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Synthesis of Highly Functionalized Anthraquinones and Evaluation of Their Antitumor Activity

Lutz F. Tietze,*[a] Kersten M. Gericke,[a] and Ingrid Schuberth[a]

Dedicated to Professor Theophil Eicher on the occasion of his 75th birthday

Keywords: Anthraquinones / Antitumor agents / Cycloaddition / Epoxides / Natural product analogs

Highly functionalized anthraquinones which derive from the natural products mensacarcin, islandicin, and chrysophanol have been efficiently synthesized using a Diels–Alder reaction as key step. The introduction of the proposed pharmacophoric side chain unit has been achieved by an addition of an aryllithium species onto different aldehydes. Furthermore, the antitumor activity of these novel compounds has been studied by the in vitro growth inhibition of human lung carcinoma cells of line A549.

Introduction

Anthraquinones represent the largest group of naturally occurring quinones and most of these substances have been isolated from higher plants and fungi.[1] Beside their potential applications as safe and ecofriendly natural colorants in foods, drugs, cosmetics, and textiles,[2–4] their use has been extended as chemical sensors,[5] organogelators,[6] liquid crystals,[7–11] and DNA photooxidants.[12] Moreover, anthraquinones are well known to be the major active components in many traditional Chinese medicinal herbs. Due to the large number of different biological activities,[1] including purgative, antiinflammatory, astringent,[13] antioxidant,[14,15] antifungal,[16–18] antimicrobial,[19–22] antitumor,[23–27] larvicidal,[28] antiparasidal,[29,30] casein kinase II inhibitory,[31] antiviral,[32,33] and glucose-6-phosphate translocase (G6P-T1) inhibitory[34] properties, these compounds have become an attractive target for organic chemists.[35,36] In 1998, Arnold and co-workers[37] isolated a novel anthracene derivative **1** from the culture broth of *Streptomyces* sp. Gö C4/4 (Figure 1). This polyketidal compound, called mensacarcin (**1**), has a similar anticancer potency as doxorubicin,[38] another agent currently used in the treatment of malignant lymphomas and leukemias.[39] Mensacarcin represents a rather unique compound containing nine stereogenic centers and two epoxide moieties. Beside our efforts towards the total synthesis of mensacarcin (**1**),[26,40,41] we were also interested in preparing simplified analogs and partial structures for further investigations of the structure-activity relationship. Basic studies of mensacarcin (**1**) have already shown that the epoxide-containing side chain acts as the main pharmacophore and that a reductive opening of the latter led to a dramatic decrease of the cytotoxicity.[37] For that reason, the installation of this moiety was one of the main tasks in our synthetic approach. As carrier for this pharmacophoric group we have chosen the anthraquinone natural products chrysophanol (**2**) and islandicin (**3**), which both show a distinct similarity to the structural core of mensacarcin (**1**). Thus, islandicin (**3**), having the epoxide side chain attached in the C2 position, can be regarded as an aromatized analog of mensacarcin.

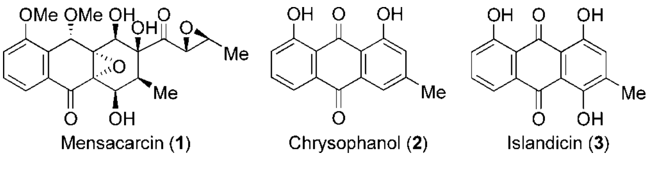

Figure 1. Natural products mensacarcin (**1**), chrysophanol (**2**) and islandicin (**3**).

Furthermore, anthraquinones with general structures like **4** and **5** (Figure 2) are known to exhibit promising in vitro and in vivo antitumor properties (e.g. GI_{50} = 1.8 ± 0.2 µM, MCF-7, breast cancer cell line).[25a,25b] Therefore, we also planned to synthesize chrysophanol and islandicin derivatives bearing an acetyl functionality in the C2 position.

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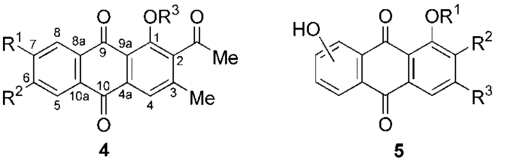
[a] Institut für Organische und Biomolekulare Chemie, Georg-August-Universität,
Tammannstr. 2, 37077 Göttingen, Germany
Fax: +49-551-399476
E-mail: ltietze@gwdg.de



4

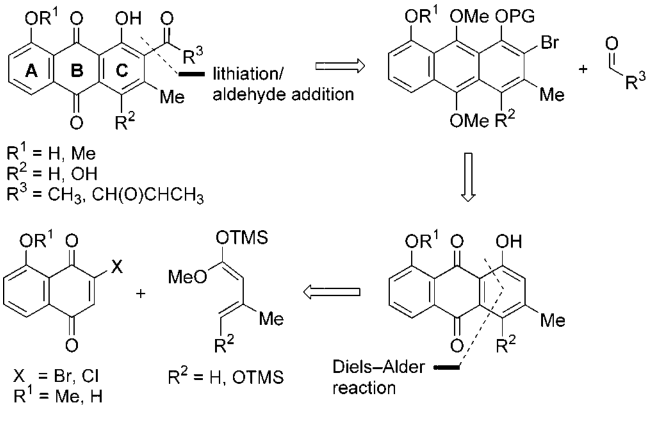
R^1 = H, Me
R^2 = H, Me
R^3 = H, Ac

5

R^1 = H, alkyl, substituted alkyl
R^2 = 1–12 C atoms, alkyl, substituted alkyl, aldehyde, hydroxy, hydroxymethyl, carboxyl, carbohydrates
R^3 = 1–12 C atoms, alkyl, substituted alkyl, aldehyde, hydroxy, hydroxymethyl, carboxyl, carbohydrates

Figure 2. Anthraquinone scaffolds **4** and **5** with in vitro and in vivo antitumor properties.

According to the retrosynthetic analysis of Scheme 1, the side chain at C2 was planned to be introduced as one of the last steps by the nucleophilic addition of an aryllithium species derived from a bromodimethoxyanthracene onto the appropriate aldehyde, a strategy which has already proven to be a reliable method within our syntheses of anthrapyran natural products.[42] In addition, the required anthracene derivative should be accessible by a Diels–Alder reaction of a juglone derivative and a silylketene acetal, followed by a regioselective bromination of the resulting anthraquinone and final reductive methylation.

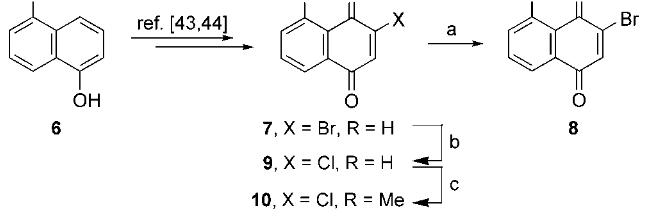


Scheme 1. Key stages in the retrosynthetic analysis of the anthraquinones.

Results and Discussion

Synthesis

The synthesis of the required dienophilic naphthoquinones commences from commercially available 1,5-dihydroxynaphthalene (**6**) which was converted into the isomeric pure 3-bromojuglone (**7**) using known procedures (Scheme 2).[43,44] The OH group of **7** was protected utilizing the mild base Ag_2O and MeI to deliver methyl ether **8** in nearly quantitative yield.[45] The corresponding protected 3-chlorojuglone (**10**) could be prepared from **7** by halogen exchange[46] by treatment with concentrated HCl in refluxing ethanol and subsequent formation of the methyl ether using again Ag_2O and MeI.



6

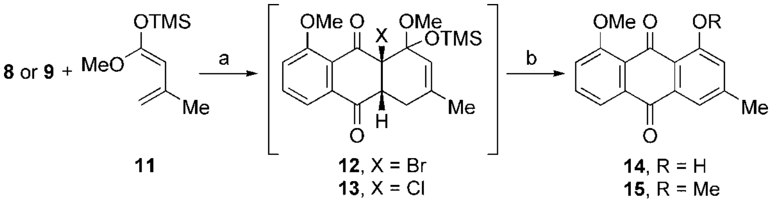
7, X = Br, R = H
9, X = Cl, R = H
10, X = Cl, R = Me

8

Scheme 2. Synthesis of juglon derivatives **8** and **10**; (a) Ag_2O, MeI, $CHCl_3$, room temp., 16 h, 98%; (b) concentrated HCl, EtOH, reflux, 10 min, 89%; (c) Ag_2O, MeI, $CHCl_3$, room temp., 16 h, 100%.

The Diels–Alder reaction of **8** and 1-methoxy-3-methyl-1-trimethylsiloxy-1,3-butadiene **11**[42c,47] was first carried out in benzene using the same conditions, as were originally described by Brassard et al. (Scheme 3).[47] Therefore, after the complete consumption of **8** and the formation of the primary cycloadduct **12** (monitored by TLC), the reaction mixture was subjected to slow percolation through a column of silica gel to induce the aromatization to the corresponding anthraquinone. To our surprise, we were only able to obtain trace amounts of the desired aromatized product **14** using this methodology. Unfortunately, changing the dienophile to 3-chlorojuglone (**10**), which was used in the original procedure by Brassard et al., gave the same unexpected result. Finally, we observed that a slight modification of the aromatization procedure led to a highly efficient and selective formation of the desired chrysophan-8-yl methyl ether (**14**), which is a common precursor of naturally occurring anthraquinone antibiotics. We discovered that the hydrolysis of the TMS ether of either cycloadduct **12** or **13** could be induced by treatment with silica gel as a mild acid in dichloromethane for a prolonged reaction time (24 h). Furthermore, it was crucial to adsorb the hydrolyzed product onto the silica gel by simply removing the solvent using a rotary evaporator to allow a complete conversion into the thermodynamically more stable anthraquinone derivative by elimination of HX and MeOH. Applying this methodology, **14** could be obtained in 87% yield (X = Cl) or 91% yield (X = Br) yield without observing the formation of the *O*-methyl ether **15**, which was a major side-product in Brassard's synthesis (**14**: 50% yield, **15**: 44% yield) and has been proven to be unfavorable for further transformations of the C-ring moiety. It is worthwhile to note that the halogen acts as a regiochemical control element directing carbon–carbon bond formation during the Diels–Alder reaction.[48] For that reason, the cycloaddition proceeded with high selectivity and without any formation of the undesired regioisomer.

With compound **14** in hand, we next turned our attention to the functionalization of the C2 position of the anthraquinone core. The first attempts to introduce the desired acetyl group by a Lewis-acid-promoted Fries rearrangement of the corresponding acetyl-protected phenol of **14** were not successful, probably due to the electron de-

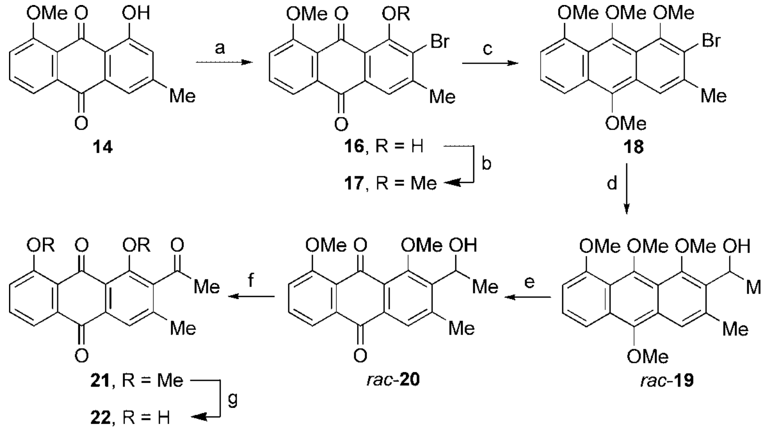


Scheme 3. Synthesis of chrysophan-8-yl methyl ether (**14**); (a) benzene, room temp., 7 h; (b) SiO_2, CH_2Cl_2, room temp., 24 h, then removal of solvent, 91% (X = Br), 87% (X = Cl) overall yield of **14** for two steps.

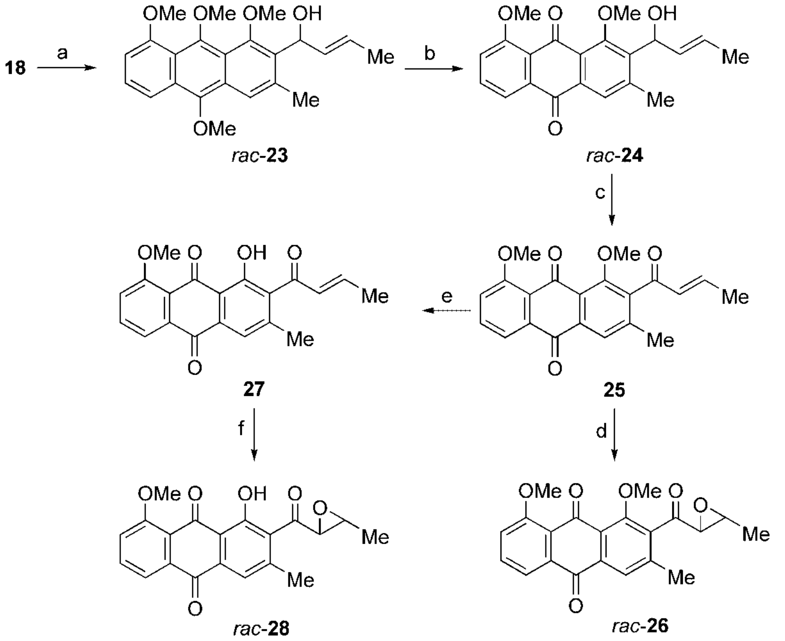
ficiency of the C ring. To our delight, a regioselective bromination of anthraquinone **14** was feasible using NBS in dichloromethane in the presence of a catalytic amount of a secondary amine (Scheme 3).[49] Under these conditions, the strong *ortho*-directing effect of the hydroxy group led to the formation of monobromoanthraquinone **16** in excellent yield (96%). At this point, the desired bromination site as well as the correct regioselectivity during the Diels–Alder reaction were unambiguously deduced from HMBC experiments.

