DOI: 10.1002/ejoc.200700015

Total Synthesis of *rac*-γ-Indomycinone by Baker–Venkataraman Rearrangement

Karsten Krohn,*[a] Hoan Trang Tran-Thien,[a] Jürgen Vitz,[a] and Anne Vidal[a]

Dedicated to Professor Burchard Franck on the occasion of his 80th birthday

Keywords: Total synthesis / Anthrapyranone antibiotics / γ-Indomycinone / Baker–Venkataraman rearrangement / Radical bromination

The total synthesis of racemic γ-indomycinone (*rac*-**3**) was achieved by Baker–Venkataraman rearrangement of ester **11** to the diketone **12**, acid-catalyzed cyclization to the anthrapyranone **13**, followed by methyl ether cleavage and acetylation to **16**, selective bromination of the branched side chain with simultaneous S_N1-type hydroxy substitution to **23** and transesterification to *rac*-**3**. The corresponding γ-indomycinone 11-methyl ether (*rac*-**20**) was prepared in a similar reaction sequence.

Introduction

γ-Indomycinone[1] is a member of the large family of anthrapyran antibiotics which mostly occur as the C-glycosides such as the pluramycines, hedamycines, riboflavines, altromycines and indomycines.[2,3] These antibiotics found renewed interest in structural biology[4] due to their selective binding to DNA and their specific alkylation of guanine.[5,6] In addition to the C-glycosides, a number of aglycones with the anthra[*b*]pyran skeleton are also found in nature. Some of these have a C-6 side chain at C-2 such as β-indomycinone (**1**)[7] and δ-indomycinone (**2**)[7,8] or a C-4 side chain, exemplified by γ-indomycinone (**3**),[1] kidamycinone (**4**),[9] the antihepatitic antibiotic AH-1763 IIa (**5**),[10] and the neuroprotective espicufolin (**6**)[11] (Figure 1). The remarkable biological properties of some derivatives have aroused great interest, which recently resulted in several syntheses including those of premithramycinone,[12] espicufolin,[13,14] altromycinone and kidamycinone,[15] and AH-1763 IIa.[16] The recent publication of the synthesis of *ent*-γ-indomycinone by Tietze et al.[17] prompted us to disclose our alternative synthesis of *rac*-**3**. In the syntheses published to date, the construction of the appropriately substituted skeleton and the attachment of the C-2 side chain have found different solutions. Diels–Alder reactions[13,14,16,17] or biomimetic-type dianion condensations[12,15] were mainly used for the construction of the anthra[*b*]pyran skeleton. Carbanion methodology, not possible at the anthraquinone level, was often employed on naphthalene derivatives for

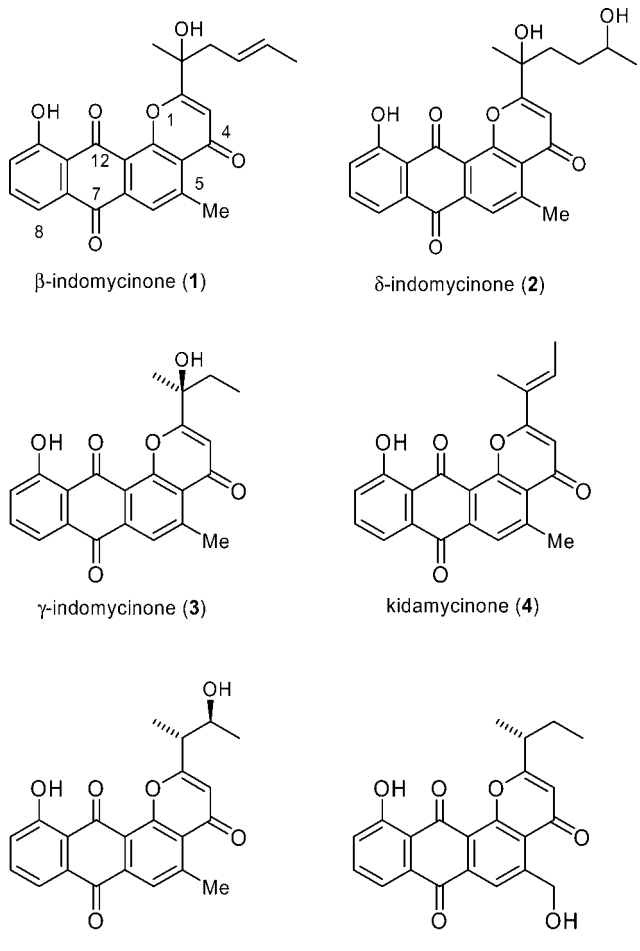


Figure 1. Representative anthrapyranone antibiotics with C-6 or C-4 side chains.