After the protection of the hydroxy group of compound **16** as its methyl ether **17** in 91% yield by treatment with dimethyl sulfate and K_2CO_3,[50] the reductive methylation of the quinone moiety in **17** was realized using aq. sodium dithionite to furnish the corresponding air-sensitive hydroquinone, which directly underwent methylation by its treatment with KOH and dimethyl sulfate under phase-transfer catalysis to obtain the bromodimethoxyanthracene **18** in an excellent overall yield. After the conversion of **18** into the corresponding lithium derivative by bromine/lithium exchange using *n*BuLi at low temperature, the subsequent reaction with an excess of freshly distilled acetaldehyde proceeded smoothly to give the racemic alcohol *rac*-**19** in nearly quantitative yield. It is noteworthy that the aldehyde had to be added immediately after the generation of the organolithium compound to avoid the formation of debrominated side product. The oxidative demethylation of the anthracene derivative *rac*-**19** using AgO/HNO_3[51] yielded the anthraquinone *rac*-**20**, which was subsequently subjected to Dess–Martin oxidation[52] to afford compound **21** in very high yield. Finally, the cleavage of both methyl ethers was achieved by treatment with HBr in acetic acid at high temperature to deliver the anthraquinone **22** nearly quantitatively (Scheme 4).[53]

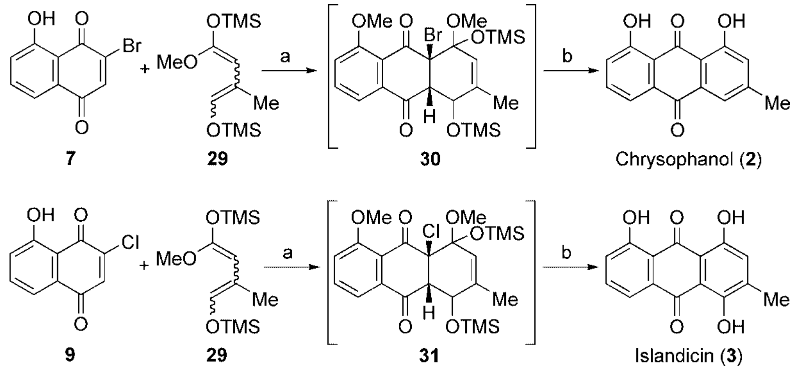
For the introduction of the epoxide-containing side chain as in mensacarcin (**1**) we followed again the previously described lithiation strategy. Therefore, compound **18** was treated after bromine/lithium exchange with an excess of (*E*)-crotonaldehyde to give the desired alcohol *rac*-**23** in 72% yield (Scheme 5). In this case, the formation of the debrominated side-product could not be completely avoided due to the lower reactivity of the α,β-unsaturated aldehyde. Afterwards, the reoxidation of the anthracene derivative *rac*-**23** to the corresponding anthraquinone and subsequent Dess–Martin oxidation furnished compound **25**. The α,β-unsaturated ketone moiety of the latter could then be quantitatively epoxidized under basic conditions using hydrogen peroxide to deliver the first target compound *rac*-**26**.[54] Furthermore, due to an activation by two carbonyl functionalities in *ortho* position, it was feasible to cleave the C-ring methyl ether of **25** selectively with BBr_3 at low temperature to yield phenol **27** in good yield. The epoxidation of **27** was then achieved under neutral conditions with an excess of dimethyl dioxirane (DMDO).[55] Although the reaction was rather sluggish, *rac*-**28** could be isolated in very good yield after 6 d of reaction time.



Scheme 4. Synthesis of chrysophanol analogs **21** and **22**; (a) NBS, cat. *i*Pr_2NH, CH_2Cl_2, room temp., 6 h, 96%; (b) K_2CO_3, Me_2SO_4, acetone, reflux, 22 h, 91%; (c) $Na_2S_2O_4$, TBABr, KOH, H_2O, Me_2SO_4, THF, room temp., 40 h, 94%; (d) *n*BuLi, acetaldehyde, THF, –78 °C, 1 h, 98%; (e) AgO, dioxane, 4 N HNO_3, room temp., 15 min, 99%; (f) Dess–Martin reagent, CH_2Cl_2, room temp., 2 h, 97%; (g) 33% HBr (in HOAc), HOAc, 100 °C, 2 h, 99%.



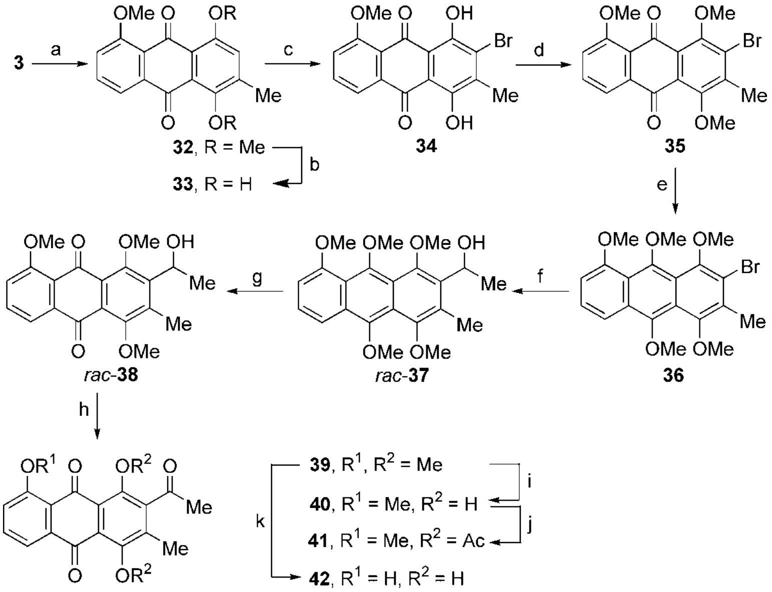
Scheme 5. Synthesis of mensacarcin analogs *rac*-**26** and *rac*-**28**; (a) *n*BuLi, (*E*)-crotonaldehyde, THF, –78 °C, 1 h, 72%; (b) AgO, dioxane, 4 N HNO_3, room temp., 15 min, 77%; (c) Dess–Martin reagent, CH_2Cl_2, room temp., 2 h, 92%; (d) 30% H_2O_2, NaOH, MeOH, room temp., 12 h, 100%; (e) BBr_3, CH_2Cl_2, –78 °C, 30 min, 66% (73% based upon recovered starting material); (f) DMDO, acetone, room temp., 6 d, 90%.



Scheme 6. Synthesis of chrysophanol (**2**) and islandicin (**3**); (a) benzene, reflux, 5 h; (b) concentrated HCl, THF, reflux, 2 h, 79% (**2**), 89% (**3**) overall yield for two steps.

The preparation of the islandicin-derived compounds started with the synthesis of islandicin applying the methodology developed by Brassard et al.[56] Utilizing 3-bromojuglon (**7**) and diene **29** for the Diels–Alder cycloaddition, the outcome of the reaction was again unexpected. After the treatment of cycloadduct **30** with concentrated HCl in THF at reflux, we could only isolate chrysophanol (**2**) in 79% yield instead of the desired islandicin (**3**, Scheme 6). However, using 3-chlorojuglon for the cycloaddition as described by Brassard et al., the required islandicin (**3**) was formed in 89% yield. An explanation for this unusual halogen effect is still missing to date.

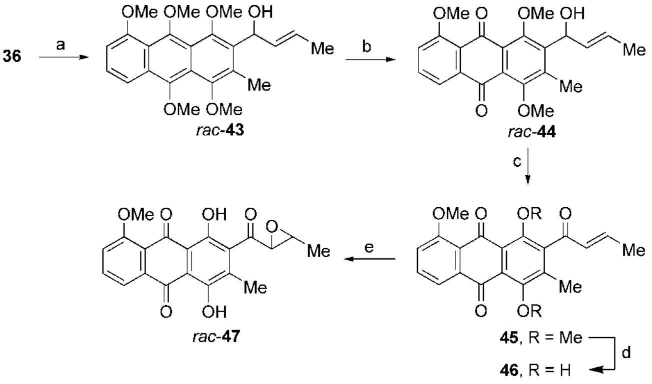
The direct bromination of islandicin (**3**) at the C2 position using bromine under different reaction conditions failed because of the competing oxidation of the hydroquinone motif in the C ring to the corresponding quinone. On the other hand, the usage of the amine-catalyzed NBS bromination required the selective protection of the A-ring moiety to avoid the competing reaction at C7. Therefore, permethylation of islandicin (**3**) was carried out under standard conditions to furnish **32** in quantitative yield (Scheme 7).[57] The selective deprotection of the C-ring functionalities was accomplished by oxidation to the bis(quinone) with AgO/HNO_3 and subsequent reduction with $NaHSO_3$ to deliver the monoprotected islandicin (**33**).[57] The following amine-catalyzed NBS bromination turned out to be very sluggish and was again accompanied by an oxidation of the C ring. Nonetheless, it was possible to obtain the desired bromination product **34** in 54% yield by using a large excess of NBS (10 equiv.), a long reaction time



Scheme 7. Synthesis of islandicin analogs **39**–**42**; (a) K_2CO_3, Me_2SO_4, acetone, reflux, 20 h, 99%, (b) (i) AgO, acetone, 6 N HNO_3, room temp., 20 min, (ii) aq. $NaHSO_3$, 82%; (c) (i) NBS, cat. *i*Pr_2NH, CH_2Cl_2, room temp., 16 d; (ii) aq. $NaHSO_3$, 54%; (d) K_2CO_3, Me_2SO_4, acetone, reflux, 18 h, 88%; (e) $Na_2S_2O_4$, TBABr, KOH, H_2O, Me_2SO_4, THF, room temp., 18 h, 95%; (f) *n*BuLi, acetaldehyde, THF, –78 °C, 1 h, 81%; (g) AgO, dioxane, 4 N HNO_3, room temp., 15 min, 94%; (h) Dess–Martin reagent, CH_2Cl_2, room temp., 2 h, 85%; (i) BCl_3, CH_2Cl_2, 0 °C, 5 min, 87%; (j) Ac_2O, py, cat. DMAP, room temp., 24 h, 94%; (k) 33% HBr (in HOAc), HOAc, 100 °C, 135 min, 95%.

(16 d) and a subsequent reductive workup with $NaHSO_3$. After protection of the phenolic hydroxy groups in ring C with dimethyl sulfate and K_2CO_3, the reductive methylation of the anthraquinone with aq. sodium dithionite and treatment of the resulting hydroquinone with KOH and dimethyl sulfate under phase-transfer catalysis was performed to obtain the bromodimethoxyanthracene **36** in very good yield. According to our established strategy for the C2 functionalization, reaction with *n*BuLi and acetaldehyde led to the formation of alcohol *rac*-**37** in nearly quantitative yield. Oxidative demethylation utilizing AgO/HNO_3 yielded the anthraquinone *rac*-**38**, which was oxidized to the corresponding ketone **39** using the Dess–Martin periodinane. For evaluating the influence of the hydroxy functionalities on the bioactivity, we finally carried out a few protecting group manipulations. Therefore, the selective deprotection of the C ring was accomplished with BCl_3 to give compound **40** in 87% yield.[58] A variation of the protecting groups was achieved by acetylation under standard conditions using acetic anhydride, pyridine and catalytic amounts of DMAP to furnish derivative **41**. However, an exhaustive deprotection of the methyl ethers of **39** could be realized by treatment with HBr in acetic acid at high temperature to furnish the anthraquinone **42**.

The introduction of the epoxide-containing side chain was performed by using the same conditions as described earlier (Scheme 8). Thus, the treatment of compound **36** with *n*BuLi and (*E*)-crotonaldehyde led to the formation of *rac*-**43**. Subsequent oxidative demethylation and Dess–Martin oxidation furnished anthraquinone **45**, whose C ring could be selectively deprotected using BCl_3 under a strict reaction time control yielding derivative **46**. The final epoxidation was again accomplished under neutral conditions employing an excess of DMDO for a long reaction time to deliver the racemic epoxide *rac*-**47** in 58% yield.



Scheme 8. Synthesis of mensacarcin analog *rac*-**47**; (a) *n*BuLi, (*E*)-crotonaldehyde, THF, –78 °C, 1 h, 75%; (b) AgO, dioxane, 4 N HNO_3, room temp., 15 min, 74%; (c) Dess–Martin reagent, CH_2Cl_2, room. temp., 2 h, 92%; (d) BCl_3, CH_2Cl_2, 0 °C, 5 min, 90%; (e) DMDO, acetone, room temp., 6 d, 58%.