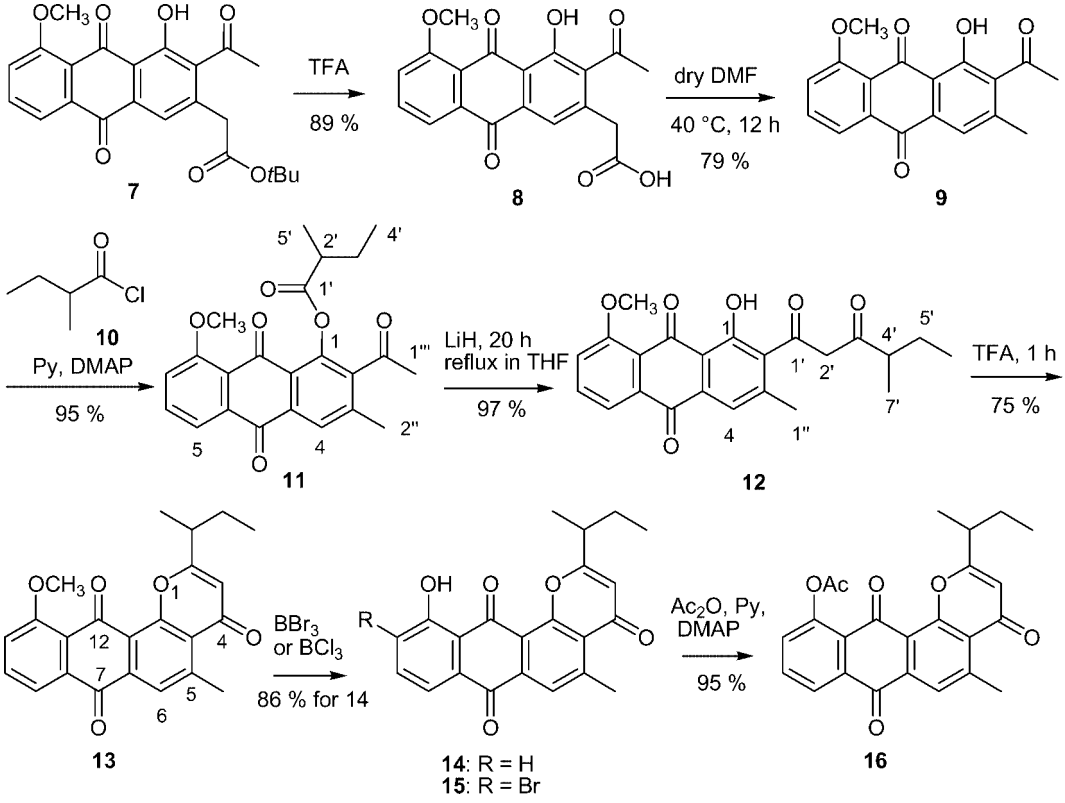
[a] Department of Chemistry, University of Paderborn, Warburger Straße 100, 33098 Paderborn, Germany
Fax: +49-5251603245
E-mail: k.krohn@uni-paderborn.de

the attachment of the side chains.[13–17] Alternatively, in our approach, we used an acyl transfer of the Baker–Venkataraman-type for chain elongation to avoid the reduction and/or oxidation steps connected with the organometallic reactions on the anthraquinone skeleton.[12,18]