Antitumor Activity

Based on the significant antitumor activity of mensacarcin (**1**) and patented compounds like **4** and **5**, we were highly interested in the biological properties of the novel anthraquinones prepared by us. The cytotoxicity was studied by in vitro growth inhibition of human lung carcinoma cells of line A549. The adherent cells were sown in different numbers and, after incubation with different concentrations of the compound, the numbers of formed colonies were counted. Unfortunately, due to a low solubility of some compounds in the incubation medium, only a few anthraquinones could be tested. However, comparing the bioactivity by taking the ED_{50} values for the relative colony-forming rates into account, we observed that the highly complex natural product mensacarcin (**1**) is the most bioactive of the tested compounds (ED_{50} = 1.6 μM). Interestingly, the structurally much simpler anthraquinones *rac*-**26**, *rac*-**28**, **41** and *rac*-**47** all show cytotoxic properties, although their activity is lower than 1.6 μM (Table 1). It is noteworthy that the racemic compound *rac*-**47**, the so-called "aromatic" mensacarcin, shows an ED_{50} value of 11.6 μM and is only approximately 7 times less active than **1**. Another interesting fact is the observed influence of the amount of free hydroxy groups on the bioactivity. According to this, a higher number of unprotected phenol groups on the C ring leads to a clear increase of the antitumor activity (11.6 μM < 25.0 μM < 41.5 μM). Finally, a comparison of epoxide *rac*-**26** and compound **41** shows that the epoxide side chain is not necessarily crucial for biological activity.

Table 1. ED_{50} values (μM) of the in vitro cytotoxicity of mensacarcin (**1**), and anthraquinones *rac*-**26**, *rac*-**28**, **41** and *rac*-**47** against the human bronchial carcinoma cell line A549.

Entry	Compound	Antitumor activity in cell line A549 (ED_{50} [μM])
1	mensacarcin (**1**)	1.6
2	*rac*-**26**	41.5
3	*rac*-**28**	25.0
4	**41**	39.4
5	*rac*-**47**	11.6

Conclusions

The present work reveals an efficient and reliable method for the synthesis of natural product-derived hydroxylated anthraquinones and their functionalization at the C2 position. The novel epoxide- and acetyl-containing compounds show in vitro cytotoxicity against the human bronchial carcinoma cell line A549 with ED_{50} values in the lower μM concentrations. Due to their structural complexities these compounds bear good prospects to show further biological activities, for instance antifungal or antimicrobial properties.

Experimental Section

General: All reactions were performed in flame-dried glassware under argon. Solvents were dried and purified according to the method defined by Perrin and Armarego.[59] Dimethyl dioxirane (DMDO) was prepared using a literature procedure.[60] Commercial reagents were used without further purification. Thin-layer chromatography (TLC) was carried out with precoated Alugram SIL G/UV$_{254}$ (0.25 mm) plates from Macherey–Nagel & Co. Column chromatography was carried out with Kieselgel 60 from Merck with particle size 0.063–0.200 mm for normal-pressure chromatography and 0.020–0.063 mm for flash chromatography. Melting points were recorded with a Mettler FP61 apparatus and are uncorrected. IR spectra were determined with a Bruker Vektor 22 spectrometer, UV/Vis spectra were recorded with a Perkin–Elmer Lambda 2 spectrometer, and mass spectra were recorded with a Varian MAT 311A spectrometer, a Varian MAT 731 spectrometer (for EI-HRMS), or a Bioapex fourier-transformation ion cyclotron resonance mass spectrometer (for ESI-HRMS). ^{1}H NMR spectra were recorded with a Varian UNITY-300 MHz spectrometer, and ^{13}C NMR spectra were recorded at 75 MHz. Spectra were taken at room temperature in deuterated solvents as indicated, using the solvent peak as an internal standard. Elemental analysis was performed at the Mikroanalytisches Labor des Institutes für Organische und Biomolekulare Chemie der Universität Göttingen.

Synthesis

3-Bromo-5-methoxy-1,4-naphthoquinone (8): To a mixture of 3-bromojuglone (**7**) (9.50 g, 37.5 mmol) and Ag_2O (17.4 g, 75.0 mol) in $CHCl_3$ (400 mL) was added iodomethane (7.03 mL, 113 mmol), and the resulting suspension was stirred in the dark at 25 °C for 16 h. Additional Ag_2O (8.73 g, 37.5 mmol) and iodomethane (2.33 mL, 37.5 mmol) were then added, and stirring was continued for another 8 h (monitored by TLC). The mixture was filtered trough a plug of Celite®, and the filter cake was rinsed thoroughly with CH_2Cl_2. After the removal of the solvent under reduced pressure, the crude product was filtered through a plug of silica gel (CH_2Cl_2) to afford naphthoquinone **8** (9.80 g, 98% yield) as a yellow solid. R_f = 0.19 [petroleum ether (PE)/EtOAc, 4:1]; m.p. 155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.02 (s, 3 H, OCH_3), 7.33 (m_c, 1 H, 6-H), 7.44 (s, 1 H, 2-H), 7.68–7.74 (m, 2 H, 7-H, 8-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 56.52, 118.1, 118.6, 119.4, 133.8, 135.5, 138.3, 142.6, 160.3, 176.1, 182.5 ppm. IR (KBr): $\tilde{\nu}$ = 3043, 1673, 1652, 1581, 1470, 1444, 1336, 1311, 1276, 1212 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 257.0 (4.549), 247.5 (3.981), 277.0 (4.117), 401.5 (3.578) nm. MS (EI, 70 eV): *m/z* (%) = 267.9 (100), 265.9 (93) [M]$^+$, 186.0 (39) [M – Br]$^+$, 159.0 (42) [M – Br – CO]$^+$, 129.0 (51) [M – Br – 2 CO]$^+$. $C_{11}H_7BrO_3$ (267.08): calcd. C 49.47, H 2.64; found C 49.71, H 2.52.

3-Chloro-5-hydroxy-1,4-naphthoquinone (9): A solution of 3-bromojuglone (**7**) (8.91 g, 35.2 mmol) in EtOH (800 mL) was treated at reflux with concentrated HCl (90 mL). After stirring at reflux for 10 min, the reaction mixture was poured onto ice. The resulting suspension was extracted with CH_2Cl_2 (3 × 200 mL), and the combined organic phases were dried with Na_2SO_4, filtered and concentrated in vacuo. The crude product was filtered through a plug of silica gel (CH_2Cl_2) to afford naphthoquinone **9** (6.52 g, 89% yield) as a yellow-orange solid. R_f = 0.43 (PE/EtOAc, 8:1); m.p. 167 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20 (s, 1 H, 2-H), 7.31 (dd, J = 7.7, 1.9 Hz, 1 H, 6-H), 7.64 (dd, J = 7.4, 1.9 Hz, 1 H, 8-H), 7.68 (t, J = 7.5 Hz, 1 H, 7-H), 11.68 (s, 1 H, OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 114.3, 119.8, 124.8, 131.7, 136.7, 137.3, 145.7, 162.1, 181.8, 182.9 ppm. IR (KBr): $\tilde{\nu}$ = 3424, 3060, 1659, 1640, 1593, 1486, 1455, 1362, 1271, 1215 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 211.5 (4.550), 272.5 (4.132), 424.5 (3.591) nm. MS (EI, 70 eV): *m/z* (%) = 210.1 (22), 208.1 (68) [M]$^+$, 180.1 (21) [M – CO]$^+$, 173.1 (40) [M – Cl]$^+$, 145.1 (100) [M – CO – Cl]$^+$. $C_{10}H_5ClO_3$ (208.60): calcd. C 57.58, H 2.42; found C 57.34, H 2.36.

3-Chloro-5-methoxy-1,4-naphthoquinone (10): To a mixture of 3-chlorojuglone (**9**) (6.50 g, 31.2 mmol) and Ag_2O (14.5 g, 62.4 mol) in $CHCl_3$ (400 mL) was added iodomethane (5.82 mL, 93.6 mmol), and the resulting suspension was stirred in the dark at 25 °C for 16 h. Additional Ag_2O (7.46 g, 32.2 mmol) and iodomethane (2.00 mL, 32.2 mmol) were then added, and stirring was continued for another 8 h (monitored by TLC). The mixture was filtered trough a plug of Celite®, and the filter cake was rinsed thoroughly with CH_2Cl_2. After the removal of the solvent under reduced pressure, the crude product was filtered through a plug of silica gel (CH_2Cl_2) to afford naphthoquinone **10** (6.72 g, 100% yield) as a yellow solid. R_f = 0.20 (PE/EtOAc, 4:1); m.p. 167 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.03 (s, 3 H, OCH_3), 7.15 (s, 1 H, 2-H), 7.34 (m_c, 1 H, 6-H), 7.69–7.75 (m, 2 H, 7-H, 8-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 56.53, 118.1, 119.0, 119.3, 133.8, 133.9, 135.6, 148.0, 160.3, 176.1, 182.8 ppm. IR (KBr): $\tilde{\nu}$ = 3045, 1680, 1661, 1602, 1582, 1470, 1444, 1338, 1314, 1279, 1212 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 209.5 (4.545), 263.5 (4.127), 401.5 (3.549) nm. MS (EI, 70 eV): m/z (%) = 224.1 (24), 222.1 (100) $[M]^+$, 187.1 (12) $[M - Cl]^+$, 159.1 (28) $[M - Cl - CO]^+$, 129.1 (62) $[M - Cl - 2\ CO]^+$. HRMS (EI): calcd. for $C_{11}H_7ClO_3$ 222.0084; found 222.0084. $C_{11}H_7ClO_3$ (222.62): calcd. C 59.35, H 3.17; found C 59.40, H 3.14.

1-Hydroxy-8-methoxy-3-methylanthraquinone (14): To a solution of juglone derivative **8** (6.00 g, 22.5 mmol) in benzene (100 mL) was added at 25 °C dropwise with stirring diene **11** (8.37 g, 44.9 mmol) over 10 min. Stirring was continued at 25 °C for 3.5 h, and another portion of diene **11** (2.93 g, 15.7 mmol) was added, and stirring was continued for an additional 3.5 h. Afterwards, the reaction mixture was poured onto silica gel (100 g), CH_2Cl_2 (500 mL) was added, and the suspension was stirred for 24 h. After removing the solvent under reduced pressure, the silica gel was eluted thoroughly with CH_2Cl_2/MeOH (10:1), and the combined organic fractions were concentrated in vacuo to afford the crude product. This material was subjected to silica gel flash chromatography (CH_2Cl_2), and the concentration of the appropriate fractions in vacuo furnished anthraquinone **14** (5.50 g, 91% yield) as a yellow solid. R_f = 0.18 (PE/EtOAc, 4:1); m.p. 195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, Ar-CH_3), 4.06 (s, 3 H, OCH_3), 7.06 (d, J = 0.7 Hz, 1 H, 2-H), 7.33 (dd, J = 8.4, 0.6 Hz, 1 H, 7-H), 7.55 (d, J = 1.1 Hz, 1 H, 4-H), 7.71 (t, J = 8.4 Hz, 1 H, 6-H), 7.92 (dd, J = 7.5, 0.8 Hz, 1 H, 5-H), 12.90 (s, 1 H, OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.01, 56.56, 114.9, 118.0, 119.9, 120.0, 120.6, 124.5, 132.3, 135.5, 135.7, 147.5, 160.7, 162.6, 182.8, 188.4 ppm. IR (KBr): $\tilde{\nu}$ = 2948, 1677, 1637, 1584, 1490, 1446, 1370, 1302, 1276, 1245, 1210 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 222.5 (4.565), 256.5 (4.331), 280.0 (4.055), 412.0 (3.962) nm. MS (EI, 70 eV): m/z (%) = 268.0 (100) $[M]^+$, 250.1 (40) $[M - H_2O]^+$, 239.1 (18), 222.0 (48) $[M - H_2O - CO]^+$. HRMS (EI): calcd. for $C_{16}H_{12}O_4$ 268.0736; found 268.0736. $C_{16}H_{12}O_4$ (268.26): calcd. C 71.64, H 4.41; found C 71.57, H 4.41.

2-Bromo-1-hydroxy-8-methoxy-3-methylanthraquinone (16): A solution of anthraquinone **14** (3.00 g, 11.2 mmol) in CH_2Cl_2 (120 mL) was treated at 25 °C with a catalytic amount of diisopropylamine (10 drops), and then a solution of NBS (2.95 g, 16.8 mmol) in CH_2Cl_2 (100 mL) was added dropwise over 10 min. Stirring at 25 °C was continued for 3 h during which an orange precipitate was formed. Afterwards, this solid was dissolved by adding CH_2Cl_2 (500 mL), and the resulting solution was washed subsequently with aq. HCl (0.1 N, 2 × 500 mL) and H_2O (500 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was recrystallized (EtOAc) to afford anthraquinone **16** (3.72 g, 96% yield) as orange needles. R_f = 0.18 (PE/EtOAc, 4:1); m.p. 257 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, Ar-CH_3), 4.09 (s, 3 H, OCH_3), 7.38 (dd, J = 8.7, 1.0 Hz, 1 H, 7-H), 7.67 (s, 1 H, 4-H), 7.76 (dd, J = 8.3, 7.6 Hz, 1 H, 6-H), 7.96 (dd, J = 7.5, 1.0 Hz, 1 H, 5-H), 13.79 (s, 1 H, OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.22, 56.71, 115.2, 118.3, 120.2, 120.3, 120.3, 121.7, 130.4, 135.5, 136.1, 147.4, 159.1, 161.0, 182.37, 188.2 ppm. IR (KBr): $\tilde{\nu}$ = 2954, 1671, 1634, 1583, 1482, 1442, 1381, 1348, 1299, 1264, 1240 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 195.0 (4.360), 227.5 (4.463), 261.0 (4.338), 286.0 (3.954), 415.5 (3.965) nm. MS (EI, 70 eV): m/z (%) = 348.1 (100) $[M]^+$, 330.0 (48) $[M - H_2O]^+$, 302.0 (36) $[M - H_2O - CO]^+$. HRMS (EI): calcd. for $C_{16}H_{11}BrO_4$ 345.9841; found 345.9841. $C_{16}H_{11}BrO_4$ (347.16): calcd. C 55.36, H 3.19; found C 55.29, H 3.03.

2-Bromo-1,8-dimethoxy-3-methylanthraquinone (17): A solution of anthraquinone **16** (6.90 g, 19.9 mmol) in acetone (950 mL) was treated subsequently at 25 °C with K_2CO_3 (33.8 g, 245 mmol) and Me_2SO_4 (20 mL). After being stirred at reflux for 22 h, the reaction mixture was filtered through a plug of Celite®. The filter cake was rinsed thoroughly with CH_2Cl_2, and then the combined organic phases were concentrated under reduced pressure. The crude product was subjected to silica gel flash chromatography (CH_2Cl_2), and the concentration of the appropriate fractions in vacuo afforded anthraquinone **17** (6.54 g, 91% yield) as a pale yellow solid. R_f = 0.42 (PE/EtOAc, 3:2); m.p. 202 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.55 (s, 3 H, Ar-CH_3), 4.03 (s, 3 H, OCH_3), 4.05 (s, 3 H, OCH_3), 7.32 (d_{br}, J = 8.5, 1.0 Hz, 1 H, 6-H), 7.66 (t, J = 8.0 Hz,1 H, 6-H), 7.83 (dd, J = 7.7, 0.8 Hz, 1 H, 4-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.16, 56.56, 61.98, 118.1, 119.0, 123.2, 124.2, 126.8, 130.2, 132.4, 134.7, 145.4, 156.9, 159.6, 181.5, 183.2 ppm. IR (KBr): $\tilde{\nu}$ = 2962, 1672, 1585, 1470, 1388, 1282, 1239 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.5 (4.512), 261.0 (4.533), 371.5 (3.796) nm. MS (EI, 70 eV): m/z (%) = 362.1 (42) $[M]^+$, 345.1 (100) $[M - OH]^+$. HRMS (EI): calcd. for $C_{17}H_{13}BrO_4$ 359.9997; found 359.9997. $C_{17}H_{13}BrO_4$ (361.19): calcd. C 56.53, H 3.63; found C 56.25, H 3.80.

2-Bromo-1,8,9,10-tetramethoxy-3-methylanthracene (18): A solution of anthraquinone **17** (2.95 g, 8.17 mmol) and tetra-*n*-butylammonium bromide (1.32 g, 4.09 mmol) in THF (400 mL) was treated at 25 °C with a solution of $Na_2S_2O_4$ (8.53 g, 49.0 mmol) in H_2O (75 mL) and stirred for 25 min. Afterwards, a solution of KOH (13.8 g, 245 mmol) in H_2O (75 mL) was added (the yellow solution turned deep red), and stirring was continued for an additional 15 min. After the addition of Me_2SO_4 (10 mL), the reaction mixture was stirred for 12 h (the solution turned back to yellow) and then poured into H_2O (400 mL). The resulting solution was extracted with CH_2Cl_2 (3 × 250 mL), and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was subjected to silica gel column filtration (CH_2Cl_2), and the concentration of the appropriate fractions in vacuo afforded anthracene **18** (3.00 g, 94% yield) as a yellow oil which solidified under high vacuum. R_f = 0.55 (PE/EtOAc, 4:1); m.p. 124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (d, J = 1.0 Hz, 3 H, Ar-CH_3), 3.96 (s, 3 H, OCH_3), 3.99 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 4.08 (s, 3 H, OCH_3), 6.79 (d_{br}, J = 7.3 Hz, 1 H, 7-H), 7.39 (dd, J = 8.7, 7.8 Hz, 1 H, 6-H), 7.83 (dd, J = 8.7, 0.6 Hz, 1 H, 5-H), 7.93 (d, J = 0.9 Hz, 1 H, 4-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.35, 56.32, 61.60, 62.71, 64.11, 104.1, 114.6, 118.3, 125.9, 119.3, 119.5, 119.9, 125.9, 127.5, 136.0, 147.4, 148.9, 153.1, 157.2 ppm. IR (KBr): $\tilde{\nu}$ = 3063, 2926, 2833, 1620, 1556, 1452, 1397, 1353, 1309, 1256 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 201.0 (4.305), 229.5 (4.080), 267.5 (4.962), 360.5 (3.719), 379.0 (4.000), 396.5 (3.890), 419.0 (3.741) nm. MS (EI, 70 eV): m/z (%) = 392.1 (100) $[M]^+$, 377.1 (74) $[M - CH_3]^+$, 145.0 (17) $[M - 3\ CH_3]^+$. HRMS (EI): calcd. for $C_{19}H_{19}BrO_4$ 390.0467; found 390.0467. $C_{16}H_{11}BrO_4$ (391.26): calcd. C 58.88, H 4.89; found C 58.09, H 4.68.

***rac*-1-(1,8,9,10-Tetramethoxy-3-methylanthracen-2-yl)ethanol (*rac*-19):** A solution of anthracene **18** (500 mg, 1.28 mmol) in THF (15 mL) was treated at –78 °C dropwise with *n*BuLi (0.61 mL, 1.53 mmol, 2.5 M in *n*-hexane) over 1 min. After being stirred for

1 min, freshly distilled acetaldehyde (0.36 mL, 6.40 mmol) was added quickly. Stirring was continued at –78 °C for 15 min, and then the reaction mixture was warmed to 25 °C over 1 h. The reaction mixture was treated with saturated aq. NH_4Cl (9 mL), stirred for 5 min and then poured into H_2O (50 mL). Afterwards, the resulting solution was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to silica gel flash chromatography (PE/EtOAc, 4:1 → 1:1), and the concentration of the appropriate fractions in vacuo afforded alcohol *rac*-**19** (450 mg, 98% yield) as a yellow oil which solidified under high vacuum. R_f = 0.55 (PE/EtOAc, 3:2); m.p. 152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (d, *J* = 6.7 Hz, 3 H, 2-H_3), 2.55 (s, 3 H, Ar-CH_3), 3.89 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 5.29 (s_{br}, 1 H, 1-H), 6.78 (d_{br}, *J* = 7.3 Hz, 1 H, 7′-H), 7.36 (dd, *J* = 7.9, 7.7 Hz, 1 H, 6′-H), 7.81 (s, 1 H, 4′-H), 7.83 (dd, *J* = 7.6, 0.9 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.84, 24.97, 56.36, 62.63, 63.63, 63.99, 67.59, 104.0, 114.6, 118.8, 118.9, 118.9, 125.6, 126.5, 127.3, 133.5, 134.1, 147.2, 148.9, 153.9, 157.2 ppm. IR (KBr): ṽ = 2932, 1621, 1557, 1396, 1453, 1362, 1332, 1316, 1268 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 199.5 (4.342), 227.5 (4.087), 264.0 (4.987), 359.5 (3.743), 377.5 (4.011), 393.0 (3.915), 415.5 (3.753) nm. MS (EI, 70 eV): *m*/*z* (%) = 356.4 (15) [M]$^+$, 341.3 (11) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{21}H_{24}O_5$ 356.1624; found 356.1624. $C_{21}H_{24}O_5$ (356.41): calcd. C 70.77, H 6.79; found C 70.49, H 6.49.

***rac*-2-(1-Hydroxyethyl)-1,8-dimethoxy-3-methylanthraquinone (*rac*-20):** A solution of anthracene *rac*-**19** (450 mg, 1.26 mmol) in 1,4-dioxane (50 mL) was treated at 25 °C with AgO (782 mg, 6.31 mmol) stirred for 5 min until a suspension was formed. Afterwards, HNO_3 (4 N, 10 mL) was added dropwise over 5 min until the AgO was completely dissolved. After being stirred for another 10 min, the reaction mixture was poured into H_2O (150 mL) and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2/EtOAc, 1:1) to afford anthraquinone *rac*-**20** (407 mg, 99% yield) as a yellow oil which solidified under high vacuum. R_f = 0.55 (PE/EtOAc, 1:2); m.p. 187 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59 (d, *J* = 7.0 Hz, 3 H, 2′-H_3), 2.48 (s, 3 H, Ar-CH_3), 4.00 (s, 3 H, OCH_3), 4.01 (s, 3 H, OCH_3), 5.24 (q, *J* = 7.0 Hz, 1 H, 1′-H), 7.31 (dd, *J* = 8.2, 0.9 Hz, 1 H, 7-H), 7.64 (t, *J* = 8.4 Hz, 1 H, 6-H), 7.75 (s, 1 H, 4′-H), 7.81 (dd, *J* = 8.0, 0.9 Hz, 1 H, 5-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.36, 23.39, 56.52, 63.32, 66.54, 118.0, 118.9, 124.8, 125.5, 134.1, 123.6, 132.72, 134.7, 142.3, 143.6, 158.7, 159.3, 182.6, 183.2 ppm. IR (KBr): ṽ = 3474, 2983, 2849, 1661, 1583, 1472, 1445, 1315, 1273, 1241 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 220.0 (4.496), 259.5 (4.448), 372.5 (3.786) nm. MS (EI, 70 eV): *m*/*z* (%) = 326.1 (38) [M]$^+$, 311.1 (100) [M – CH_3]$^+$, 293.1 (34) [M – CH_3 – H_2O]$^+$, 281.1 (18) [M – C_2H_5O]$^+$. HRMS (EI): calcd. for $C_{19}H_{18}O_5$ 326.1154; found 326.1154. $C_{19}H_{18}O_5$ (326.34): calcd. C 69.93, H 5.56; found C 69.66, H 5.38.

2-Acetyl-1,8-dimethoxy-3-methylanthraquinone (21): A solution of anthraquinone *rac*-**20** (200 mg, 0.613 mmol) in CH_2Cl_2 (20 mL) was treated at 25 °C with the Dess–Martin periodinane (390 mg, 0.920 mmol) and stirred for 30 min. Afterwards, saturated aq. $NaHCO_3$ (3 mL) and aq. $Na_2S_2O_3$ (1 M, 3 mL) were added simultaneously, and the resulting cloudy reaction mixture was stirred for 30 min until a clear solution was formed. The mixture was poured into H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 9:1) to afford anthraquinone **21** (193 mg, 97% yield) as a yellow solid. R_f = 0.41 (PE/EtOAc, 1:1); m.p. 188 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, Ar-CH_3), 2.56 (s, 3 H, 2-H_3), 3.93 (s, 3 H, C-1-OCH_3), 4.03 (s, 3 H, C-8-OCH_3), 7.34 (d_{br}, *J* = 8.2 Hz, 1 H, 7-H), 7.66 (t, *J* = 8.3 Hz, 1 H, 6-H), 7.82–7.90 (m, 2 H, 4-H, 5-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.15, 31.93, 56.54, 63.56, 118.1, 119.1, 123.2, 124.8, 134.4, 125.5, 134.1, 134.7, 140.5, 143.5, 156.6, 159.6, 181.9, 183.1, 204.2 ppm. IR (KBr): ṽ = 2954, 1691, 1672, 1586, 1446, 1393, 1322, 1286, 1230 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.0 (4.454), 257.0 (4.420), 376.0 (3.747) nm. MS (EI, 70 eV): *m*/*z* (%) = 324.1 (28) [M]$^+$, 309.1 (100) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{19}H_{16}O_5$ 324.0998; found 324.0998. $C_{19}H_{16}O_5$ (324.33): calcd. C 70.36, H 4.97; found C 69.66, H 5.03.

2-Acetyl-1,8-dihydroxy-3-methylanthraquinone (22): A suspension of anthraquinone **21** (200 mg, 0.617 mmol) in HOAc (10 mL) was treated at 25 °C with HBr (15 mL, 33% in HOAc) and stirred at 100 °C for 1.5 h. Afterwards, the mixture was poured into H_2O (250 mL) and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2) to afford anthraquinone **22** (181 mg, 99% yield) as a yellow solid. R_f = 0.49 (PE/EtOAc, 4:1); m.p. 203 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, Ar-CH_3), 2.62 (s, 3 H, 2′-H_3), 7.32 (dd, *J* = 8.5, 1.1 Hz, 1 H, 7-H), 7.68 (s_{br}, 1 H, 4-H), 7.70 (t, *J* = 8.5 Hz, 1 H, 6-H), 7.84 (dd, *J* = 7.6, 1.0 Hz, 1 H, 5-H), 11.98 (s, 1 H, 8-OH), 12.36 (s, 1 H, 1-OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.36, 31.82, 114.2, 115.8, 120.2, 122.2, 124.8, 133.1, 133.5, 136.2, 137.4, 145.6, 159.5, 162.6, 181.3, 192.6, 202.5 ppm. IR (KBr): ṽ = 3057, 1705, 1673, 1622, 1558, 1449, 1374, 1350, 1291, 1268, 1247 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 225.0 (4.496), 255.0 (4.354), 277.0 (4.041), 287.0 (4.035), 428.0 (4.048) nm. MS (EI, 70 eV): *m*/*z* (%) = 296.1 (58) [M]$^+$, 281.1 (100) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{17}H_{12}O_5$ 296.0685; found 296.0685. $C_{17}H_{12}O_5$ (296.27): calcd. C 68.92, H 4.08; found C 68.65, H 3.86.