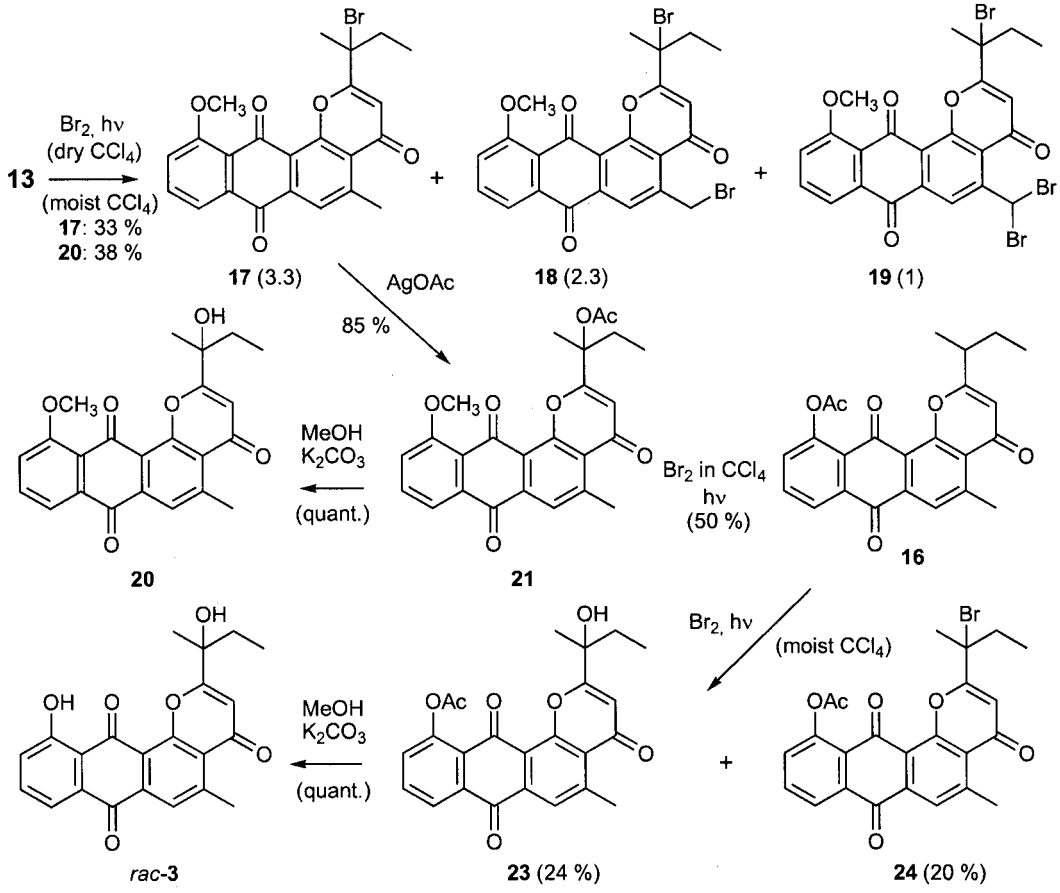
Results and Discussion

The synthesis of *rac*-γ-indomycinone started from the known 2-acetyl-1-hydroxy derivative **7**, prepared in a biomimetic-type dianion reaction during the synthesis of aklanonic acid.[19] The first task was the decarboxylation of the ester group to obtain the methyl group at C-5 as present in γ-indomycinone (**3**). To this end, the *tert*-butyl ester **7** was dissolved in trifluoroacetic acid to afford the acid **8** in 89% yield (Scheme 1). As communicated earlier,[18] the decarboxylation of the acid **8** was particularly rapid in rigorously dried DMF solutions, and the decarboxylated anthraquinone **9** was isolated in 79% yield after stirring for 12 h at 40 °C. The poor nucleophilicity of the strongly chelated phenolic hydroxy group at C-1 in **9** in the esterification with the racemic α-branched acyl chloride **10**[20] was overcome by addition of 4-(dimethylamino)pyridine (DMAP)[21] to afford the ester **11** in 95% yield. The key step was the subsequent Baker–Venkataraman rearrangement induced by heating of the ester **11** under reflux with lithium hydride to afford the anthraquinone **12** with a branched β-diketo side chain in 97% yield. The NMR spectra clearly showed that the β-diketone **12** existed in a tautomeric equilibrium with the enol form in $CDCl_3$ solution. The next task was the cyclization of the open-chain β-diketone **12** to the anthra[*b*]pyran skeleton. Simple solution in trifluoroacetic acid induced this transformation and the 2′-deoxy-γ-indomycinone methyl ether **13** was isolated in 75% yield. At this point, we wanted to test the cleavage of the methyl ether at C-11. Interestingly, using boron tribromide, the bromination product **15** (56%) was isolated in addition to the expected phenol **14** (34%). This side reaction has to be kept in mind generally in the employment of boron tribromide in phenol methyl ether cleavage. Not unexpectedly, the methyl ether cleavage using boron trichloride went without formation of any side products and the phenol **14** was isolated in 86%. Acetylation of the phenol **14** afforded the acetate **16** in 95% yield, providing another molecule in addition to **13** for subsequent bromination experiments (see below).