***rac*-(2*E*)-1-(1,8,9,10-Tetramethoxy-3-methylanthracene-2-yl)but-2-en-1-ol (*rac*-23):** A solution of anthracene **18** (978 mg, 2.50 mmol) in THF (30 mL) was treated at –78 °C dropwise with *n*BuLi (1.20 mL, 3.00 mmol, 2.5 M in *n*-hexane) over 1 min, and stirring was continued for 1 min. (*E*)-Crotonaldehyde (1.02 mL, 12.5 mmol) was added quickly. Stirring was continued at –78 °C for 15 min, and then the reaction mixture was warmed to 25 °C over 1 h. The reaction mixture was treated with saturated NH_4Cl (20 mL), stirred for 5 min and then poured into H_2O (100 mL). Afterwards, the resulting solution was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to silica gel flash chromatography (PE/EtOAc, 10:1 → 4:1), and the concentration of the appropriate fractions in vacuo afforded alcohol *rac*-**23** (688 mg, 72% yield) as a yellow foam. R_f = 0.15 (PE/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73 (d_{br}, *J* = 6.2 Hz, 3 H, 4-H_3), 2.55 (s, 3 H, Ar-CH_3), 3.89 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 4.05 (s, 3 H, OCH_3), 5.52–5.76 (m, 2 H, 1-H, 3-H), 5.94 (dd_{br}, *J* = 18.3, 3.7 Hz, 1 H, 2-H), 6.76 (d_{br}, *J* = 7.4 Hz, 1 H, 7′-H), 7.35 (dd, *J* = 8.7, 7.8 Hz, 1 H, 6′-H), 7.80–7.85 (m, 2 H, 4′-H, 5′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 17.71, 20.87, 56.29, 62.56, 63.49, 63.63, 71.00, 71.17, 71.29, 103.9, 114.5, 118.7, 118.9, 118.9, 125.6, 125.9, 126.6, 127.4, 131.6, 133.8, 134.6, 147.1, 149.0, 154.1, 157.2 ppm. IR (KBr): ṽ = 3462, 2931, 2834, 1620, 1557, 1515, 1452, 1396, 1359, 1316, 1259 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 199.0 (4.379), 228.0 (4.090), 266.0 (4.941), 359.5 (3.710), 377.5 (3.975), 393.5 (3.873), 415.5

(3.709) nm. MS (EI, 70 eV): *m*/*z* (%) = 382.2 (100) $[M]^+$, 367.2 (68) $[M - CH_3]^+$, 305.2 (36). HRMS (EI): calcd. for $C_{23}H_{26}O_5$ 382.1780; found 382.1780.

***rac*-2-[(2*E*)-1-Hydroxybut-2-en-1-yl]-1,8-dimethoxy-3-methylanthraquinone (*rac*-24):** A solution of anthracene *rac*-**23** (550 mg, 1.44 mmol) in 1,4-dioxane (40 mL) was treated at 25 °C with AgO (891 mg, 7.19 mmol) stirred for 5 min until a suspension was formed. Afterwards, HNO_3 (4 N, 10 mL) was added dropwise over 5 min until the AgO was completely dissolved. After being stirred for another 15 min, the reaction mixture was poured into H_2O (150 mL) and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 4:1) to afford anthraquinone *rac*-**24** (390 mg, 77% yield) as a yellow foam. R_f = 0.30 (PE/EtOAc, 3:2); m.p. 187 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.72 (m_c, 3 H, 4′-H_3), 2.48 (s, 3 H, Ar-CH_3), 3.95 (s, 3 H, OCH_3), 4.01 (s, 3 H, OCH_3), 5.45 (s_{br}, 1 H, 1′-H), 5.58–5.72 (m, 1 H, 3′-H), 5.83 (ddd_{br}, *J* = 15.5, 5.5, 1.7 Hz, 1 H, 2′-H), 7.31 (dd, *J* = 8.4, 0.8 Hz, 1 H, 7-H), 7.65 (t, *J* = 7.4 Hz, 1 H, 6-H), 7.78 (s, 1 H, 4-H), 7.82 (dd, *J* = 7.4, 1.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 17.68, 20.48, 56.54, 63.36, 66.54, 118.0, 118.9, 123.5, 124.8, 125.5, 126.9, 132.1, 133.0, 134.1, 134.7, 142.0, 143.0, 158.6, 159.4, 182.6, 183.2 ppm. IR (KBr): $\tilde{\nu}$ = 3481, 2937, 1673, 1585, 1445, 1401, 1316, 1277 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 220.5 (4.536), 260.0 (4.490), 372.0 (3.821) nm. MS (EI, 70 eV): *m*/*z* (%) = 352.2 (30) $[M]^+$, 337.2 (72) $[M - CH_3]^+$, 320.2 (76) $[M - CH_3 - OH]^+$, 295.1 $[M - C_3H_5O]^+$ (100). HRMS (EI): calcd. for $C_{21}H_{20}O_5$ 352.1311; found 352.1311. $C_{21}H_{20}O_5$ (352.38): calcd. C 71.58, H 5.72; found C 71.31, H 5.63.

2-[(2*E*)-But-2-enoyl]-1,8-dimethoxy-3-methylanthraquinone (25): A solution of anthraquinone *rac*-**24** (300 mg, 0.851 mmol) in CH_2Cl_2 (30 mL) was treated at 25 °C with the Dess–Martin periodinane (541 mg, 1.28 mmol) stirred for 2 h. Afterwards, saturated aq. $NaHCO_3$ (5 mL) and aq. $Na_2S_2O_3$ (1 M, 5 mL) were added simultaneously, and the resulting cloudy reaction mixture was stirred for 30 min until a clear solution was formed. The mixture was poured into H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 10:1) to afford anthraquinone **25** (274 mg, 92% yield) as a yellow solid. R_f = 0.22 (PE/EtOAc, 3:2); m.p. 175 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.94 (dd, *J* = 6.6, 1.3 Hz, 3 H, 4′-H_3), 2.31 (s, 3 H, Ar-CH_3), 3.90 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 6.40 (dd_{br}, *J* = 16.1, 1.7 Hz, 1 H, 2′-H), 6.58 (dq, *J* = 15.8, 6.6 Hz, 1 H, 3′-H), 7.34 (dd, *J* = 8.3, 0.7 Hz, 1 H, 7-H), 7.68 (t, *J* = 7.8 Hz, 1 H, 6-H), 7.86 (dd, *J* = 7.8, 1.0 Hz, 1 H, 5-H), 7.88 (d, *J* = 0.5 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 18.57, 19.27, 56.54, 63.60, 118.1, 119.1, 123.3, 124.3, 125.6, 133.1, 134.2, 134.3, 134.7, 141.8, 148.7, 157.1, 159.6, 181.8, 183.3, 196.3 ppm. IR (KBr): $\tilde{\nu}$ = 2953, 1670, 1586, 1442, 1398, 1326, 1280, 1231 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 217.5 (4.557), 257.5 (4.430), 374.5 (3.749) nm. MS (EI, 70 eV): *m*/*z* (%) = 350.2 (12) $[M]^+$, 335.2 (28) $[M - CH_3]^+$, 295.1 (100) $[M - C_3H_3O]^+$. HRMS (EI): calcd. for $C_{21}H_{18}O_5$ 350.1154; found 350.1154. $C_{21}H_{18}O_5$ (350.37): calcd. C 71.99, H 5.18; found C 71.70, H 5.06.

***rac*-1,8-Dimethoxy-3-methyl-2-[(3-methyloxiran-2-yl)carbonyl]anthraquinone (*rac*-26):** A solution of anthraquinone **25** (100 mg, 0.285 mmol) in MeOH (60 mL) was treated at 0 °C with NaOH (1 M, 5 mL) and H_2O_2 (30%, 5 mL). After being warmed to 25 °C, the reaction mixture was stirred for 14 h. Afterwards, the mixture was poured into H_2O (150 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2/EtOAc, 10:1) to afford anthraquinone *rac*-**26** (104 mg, 100% yield) as a yellow solid. R_f = 0.31 (PE/EtOAc, 1:1); m.p. 206 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, *J* = 5.2 Hz, 3 H, 4′-H_3), 2.38 (s, 3 H, Ar-CH_3), 3.27 (dq, *J* = 5.9, 1.9 Hz, 1 H, 3′-H), 3.58 (d, *J* = 1.8 Hz, 1 H, 2′-H), 3.94 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 7.35 (dd, *J* = 8.4, 0.9 Hz, 1 H, 7-H), 7.69 (t, *J* = 7.8 Hz, 1 H, 6′-H), 7.87 (dd, *J* = 7.7, 1.0 Hz, 1 H, 5-H), 7.88 (d, *J* = 0.6 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 17.46, 19.47, 55.79, 56.60, 60.98, 64.00, 118.23, 119.2, 123.2, 124.6, 125.5, 134.5, 134.7, 135.0, 139.3, 142.8, 157.8, 159.7, 181.8, 183.2, 202.4 ppm. IR (KBr): $\tilde{\nu}$ = 2950, 1673, 1585, 1445, 1391, 1354, 1289, 1234 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.0 (4.481), 257.5 (4.457), 376.5 (3.799) nm. MS (EI, 70 eV): *m*/*z* (%) = 366.2 (2) $[M]^+$, 351.2 (4) $[M - CH_3]^+$, 309.2 (100) $[M - C_3H_5O]^+$. HRMS (EI): calcd. for $C_{21}H_{18}O_6$ 366.1103; found 366.1103. $C_{21}H_{18}O_6$ (366.36): calcd. C 68.85, H 4.95; found C 68.58, H 4.94.

2-[(2*E*)-But-2-enoyl]-1-hydroxy-8-methoxy-3-methylanthraquinone (27): A solution of anthraquinone *rac*-**26** (120 mg, 0.343 mmol) in CH_2Cl_2 (12 mL) was treated at –78 °C dropwise with BBr_3 (1.71 mL, 1.71 mmol, 1 M in CH_2Cl_2) and stirred for 10 min. Afterwards, MeOH (10 mL) was slowly added, and the reaction mixture was warmed to 25 °C. After being stirred for 30 min, the reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed H_2O (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was subjected to silica gel flash chromatography (CH_2Cl_2, CH_2Cl_2/EtOAc, 20:1), and the concentration of the appropriate fractions in vacuo furnished anthraquinone **27** [76 mg, 66% yield (73% based upon recovered starting material)] as a yellow solid. R_f = 0.31 (PE/EtOAc, 3:2); m.p. 209 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.97 (dd, *J* = 6.9, 1.6 Hz, 3 H, 4′-H_3), 2.32 (s, 3 H, Ar-CH_3), 4.06 (s, 3 H, OCH_3), 6.44 (dq, *J* = 14.2, 1.6 Hz, 1 H, 2′-H), 6.71 (dq, *J* = 15.8, 6.8 Hz, 1 H, 3′-H), 7.36 (dd, *J* = 8.4, 0.9 Hz, 1 H, 7-H), 7.60 (s, 1 H, 4-H), 7.74 (t, *J* = 7.8 Hz, 1 H, 6′-H), 7.92 (dd, *J* = 7.8, 1.0 Hz, 1 H, 5-H), 13.07 (s, 1 H, OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 18.63, 19.80, 56.61, 115.0, 118.3, 120.1, 120.4, 120.5, 132.1, 133.1, 135.0, 135.4, 135.8, 144.2, 148.2, 159.4, 160.8, 182.3, 188.3, 195.8 ppm. IR (KBr): $\tilde{\nu}$ = 2940, 1655, 1628, 1585, 1444, 1392, 1318, 1280, 1218 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 221.0 (4.633), 257.5 (4.391), 413.5 (3.983) nm. MS (EI, 70 eV): *m*/*z* (%) = 336.2 (62) $[M]^+$, 321.2 (100) $[M - CH_3]^+$, 293.1 (15) $[M - CH_3 - CO]^+$. HRMS (EI): calcd. for $C_{20}H_{16}O_5$ 336.0998; found 336.0998. $C_{20}H_{16}O_5$ (336.24): calcd. C 71.42, H 4.79; found C 71.19, H 4.86.

***rac*-1-Hydroxy-8-methoxy-3-methyl-2-[(3-methyloxiran-2-yl)carbonyl]anthraquinone (*rac*-28):** A solution of anthraquinone **27** (40.0 mg, 0.119 mmol) in acetone (30 mL) was treated at 25 °C with a freshly produced solution of DMDO in acetone (10 mL, ca. 0.07–0.09 M). The reaction mixture was stirred for 6 d with the addition of DMDO after each 24 h (5 × 3 mL). Afterwards, the mixture was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2/EtOAc, 10:1) to afford anthraquinone *rac*-**28** (38.0 mg, 90% yield) as a yellow solid. R_f = 0.38 (PE/EtOAc, 1:1 + 1% HOAc); m.p. 185 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.46 (d, *J* = 5.1 Hz, 3 H, 4′-H_3), 2.40 (s, 3 H, Ar-CH_3), 3.26 (dq, *J* = 5.1, 2.0 Hz, 1 H, 3′-H), 3.71 (d, *J* = 2.0 Hz, 1 H, 2′-H), 4.07 (s, 3 H, OCH_3), 7.37 (d_{br}, *J* = 8.2 Hz, 1 H, 7-H), 7.58 (s, 1 H, 4-H), 7.75 (t, *J* = 8.1 Hz, 1 H, 6-H), 7.92 (dd, *J* = 7.8, 0.7 Hz, 1 H, 5-H), 13.37 (s, 1 H, OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 17.55, 20.32, 56.46, 56.67, 61.25, 115.1, 118.4, 120.3, 120.4, 120.7, 132.2, 132.9, 135.4, 136.1, 146.0, 160.7, 160.9, 182.2, 188.4, 200.9 ppm. IR (KBr): $\tilde{\nu}$ = 2926, 1708, 1675, 1630, 1585, 1566, 1468, 1444, 1389, 1360, 1298, 1266, 1245, 1215 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.0 (4.510), 254.0 (4.352), 413.0 (3.972) nm. MS (EI, 70 eV): *m/z* (%) = 352.2 (12) [M]$^+$, 334.2 (6) [M – H_2O]$^+$, 308.1 (18) [M – C_2H_4O]$^+$, 295.1 (100) [M – C_3H_5O]$^+$. HRMS (ESI): calcd. for $C_{20}H_{16}O_6$ + H 353.10196; found 353.10193; calcd. for $C_{20}H_{16}O_6$ + Na 375.08391; found 375.08395.

1,4,5-Trihydroxy-2-methylanthraquinone (Islandicin, 3): To a suspension of juglone derivative **9** (1.00 g, 4.78 mmol) in benzene (15 mL) was added at 25 °C dropwise with stirring diene **29** (2.63 g, 9.57 mmol) in benzene (10 mL) over 5 min. After being stirred at 25 °C for 1 h, the reaction mixture was heated at reflux for 1 h. Another portion of diene **29** (0.66 g, 2.39 mmol) was then added, and stirring at reflux was continued for an additional 2 h. Afterwards, the reaction mixture was concentrated under reduced pressure, and the residue was dissolved in THF (50 mL). Concentrated HCl (10 mL) was then added dropwise at 25 °C over 2 min. The reaction mixture was stirred at 25 °C for 1 h and then at reflux for 1 h (formation of a red precipitate). The reaction mixture was poured into H_2O (300 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic phases were extracted with NaOH (2%, 3 × 600 mL), and the resulting violet aq. phase was acidified with 6 N HCl (the color changed to yellow). After the mixture was extracted with CH_2Cl_2 (3 × 500 mL), the combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2 + 1% HOAc) to afford islandicin (**3**, 1.15 g, 89% yield) as a dark red solid. R_f = 0.138 (PE/EtOAc, 20:1); m.p. 219 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (d, *J* = 0.6 Hz, 3 H, CH_3), 7.15 (s, 1 H, 3-H), 7.30 (dd, *J* = 8.4, 1.0 Hz, 1 H, 6-H), 7.69 (t, *J* = 8.3 Hz, 1 H, 7-H), 7.88 (dd, *J* = 7.6, 1.1 Hz, 1 H, 8-H), 12.28 (s, 1 H, 4-OH*), 12.32 (s, 1 H, 5-OH*), 13.48 (s, 1 H, 1-OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.63, 110.7, 111.7, 116.3, 119.4, 124.5, 129.0, 133.6, 136.7, 141.8, 157.7, 157.9, 162.5, 186.6, 190.4 ppm. IR (KBr): $\tilde{\nu}$ = 3423, 3125, 1598, 1446, 1380, 1249 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 231.0 (4.580), 252.0 (4.377), 289.5 (3.947), 490.5 (4.131), 522.5 (3.937, sh) nm. MS (EI, 70 eV): *m/z* (%) = 270.1 (100) [M]$^+$. HRMS (EI): calcd. for $C_{15}H_{10}O_5$ 270.0528; found 270.0528. $C_{15}H_{10}O_5$ (270.24): calcd. C 66.67, H 3.73; found C 66.38, H 3.55.

1,4,5-Trimethoxy-2-methylanthraquinone (32): A suspension of islandicin (**3**, 6.00 g, 22.2 mmol) in acetone (1.6 L) was treated subsequently at 25 °C with K_2CO_3 (92.0 g, 0.666 mol) and Me_2SO_4 (15 mL). After being stirred at reflux for 36 h, the reaction mixture was filtered through a plug of Celite®. The filter cake was rinsed carefully with CH_2Cl_2, and then the combined organic phases were concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (300 mL), washed with H_2O (200 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 5:1) to afford anthraquinone **32** (6.86 g, 99% yield) as an orange yellow solid. R_f = 0.16 (PE/EtOAc, 1:1); m.p. 160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 3.99 (s, 3 H, OCH_3), 7.12 (s, 1 H, 3-H), 7.23 (dd, *J* = 8.3, 0.9 Hz, 1 H, 6-H), 7.60 (t, *J* = 7.5 Hz, 1 H, 7-H), 7.72 (dd, *J* = 8.5, 1.1 Hz, 1 H, 8-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.84, 56.43, 56.76, 61.47, 116.9, 118.5, 120.9, 123.4, 123.7, 126.7, 133.7, 136.5, 140.3, 151.4, 154.9, 158.5, 183.1, 184.03 ppm. IR (KBr): $\tilde{\nu}$ = 3076, 2937, 2843, 1669, 1588, 1562, 1449, 1428, 1392, 1374, 1322, 1268, 1236 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 223.0 (4.591), 252.5 (4.351), 382.0 (3.866), 389.5 (3.869) nm. MS (EI, 70 eV): *m/z* (%) = 312.2 (100) [M]$^+$, 297.2 (72) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{18}H_{16}O_4$ 312.0998; found 312.0998. $C_{18}H_{16}O_5$ (312.32): calcd. C 69.22, H 5.16; found C 69.06, H 5.49.

1,4-Dihydroxy-5-methoxy-2-methylanthraquinone (33): A solution of anthraquinone **32** (8.00 g, 25.6 mmol) in acetone (500 mL) was treated at 25 °C with AgO (12.7 g, 102 mmol) and stirred for 5 min until a suspension was formed. Afterwards, HNO_3 (6 N, 60 mL) was added dropwise over 5 min until the AgO was completely dissolved. After being stirred for another 20 min, the reaction mixture was treated with aq. $NaHSO_3$ (1%, 350 mL) and stirred vigorously for 5 min. After the addition of H_2O (300 mL), the mixture was extracted with CH_2Cl_2 (3 × 300 mL), and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was subjected to silica gel flash chromatography (CH_2Cl_2) to afford anthraquinone **33** (5.97 g, 82% yield) as a red solid. R_f = 0.19 (PE/EtOAc, 4:1); m.p. 195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 4.07 (s, 3 H, OCH_3), 7.12 (s, 1 H, 3-H), 7.35 (dd, *J* = 8.4, 0.7 Hz, 1 H, 6-H), 7.74 (t, *J* = 7.6 Hz, 1 H, 7-H), 7.99 (dd, *J* = 7.7, 1.1 Hz, 1 H, 8-H), 13.28 (s, 1 H, OH), 13.30 (s, 1 H, OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.32, 56.61, 111.53, 111.69, 118.07, 119.62, 121.02, 129.48, 135.33, 135.58, 139.43, 156.76, 157.34, 160.84, 186.68, 186.83 ppm. IR (KBr): $\tilde{\nu}$ = 3007, 1620, 1578, 1447, 1401, 1379, 1352, 1296, 1278, 1231 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 230.0 (4.573), 249.5 (4.349), 285.5 (3.975), 474.5 (4.035), 489.5 (4.023, sh) nm. MS (EI, 70 eV): *m/z* (%) = 284.2 (100) [M]$^+$, 266.2 (50) [M – H_2O]$^+$, 238.2 (54) [M – H_2O – CO]$^+$. HRMS (EI): calcd. for $C_{16}H_{12}O_5$ 284.0685; found 284.0685. $C_{16}H_{12}O_5$ (284.26): calcd. C 67.60, H 4.25; found C 67.88, H 4.38.

3-Bromo-1,4-dihydroxy-5-methoxy-2-methylanthraquinone (34): A solution of anthraquinone **33** (2.70 g, 9.50 mmol) in CH_2Cl_2 (450 mL) was treated at 25 °C with a catalytic amount of diisopropylamine (0.20 mL), and then NBS (16.9 g, 95.5 mmol) was added in one portion. Stirring at 25 °C was continued for 16 d. Afterwards, the reaction mixture was treated with aq. $NaHSO_3$ (10%, 500 mL) and stirred vigorously for 10 min. After separation of the phases, the organic layer was washed subsequently with aq. HCl (0.1 N, 2 × 500 mL) and H_2O (500 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was subjected to silica gel flash chromatography (CH_2Cl_2) to afford anthraquinone **34** (31.9 g, 54% yield) as a red solid. R_f = 0.17 (PE/EtOAc, 4:1); m.p. 250 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (s, 3 H, CH_3), 4.09 (s, 3 H, OCH_3), 7.39 (dd, *J* = 8.4, 0.9 Hz, 1 H, 6-H), 7.78 (t, *J* = 7.9 Hz, 1 H, 7-H), 8.03 (dd, *J* = 7.7, 1.0 Hz, 1 H, 8-H), 13.49 (s, 1 H, OH), 14.21 (s, 1 H, OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.64, 56.73, 110.6, 111.4, 118.4, 119.7, 120.4, 126.6, 135.4, 135.8, 139.4, 154.6, 155.9, 161.1, 186.6, 186.7 ppm. IR (KBr): $\tilde{\nu}$ = 1619, 1583, 1443, 1405, 1375, 1291, 1234 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.0 (4.362), 236.0 (4.491), 253.5 (4.390), 293.0 (3.922), 476.5 (4.065) nm. MS (EI, 70 eV): *m/z* (%) = 364.0, 362.0 (100) [M]$^+$, 346.0, 344.0 (48) [M – H_2O]$^+$, 318.0, 316.0 (20) [M – H_2O – CO]$^+$. HRMS (EI): calcd. for $C_{16}H_{11}BrO_5$ 361.9790; found 361.9790. $C_{16}H_{11}BrO_5$ (363.16): calcd. C 52.92, H 3.05; found C 53.04, H 2.98.

3-Bromo-1,4,5-trimethoxy-2-methylanthraquinone (35): A solution of anthraquinone **34** (530 mg, 1.46 mmol) in acetone (350 mL) was treated subsequently at 25 °C with K_2CO_3 (8.07 g, 58.4 mol) and Me_2SO_4 (5.0 mL). After being stirred for 18 h at reflux, the reaction mixture was filtered through a plug of Celite®. The filter cake was rinsed carefully with CH_2Cl_2, and then the combined organic phases were concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (300 mL), washed with H_2O (200 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 4:1) to afford anthraquinone **35** (502 mg, 88% yield) as a yellow solid. R_f = 0.22 (PE/EtOAc, 7:3); m.p. 205 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (s, 3 H, CH_3), 3.91 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 7.26 (dd, *J* = 8.3, 0.9 Hz, 1 H, 6-H), 7.63 (t, *J* = 8.0 Hz, 1 H, 7-H), 7.72 (dd, *J* = 7.7, 1.1 Hz, 1 H, 8-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 17.22, 56.46, 62.02, 62.48, 116.9, 118.6, 122.9, 125.2, 128.3, 130.6, 134.3, 136.5, 141.1, 152.7, 154.2, 158.6, 182.1, 183.0 ppm. IR (KBr): $\tilde{\nu}$ = 2945, 2847, 1678, 1586, 1535, 1458, 1403, 1378, 1324, 1272, 1229 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 222.5 (4.516), 259.5 (4.475), 369.0 (3.911) nm. MS (EI, 70 eV): *m/z* (%) = 392.1, 390.1 (100) [M]$^+$, 375.1 (98) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{18}H_{15}BrO_5$ 390.0103; found 390.0130. $C_{18}H_{15}BrO_5$ (391.21): calcd. C 55.26, H 3.86; found C 55.41, H 3.68.

3-Bromo-1,4,5,9,10-pentamethoxy-2-methylanthracene (36): A solution of anthraquinone **35** (360 mg, 0.920 mmol) and tetra-*n*-butylammonium bromide (148 mg, 0.460 mmol) in THF (60 mL) was treated at 25 °C with a solution of $Na_2S_2O_4$ (961 mg, 5.52 mmol) in H_2O (8.0 mL) and stirred for 20 min. Afterwards, a solution of KOH (1.55 g, 27.6 mmol) in H_2O (8.0 mL) was added (the yellow solution turned deep red), and stirring was continued for an additional 15 min. After the addition of Me_2SO_4 (2.0 mL), the reaction mixture was stirred for 18 h (the solution turned back to yellow) and then poured into H_2O (150 mL). The resulting solution was extracted with CH_2Cl_2 (3 × 75 mL), and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was subjected to silica gel column filtration (CH_2Cl_2), and the concentration of the appropriate fractions in vacuo afforded anthracene **36** (368 mg, 95% yield) as a yellow oil which solidified under high vacuum. R_f = 0.51 (PE/EtOAc, 4:1); m.p. 116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.58 (s, 3 H, Ar-CH_3), 3.81 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.07 (s, 3 H, OCH_3), 6.82 (d, *J* = 7.3 Hz, 1 H, 6-H), 7.41 (dd, *J* = 8.6, 7.6 Hz, 1 H, 7-H), 7.96 (dd, *J* = 8.9, 0.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.88, 56.40, 61.54, 61.71, 63.30, 64.04, 104.7, 115.1, 119.3, 119.5, 120.5, 121.0, 126.0, 127.7, 129.1, 147.2, 149.0, 149.2, 149.4, 156.9 ppm. IR (KBr): $\tilde{\nu}$ = 2927, 2833, 1617, 1579, 1560, 1518, 1451, 1415, 1380, 1364, 1347, 1316, 1286, 1259 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 201.0 (4.423), 230.0 (4.119), 269.0 (4.993), 365.0 (3.855), 383.0 (4.120), 399.5 (3.966), 422.5 (3.864) nm. MS (EI, 70 eV): *m/z* (%) = 422.0, 420.0 (100) [M]$^+$, 407.0, 405.0 (56) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{20}H_{21}BrO_5$ 420.0572; found 420.0572. $C_{20}H_{21}BrO_5$ (421.28): calcd. C 57.02, H 5.02; found C 57.27, H 5.05.