A key feature of our synthesis was the exploitation of selective brominations of the side chains of **13** to introduce the missing hydroxy groups. We expected that the tertiary position of the branched side chain at C-2′ would be attacked more rapidly than the C-5 methyl group. In fact, this assumption turned out to be true, in agreement with theory.[22] We tried two different conditions for the bromination reactions. In the first experiment, rigorously dried tetrachloromethane and a sixfold excess of bromine was used in the light induced bromination. After consumption of the starting material, an approximate 3.3:2.3:1 ratio (45, 32, and 13% yield, respectively) of the monobromide **17**, the dibromide **18**, and the tribromide **19** was isolated (Scheme 2). In the second series of experiments, moist tetrachloromethane was used as a solvent, only a twofold excess



Scheme 1. Synthesis of the basic anthrapyranone skeletons **13**–**16** by Baker–Venkataraman rearrangement of **12**.



Scheme 2. Synthesis of *rac*-**20** and the natural product *rac*-**3** by transesterification in basic methanol of **21** and **23**, respectively.

of bromine was used, and the irradiation time was limited to ca. 90% of starting material conversion. Under these conditions, in addition to the expected monobromination product **17**, the γ-indomycinone methyl ether (**20**) was simultaneously formed (38%). A similar in situ bromine-hydroxy group exchange was observed in the dealkyl mumbaistatin synthesis.[23] In fact, the tertiary bromide proved to be easily exchanged by SN_1-type substitution in moist solvents. For instance, the formation of the corresponding hydroxy compounds could be observed by TLC analysis of the $CDCl_3$ solution from NMR measurement. An alternative exchange of the bromine atom in the monobromide **17** was realized by the two step procedure via the acetate **21**, formed by treating bromide **17** with silver acetate in DMF (85%), followed by transesterification with basic methanol to yield γ-indomycinone methyl ether (**15**) quanitatively. It is worth mentioning that the dibromide **18** may serve to prepare a 1′-hydroxy analogue of the neuroprotective espicufolin (**6**).

Having established a route to the *rac*-γ-indomycinone methyl ether (**20**), the final task was the methyl ether cleavage in **20** to yield the natural product *rac*-**3**. However, elimination of the hydroxy group in **20** might be possible using either boron tribromide or boron trichloride for this reaction. We therefore decided to use the acetate **16**, produced by cleavage of the methyl ether and acetylation at an earlier stage (Scheme 1). The bromination reaction of **16** in moist tetrachloromethane was run with a reduced excess of bromine (2 equiv.) and incomplete conversion of the starting material (TLC monitoring) to yield the monobromide **24** (20%), the alcohol **23** (24%) and starting material **16** at 50% conversion. As described for **20**, the transesterification in basic methanol afforded the racemic γ-indomycinone (*rac*-**3**) quantitatively. The product was identical except for chiroptical properties with an authentic sample of the natural product.[24]

Experimental Section

General: For general methods and instrumentation see ref.[25]

2-(3-Acetyl-4-hydroxy-5-methoxy-9,10-dioxo-9,10-dihydroanthracen-2-yl)acetic Acid (8): Trifluoroacetic acid (3 mL) was added to a solution of the *tert*-butyl ester **7**[19] (520 mg, 1.27 mmol) in dry CH_2Cl_2 (30 mL), followed by stirring under reflux for 1 h. Dichloromethane (15 mL) was then added and the solvent was removed under reduced pressure. The procedure was repeated twice to remove traces of trifluoroacetic acid. The precipitate was purified by recrystallization from ethanol to afford the acid **8** as light yellow crystals (400 mg 89%, m.p. 237 °C). ^1H NMR (200 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, CH_3), 3.71 (s, 2 H, CH_2), 3.97 (s, 3 H, OCH_3), 7.34 (dd, $J_{6',7'}$ = 8.6 Hz, $J_{6',8'}$ = 1.0 Hz, 1 H, 6′-H), 7.54 (s, 1 H, 1′-H), 7.70 (dd, $J_{6',7'}$ = 8.6 Hz, $J_{7',8'}$ = 7.8 Hz, 1 H, 7′-H),

7.84 (dd, $J_{7',8'}$ = 7.8 Hz, $J_{6',8'}$ = 1.0 Hz, 1 H, 8′-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 35.9 (q, CH_3), 43.1 (t, CH_2), 60.9 (q, OCH_3), 120.7 (s, C-4a′), 123.1 (d, C-6′), 123.1 (s, C-3′), 123.2 (s, C-10a′), 124.6 (d, C-1′), 124.7 (s, C-8a′), 125.5 (d, C-8′), 137.0 (s, C-9a′), 139.6 (s, C-2′), 140.8 (d, C-7′), 144.9 (s, C-5′), 165.4 (s, C-4′), 176.3 (s, C-1), 186.6 (s, C-9′, C-10′), 208.6 (s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3446, 3165, 1747, 1734, 1689, 1670, 1626, 1595, 1583, 1566, 1468, 1444, 1392, 1363, 1352, 1284, 1275, 1236, 1213, 1182, 1038, 962, 835, 752, 611 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 415 (4.34) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 354 (4) [M$^+$], 310 (70) [M$^+$ – CO_2], 295 (100), 252 (10), 224 (4), 196 (3), 168 (6), 139 (6), 44 (7). HRMS (EI, 70 eV, 200 °C): $C_{19}H_{14}O_7$ calcd. for 354.07395; found 353.97786. $C_{19}H_{14}O_7$ (354.31): calcd. C 64.41, H 3.98; found C 64.29, H 3.74.

2-Acetyl-1-hydroxy-8-methoxy-3-methylanthracene-9,10-dione (9): The acid **8** (340 mg, 0.96 mmol) was dissolved in dry DMF (5 mL, addition of 1 g of 4-Å molecular sieves) and the reaction mixture was stirred overnight under protective gas at 40 °C. Ethyl acetate (40 mL) was added and the organic phase was washed successively with HCl (2 mol/L, 2 × 30 mL), saturated $NaHCO_3$ solution (2 × 20 mL), water (20 mL), and brine (20 mL). The solution was dried with $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was purified by recrystallization from ethanol to afford the methyl anthraquinone **9** as orange crystals (226 mg, 76%, m.p. 238 °C). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, $COCH_3$), 2.65 (s, 3 H, CH_3), 4.11 (s, 3 H, OCH_3), 7.41 (dd, $J_{6,7}$ = 8.3 Hz, $J_{5,7}$ = 1.0 Hz, 1 H, 7-H), 7.64 (s, 1 H, 4-H), 7.79 (dd, $J_{5,6}$ = 7.8 Hz, $J_{6,7}$ = 8.3 Hz, 1 H, 6-H), 8.00 (dd, $J_{5,6}$ = 7.8 Hz, $J_{5,7}$ = 1.0 Hz, 1 H, 5-H), 13.30 (s, 1 H, OH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.5 (q, CH_3), 32.3 (q, $COCH_3$), 57.1 (q, OCH_3), 115.6 (s, C-9a), 118.8 (d, C-4), 120.7 (d, C-7), 121.2 (d, C-5), 132.6 (s, C-8a), 136.0 (s, C-2), 136.4 (d, C-6), 136.7 (s, C-10a, C-4a), 144.2 (s, C-3), 160.0 (s, C-8), 161.4 (s, C-1), 182.8 (s, C-10), 188.9 (s, C-9), 203.9 (s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3437, 2981, 2927, 2848, 1685, 1631, 1585, 1487, 1468, 1446, 1352, 1286, 1271, 1230, 1184, 1068, 1036, 1012, 962, 849, 750 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 415 (3.59). MS (EI, 70 eV): *m*/*z* (%) = 310 (25) [M$^+$], 295 (45), 279 (4), 252 (5), 167 (4), 149 (10), 98 (100), 84 (10), 57 (14), 43 (10). HRMS (EI, 70 eV): $C_{18}H_{14}O_5$ calcd. for 310.08412; found 310.08414. $C_{18}H_{14}O_5$ (310.30): calcd. C 69.67, H 4.55; found C 69.32, H 4.05.