***rac*-1-(1,4,8,9,10-Pentamethoxy-3-methylanthracen-2-yl)ethanol (*rac*-37):** A solution of anthracene **36** (1.31 g, 3.11 mmol) in THF (40 mL) was treated at –78 °C dropwise with *n*BuLi (1.37 mL, 3.42 mmol, 2.5 M in *n*-hexane) over 1 min, and stirring was continued for 1 min. Freshly distilled acetaldehyde (1.83 mL, 31.1 mmol) was added quickly. Stirring was continued at –78 °C for 1 h, and then the reaction mixture was warmed to 25 °C over 1 h. The reaction mixture was treated with saturated aq. NH_4Cl (20 mL), stirred for 5 min and then poured into H_2O (100 mL). Afterwards, the resulting solution was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to silica gel flash chromatography (PE/EtOAc 4:1 → 1:1), and the concentration of the appropriate fractions in vacuo afforded alcohol *rac*-**37** (975 mg, 81% yield) as a yellow oil which solidified under high vacuum. R_f = 0.40 (PE/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (d, *J* = 6.8 Hz, 3 H, 2-H_3), 2.46 (s, 3 H, Ar-CH_3), 3.78 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 5.27 (s_{br}, 1 H, 1-H), 6.80 (d_{br}, *J* = 7.5 Hz, 1 H, 6′-H), 7.38 (dd, *J* = 8.8, 7.4 Hz, 1 H, 7-H), 7.95 (dd, *J* = 8.7, 0.7 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 11.96, 24.87, 56.44, 60.37, 61.45, 63.25, 63.48, 63.72, 104.5, 115.0, 119.2, 119.8, 120.9, 125.4, 125.7, 128.8, 133.5, 146.9, 148.7, 149.0, 149.8, 157.0 ppm. IR (KBr): $\tilde{\nu}$ = 3431, 2929, 2833, 1737, 1616, 1594, 1558, 1518, 1450, 1418, 1358, 1319, 1258 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 201.5 (4.358), 229.0 (4.082), 265.5 (4.952), 364.5 (3.794, sh), 397.0 (3.981), 420.5 (3.790) nm. MS (EI, 70 eV): *m/z* (%) = 386.3 (100) [M]$^+$, 371.3 (54) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{22}H_{26}O_6$ 386.1729; found 386.1729.

***rac*-3-(1-Hydroxyethyl)-1,4,5-trimethoxy-2-methylanthraquinone (*rac*-38):** A solution of anthracene *rac*-**37** (930 mg, 2.41 mmol) in 1,4-dioxane (100 mL) was treated at 25 °C with AgO (1.50 g, 12.1 mmol) and stirred for 5 min until a suspension was formed. Afterwards, HNO_3 (4 N, 25 mL) was added dropwise over 5 min until the AgO was completely dissolved. After being stirred for another 15 min, the reaction mixture was poured into H_2O (200 mL) and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2/EtOAc, 4:1 → 1:1) to afford anthraquinone *rac*-**38** (811 mg, 94% yield) as a yellow-orange oil which solidified under high vacuum. R_f = 0.24 (PE/EtOAc, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59 (d, *J* = 6.5 Hz, 3 H, 2-H_3), 2.39 (s, 3 H, Ar-CH_3), 3.87 (s, 3 H, OCH_3), 3.99 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 5.24 (m_c, 1 H, 1-H), 7.25 (dd, *J* = 8.3, 0.9 Hz, 1 H, 6′-H), 7.63 (t, *J* = 8.5 Hz, 1 H, 7′-H), 7.75 (s, 1 H, 4′-H), 7.81 (dd, *J* = 7.6, 0.9 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.18, 23.50, 56.50, 61.71, 63.80, 67.10, 116.8, 118.7, 123.4, 125.4, 127.0, 134.2, 136.5, 137.8, 145.1, 154.3, 154.4, 158.4, 183.0, 183.4 ppm. IR (KBr): $\tilde{\nu}$ = 3489, 2934, 1675, 1587, 1555, 1454, 1392, 1316, 1274, 1237 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 222.5 (4.500), 256.5 (4.416), 373.0 (3.869) nm. MS (EI, 70 eV): *m/z* (%) = 356.3 (100) [M]$^+$, 341.3 (86) [M – CH_3]$^+$, 323.2 (24) [M – CH_3 – H_2O]$^+$. HRMS (EI): calcd. for $C_{20}H_{20}O_6$ 356.1260; found 356.1260.

3-Acetyl-1,4,5-trimethoxy-2-methylanthraquinone (39): A solution of anthraquinone *rac*-**38** (809 mg, 2.27 mmol) in CH_2Cl_2 (120 mL) was treated at 25 °C with the Dess–Martin periodinane (1.44 g, 3.41 mmol) and stirred for 2 h. Afterwards, saturated aq. $NaHCO_3$ (12 mL) and aq. $Na_2S_2O_3$ (1 M, 12 mL) were added simultaneously, and the resulting cloudy reaction mixture was stirred for 1 h until a clear solution was formed. The mixture was poured into H_2O (100 mL) and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 10:1) to afford anthraquinone **39** (686 mg, 85% yield) as a yellow solid. R_f = 0.38 (PE/EtOAc, 1:1); m.p. 168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, Ar-CH_3), 2.54 (s, 3 H, 2′-H_3), 3.92 (s, 6 H, 2 × OCH_3), 4.01 (s, 3 H, OCH_3), 7.27 (dd, *J* = 8.6, 1.0 Hz, 1 H, 6-H), 7.66 (t, *J* = 8.7 Hz, 1 H, 7-H), 7.75 (dd, *J* = 7.5, 1.2 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.68, 31.93, 56.47, 61.83, 64.06, 116.9, 118.8, 122.9, 126.7, 127.7, 134.4, 135.9, 136.5, 145.0, 151.5, 154.7, 158.8, 182.2, 183.1, 203.7 ppm. IR (KBr): $\tilde{\nu}$ = 2943, 1706, 1681, 1587, 1564, 1460, 1416, 1392, 1319, 1279, 1222 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 221.0 (4.488), 254.0 (4.404), 372.5 (3.867) nm. MS (EI, 70 eV): *m/z* (%) = 354.3 (96) [M]$^+$, 339.3

(100) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{20}H_{18}O_6$ 354.1103; found 354.1103. $C_{20}H_{18}O_6$ (354.54): calcd. C 67.79, H 5.12; found C 67.48, H 5.08.

3-Acetyl-1,4-dihydroxy-5-methoxy-2-methylanthraquinone (40): A solution of anthraquinone **39** (100 mg, 0.282 mmol) in CH_2Cl_2 (40 mL) was treated at 0 °C dropwise with BCl_3 (4.00 mL, 4.00 mmol, 1 M in CH_2Cl_2) and stirred for 5 min. Afterwards, MeOH (10 mL) was slowly added, and the reaction mixture was warmed to 25 °C. After being stirred for 30 min, the reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed H_2O (100 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was subjected to silica gel flash chromatography (CH_2Cl_2), and the concentration of the appropriate fractions in vacuo furnished anthraquinone **40** (80 mg, 87% yield) as a red solid. R_f = 0.36 (PE/EtOAc, 3:2); m.p. 215 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, Ar-CH_3), 2.60 (s, 3 H, 2′-H_3), 4.08 (s, 3 H, OCH_3), 7.38 (dd, J = 8.4, 0.9 Hz, 1 H, 6-H), 7.77 (t, J = 8.4 Hz, 1 H, 7-H), 8.01 (dd, J = 7.7, 0.9 Hz, 1 H, 8-H), 13.27 (s, 1 H, OH), 13.49 (s, 1 H, OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.70, 31.83, 56.67, 111.6, 111.8, 118.4, 119.8, 120.8, 134.7, 135.7, 135.7, 141.1, 153.6, 156.2, 161.0, 186.8, 202.8 ppm. IR (KBr): $\tilde{\nu}$ = 2975, 1694, 1617, 1577, 1443, 1411, 1383, 1351, 1279 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 231.5 (4.541), 250.0 (4.308), 286.0 (3.933), 475.0 (4.029) nm. MS (EI, 70 eV): m/z (%) = 326.2 (76) [M]$^+$, 311.2 (100) [M – CH_3]$^+$. HRMS (EI): calcd. for $C_{18}H_{14}O_6$ 326.0790; found 326.0790. $C_{18}H_{14}O_6$ (326.30): calcd. C 66.26, H 4.32; found C 66.16, H 4.12.

3-Acetyl-5-methoxy-2-methyl-9,10-dioxo-9,10-dihydroanthracene-1,4-diyl Diacetate (41): A suspension of anthraquinone **40** (50 mg, 0.15 mmol) in acetic anhydride (5.0 mL) was treated at 25 °C with pyridine (10 mL) and a catalytic amount of DMAP (10 mg). After being stirred for 24 h, the reaction mixture was poured into H_2O (100 mL), and stirring was continued for 30 min. The mixture was extracted with CH_2Cl_2 (3 × 30 mL), the organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2/EtOAc, 4:1) to furnish anthraquinone **41** (58 mg, 94% yield) as a yellow solid. R_f = 0.33 (PE/EtOAc, 2:3); m.p. 215 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, Ar-CH_3), 2.37, 2.43, 2.45 (3 s, 9 H, 2′-H_3, 2 × OC(O)CH_3), 3.91 (s, 3 H, OCH_3), 7.20 (dd, J = 8.4, 1.0 Hz, 1 H, 7-H), 7.59 (t, J = 8.4 Hz, 1 H, 6-H), 7.68 (dd, J = 7.8, 1.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.25, 20.95, 21.13, 31.73, 56.71, 117.8, 119.3, 122.0, 125.2, 126.1, 134.9, 135.7, 142.8, 143.2, 146.1, 159.6, 169.0, 180.6, 181.9, 201.2 ppm. IR (KBr): $\tilde{\nu}$ = 2920, 1776, 1761, 1708, 1670, 1585, 1473, 1434, 1369, 1321, 1277, 1222, 1188, 1174 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.0 (4.438), 253.5 (4.433), 379.5 (3.747) nm. MS (EI, 70 eV): m/z (%) = 410.1 (12) [M]$^+$, 368.1 (20) [M – C_2H_2O]$^+$, 326.1 (100) [M – 2 C_2H_2O]$^+$, 311.0 (70) [M – 2 C_2H_2O – CH_3]$^+$. HRMS (EI): calcd. for $C_{22}H_{18}O_8$ 410.1002; found 410.1002.

3-Acetyl-1,4,5-trihydroxy-2-methylanthraquinone (42): A suspension of anthraquinone **39** (600 mg, 1.69 mmol) in HOAc (40 mL) was treated at 25 °C with HBr (30 mL, 33% in HOAc) and stirred at 100 °C for 1.5 h. After the addition of more HBr (20 mL), the reaction mixture was stirred for another 45 min and then poured into H_2O (500 mL). The mixture was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2) to afford anthraquinone **42** (502 mg, 95% yield) as an orange solid. R_f = 0.54 (PE/EtOAc, 4:1); m.p. 209 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, Ar-CH_3), 2.61 (s, 3 H, 2′-H_3), 7.32 (d, J = 8.4 Hz, 1 H, 6-H), 7.72 (t, J = 8.0 Hz, 1 H, 7-H), 7.89 (d, J = 7.5 Hz, 1 H, 8-H), 12.12 (s, 1 H, OH), 12.52 (s, 1 H, OH), 13.46 (s, 1 H, OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.01, 31.80, 110.8, 111.7, 116.0, 119.7, 124.9, 133.3, 137.1, 140.8, 153.7, 157.4, 162.6, 186.4, 190.6, 202.1 ppm. IR (KBr): $\tilde{\nu}$ = 2923, 1704, 1605, 1554, 1455, 1410, 1387, 1308, 1260 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 232.5 (4.545), 252.5 (4.351), 291.5 (3.909), 490.0 (4.095), 600.5 (2.850, sh) nm. MS (EI, 70 eV): m/z (%) = 312.2 (100) [M]$^+$, 297.2 (60) [M – CH_3]$^+$, 294.2 (26) [M – H_2O]$^+$. HRMS (EI): calcd. for $C_{17}H_{12}O_6$ 312.0634; found 312.0634. $C_{17}H_{12}O_6$ (312.27): calcd. C 65.39, H 3.87; found C 65.18, H 3.67.

***rac*-(2*E*)-1-(1,4,8,9,10-Pentamethoxy-3-methylanthracen-2-yl)but-2-en-1-ol (*rac*-43):** A solution of anthracene **36** (415 mg, 0.985 mmol) in THF (20 mL) was treated at –78 °C dropwise with *n*BuLi (0.47 mL, 1.18 mmol, 2.5 M in *n*-hexane) over 1 min, and stirring was continued for 1 min. (*E*)-Crotonaldehyde (0.40 mL, 4.93 mmol) was added quickly. Stirring was continued at –78 °C for 15 min, and then the reaction mixture was warmed to 25 °C over 1 h. The reaction mixture was treated with saturated aq. NH_4Cl (10 mL), stirred for 5 min and then poured into H_2O (50 mL). Afterwards, the resulting solution was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to silica gel flash chromatography (PE/EtOAc, 10:1 → 4:1), and the concentration of the appropriate fractions in vacuo afforded alcohol *rac*-**43** (306 mg, 75% yield) as a yellow foam. R_f = 0.13 (PE/EtOAc, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.75 (d_{br}, J = 6.2 Hz, 3 H, 4-H_3), 2.46 (s, 3 H, Ar-CH_3), 3.78 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 5.12 (s_{br}, 1 H, OH), 5.48–5.78 (m, 2 H, 1-H, 3-H), 5.93 (dd_{br}, J = 15.2, 3.7 Hz, 1 H, 2-H), 6.80 (d_{br}, J = 7.6 Hz, 1 H, 7′-H), 7.38 (dd, J = 8.7, 7.4 Hz, 1 H, 6′-H), 7.95 (dd, J = 8.6, 1.0 Hz, 1 H, 5′-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.17, 17.77, 56.45, 61.48, 63.26, 63.44, 63.55, 71.53, 104.5, 115.1, 119.2, 120.0, 121.1, 125.8, 126.0, 128.9, 131.7, 133.8, 146.9, 148.8, 149.2, 150.1, 157.0 ppm. IR (KBr): $\tilde{\nu}$ = 3454, 2929, 2833, 1720, 1617, 1595, 1559, 1519, 1450, 1419, 1359, 1322, 1259 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 201.0 (4.401), 230.0 (4.090), 267.0 (4.931), 365.0 (3.774, sh), 382.5 (4.031), 397.0 (3.956), 420.5 (3.759) nm. MS (EI, 70 eV): m/z (%) = 412.2 (100) [M]$^+$, 397.2 (52) [M – CH_3]$^+$, 43.0 (57) [CH_3 + CO]$^+$. HRMS (ESI): calcd. for $C_{24}H_{28}O_6$ + Na 435.17781; found 435.17771.

***rac*-3-[(2*E*)-1-Hydroxybut-2-enyl]-1,4,5-trimethoxy-2-methylanthraquinone (*rac*-44):** A solution of anthracene *rac*-**43** (89.0 mg, 0.216 mmol) in 1,4-dioxane (30 mL) was treated at 25 °C with AgO (134 mg, 1.08 mmol) and stirred for 5 min until a suspension was formed. Afterwards, HNO_3 (4 N, 3.0 mL) was added dropwise over 5 min until the AgO was completely dissolved. After being stirred for another 15 min, the reaction mixture was poured into H_2O (100 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 3:1) to afford anthraquinone *rac*-**44** (61.0 mg, 74% yield) as a yellow-orange solid. R_f = 0.25 (PE/EtOAc, 1:1); m.p. 104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73 (m_c, 3 H, 4′-H_3), 2.39 (s, 3 H, Ar-CH_3), 3.88 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 5.48–5.74 (m, 2 H, 1′-H, 3′-H), 5.83 (ddd_{br}, J = 15.5, 5.5, 1.4 Hz, 1 H, 2′-H), 7.31 (d_{br}, J = 8.4 Hz, 1 H, 6-H), 7.63 (t, J = 7.9 Hz, 1 H, 7-H), 7.73 (dd, J = 7.7, 0.9 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.40, 17.67, 56.45, 61.71, 63.80, 70.69, 116.8, 118.6, 123.3, 125.6, 127.0, 127.0, 132.0, 134.2, 136.5, 138.6, 143.4, 154.2, 154.2, 158.5, 183.1, 183.1 ppm. IR (KBr): $\tilde{\nu}$ = 3421, 2935, 2841, 1671, 1591, 1551, 1470, 1454, 1416, 1392, 1335, 1314, 1271 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 222.5 (4.505), 257.5 (4.412), 372.5 (3.896) nm. MS (EI, 70 eV): *m*/*z* (%) = 382.1 (100) $[M]^+$, 350.1 (68), 335.0 (48).

3-[(2*E*)-But-2-enoyl]-1,4,5-trimethoxy-2-methylanthraquinone (45): A solution of anthraquinone *rac*-**44** (600 mg, 0.157 mmol) in CH_2Cl_2 (15 mL) was treated at 25 °C with the Dess–Martin periodinane (100 mg, 0.235 mmol) and stirred for 2.5 h. Afterwards, saturated aq. $NaHCO_3$ (2 mL) and aq. $Na_2S_2O_3$ (1 M, 2 mL) were added simultaneously, and the resulting cloudy reaction mixture was stirred for 30 min until a clear solution was formed. The mixture was poured into H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2, CH_2Cl_2/EtOAc, 10:1) to afford anthraquinone **45** (55.0 mg, 0.144 mmol, 92% yield) as a yellow solid. R_f = 0.18 (PE/EtOAc, 3:2); m.p. 175 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.89 (dd_{br}, *J* = 6.7, 1.3 Hz, 3 H, 4′-H_3), 2.16 (s, 3 H, Ar-CH_3), 3.84 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 6.40 (dd_{br}, *J* = 16.0, 1.3 Hz, 1 H, 2′-H), 6.58 (dq, *J* = 15.4, 6.6 Hz, 1 H, 3′-H), 7.34 (d, *J* = 8.1 Hz, 1 H, 6-H), 7.61 (t, *J* = 7.9 Hz, 1 H, 7-H), 7.71 (dd, *J* = 7.8, 0.9 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.87, 18.57, 56.44, 61.82, 64.08, 116.9, 118.7, 123.0, 126.8, 127.7, 133.0, 134.3, 136.5, 137.6, 143.3, 149.0, 152.1, 154.4, 158.7, 182.2, 183.2, 195.7 ppm. IR (KBr): $\tilde{\nu}$ = 2939, 1681, 1622, 1587, 1561, 1471, 1455, 1417, 1391, 1321, 1282 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 219.5 (4.630), 254.5 (4.448), 373.5 (3.889) nm. MS (EI, 70 eV): *m*/*z* (%) = 380.1 (12) $[M]^+$, 365.1 (2) $[M - CH_3]^+$, 69.0 (32) $[C_4H_5O]^+$, 57.0 (41) $[C_3H_5O]^+$, 41.0 (100) $[C_3H_5]^+$. HRMS (ESI): calcd. for $C_{22}H_{20}O_6$ + H 381.13326; found 381.13321.

3-[(2*E*)-But-2-enoyl]-1,4-dihydroxy-5-methoxy-2-methylanthraquinone (46): A solution of anthraquinone **45** (92.0 mg, 0.242 mmol) in CH_2Cl_2 (35 mL) was treated at 0 °C dropwise with BCl_3 (3.63 mL, 3.63 mmol, 1 M in CH_2Cl_2) over 1 min and stirred at the same temperature for 3 min. Afterwards, MeOH (20 mL) was slowly added, and the reaction mixture was warmed to 25 °C. After being stirred for 30 min, the reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with H_2O (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude material was subjected to silica gel flash chromatography (CH_2Cl_2 + 2% HOAc), and the concentration of the appropriate fractions in vacuo furnished anthraquinone **46** (77.0 mg, 90% yield) as a red solid. R_f = 0.41 (PE/EtOAc, 3:2 + 1% HOAc); m.p. 212 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.94 (dd_{br}, *J* = 6.7, 1.3 Hz, 3 H, 4′-H_3), 2.16 (s, 3 H, Ar-CH_3), 4.04 (s, 3 H, OCH_3), 6.39 (dd_{br}, *J* = 16.0, 1.3 Hz, 1 H, 2′-H), 6.64 (dq, *J* = 15.4, 6.6 Hz, 1 H, 3′-H), 7.34 (d, *J* = 8.1 Hz, 1 H, 6-H), 7.72 (t, *J* = 7.9 Hz, 1 H, 7-H), 7.96 (dd, *J* = 7.8, 0.9 Hz, 1 H, 8-H), 13.26 (s, 1 H, OH), 13.34 (s, 1 H, OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.97, 18.76, 56.65, 111.6, 111.7, 118.4, 119.7, 120.8, 133.0, 135.3, 135.7, 135.7, 139.7, 149.0, 154.0, 156.1, 161.0, 186.7, 186.8, 194.9 ppm. IR (KBr): $\tilde{\nu}$ = 2946, 1657, 1616, 1576, 1446, 1397, 1350 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 229.0 (4.589), 250.5 (4.365), 283.0 (3.924, sh), 476.0 (4.041) nm. MS (EI, 70 eV): *m*/*z* (%) = 352.1 (84) $[M]^+$, 337.1 (100) $[M - CH_3]^+$, 309.0 (15) $[M - C_2H_3O]^+$, 69.0 (20) $[C_4H_5O]^+$, 41.0 (31) $[C_3H_5]^+$. HRMS (ESI): calcd. for $C_{20}H_{16}O_6$ + H 353.10196; found 353.10196.

***rac*-1,4-Dihydroxy-8-methoxy-3-methyl-2-[(3-methyloxiran-2-yl)carbonyl]anthraquinone (*rac*-47):** A solution of anthraquinone **46** (70.0 mg, 0.197 mmol) in acetone (50 mL) was treated at 25 °C with a freshly produced solution of DMDO in acetone (10 mL, ca. 0.07–0.09 M). The reaction mixture was stirred for 6 d with the addition of DMDO after each 24 h (5 × 5 mL). Afterwards, the mixture was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting crude material was filtered through a plug of silica gel (CH_2Cl_2/EtOAc, 10:1) to afford anthraquinone *rac*-**47** (42.0 mg, 58% yield) as a red solid. R_f = 0.41 (PE/EtOAc, 3:2 + 1% HOAc); m.p. 188 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.45 (d, *J* = 5.0 Hz, 3 H, 4′-H_3), 2.25 (s, 3 H, Ar-CH_3), 3.26 (dq, *J* = 5.0, 1.8 Hz, 1 H, 3′-H), 3.64 (d, *J* = 1.6 Hz, 1 H, 2′-H), 4.07 (s, 3 H, OCH_3), 7.36 (d_{br}, *J* = 8.5 Hz, 1 H, 6-H), 7.75 (t, *J* = 8.1 Hz, 1 H, 7-H), 7.97 (d_{br}, *J* = 7.7 Hz, 1 H, 8-H), 13.17 (s, 1 H, OH), 13.52 (s, 1 H, OH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.00, 17.49, 56.18, 56.59, 61.1, 111.6, 112.1, 118.5, 119.7, 120.5, 135.1, 135.8, 136.7, 137.0, 154.2, 155.7, 160.9, 186.6, 186.7, 200.7 ppm. IR (KBr): $\tilde{\nu}$ = 2926, 1710, 1619, 1574, 1446, 1383, 1282, 1223 cm^{-1}. UV (CH_3CN): λ_{max} (lg ε) = 231.0 (4.526), 250.5 (4.286), 284.5 (3.933, sh), 477.0 (4.013) nm. MS (EI, 70 eV): *m*/*z* (%) = 368.2 (68) $[M]^+$, 324.2 (44) $[M - C_2H_4O]^+$, 311.2 (100) $[M - C_3H_5O]^+$. HRMS (EI): calcd. for $C_{20}H_{16}O_7$ 368.0896; found 368.0896.

Biological Testing

Human Tumor Colony-Forming Ability (HTCF) Test: Human bronchial carcinoma cells of line A549 (ATCC CCL 185) were cultivated at 37 °C and 7.5% CO_2 in Dulbecco's modified Eagle's medium (DMEM, Biochrom) supplemented with fetal calf serum (10%, heat-inactivated for 30 min at 56 °C, GibcoBRL), $NaHCO_3$ (44 mm, Biochrom) and L-glutamine (4 mm, GibcoBRL). Adherent cells of line A549 were sown in triplicate in 6 multiwell plates at concentrations of 10^2, 10^3 and 10^4 cells per cavity. Culture medium was removed by suction after cultivating for 24 h, and the cells were washed with the incubation medium, Ultraculture (UC, serum-free special medium, Cambrex Bioproducts). Next, the cells were incubated for 24 h in Ultraculture with solutions of the compounds to be tested at various concentrations freshly prepared in DMSO (VWR) and diluted with incubation medium to a final concentration of 1% DMSO in the wells. Control wells contained 1% DMSO. After 24 h of exposure, the test substances were removed by suction, and the cells were washed with fresh medium. Cultivation was performed at 37 °C and 7.5% CO_2 in air for 12 d in culture medium. The medium was removed by suction, and the colonies were dried, stained with Löffler's methylene blue (VWR) and counted macroscopically. The relative colony-forming rate was determined according to the following formula: relative colony-forming rate [%] = [(number of colonies grown with test compound) × 100]/(number of colonies grown in the control).

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