2-Methylbutanoyl Chloride (10):[20] 2-Methylbutanoic acid (20.0 g, 196 mmol) was treated with thionyl chloride (26.2 g, 220 mmol, 16.0 mL) and a few drops of DMF. The reaction started spontaneously and the mixture was stirred for 2 h at 40 °C. The crude product was distilled to afford the acid chloride as a colorless oil (17.4 g, 85%, b.p. 32 °C/1 mbar (ref.[20] b.p. 118 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (t, $J_{3,4}$ = 7.4 Hz, 3 H, 4-H), 1.31 (d, $J_{2,1'}$ = 6.9 Hz, 3 H, 1′-H), 1.63 (m, 1 H, 3α-H), 1.86 (m, 1 H, 3β-H), 2.84 (m, 1 H, 2-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.5 (q, C-4), 16.9 (q, C-1′), 26.9 (t, C-3), 53.3 (d, C-2), 178.1 (s, CO) ppm.

2-Acetyl-8-methoxy-3-methyl-9,10-dioxo-9,10-dihydroanthracen-1-yl 2-Methylbutanoate (11): A solution of the phenol **9** (220 mg, 0.71 mmol) in dry dichloromethane (5 mL) was treated at 0 °C successively with pyridine (0.1 mL, 1.12 mmol), acid chloride **10** (0.1 mL, 1.12 mmol), and DMAP (3 mol-%). The mixture was stirred for 6 h at 20 °C (TLC monitoring). Water was then added (20 mL) and the aqueous phase was extracted with dichloromethane (2 × 50 mL). The combined organic phases were washed with saturated $NaHCO_3$ solution (20 mL), dilute HCl (2 mol/L, 20 mL), water (20 L), and brine (30 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by crystallization (CH_2Cl_2) to give the ester **11** as yellow crystals (266 mg, 95%, m.p. 158 °C). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.10 (t, $J_{3',4'}$ = 7.5 Hz, 3 H, 4′-H), 1.40 (d, $J_{2',5'}$ = 7.0 Hz, 3 H, 5′-H), 1.68 (m, 1 H, 3_α′-H), 1.97 (m, 1 H, 3_β′-H), 2.43 (s, 3 H, $COCH_3$), 2.54 (s, 3 H, CH_3), 2.87 (m, 1 H, 2′-H), 4.00 (s, 3 H, OCH_3), 7.33 (dd, $J_{6,7}$ = 8.4 Hz, $J_{5,7}$ = 1.0 Hz, 1 H, 7-H), 7.70 (dd, $J_{5,6}$ = 7.7 Hz, $J_{6,7}$ = 8.4 Hz, 1 H, 6-H), 7.89 (dd, $J_{5,6}$ = 7.7 Hz, $J_{5,7}$ = 1.0 Hz, 1 H, 5-H), 8.03 (d, $J_{4,1'''}$ = 0.5 Hz, 1 H, 4-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.8 (q, C-4′), 16.3 (q, C-5′), 19.7 (q, C-1′′′), 26.5 (t, C-3′), 32.3 (q, C-2′′), 41.3 (d, C-2′), 57.1 (q, OCH_3), 119.0 (d, C-7), 119.8 (d, C-5), 123.3 (s, C-9a), 125.6 (s, C-8a), 126.8 (d, C-4), 134.1 (s, C-10a), 135.1 (d, C-6), 135.2 (s, C-4a), 140.6 (s, C-2), 142.5 (s, C-3), 146.2 (s, C-1), 160.4 (s, C-8), 174.8 (s, C-1′), 181.5 (s, C-9), 183.2 (s, C-10), 202.6 (s, C-1′′) ppm. IR (KBr): $\tilde{\nu}$ = 3431, 2972, 2939, 2925, 1763, 1707, 1672, 1657, 1589, 1466, 1446, 1360, 1331, 1313, 1279, 1265, 1227, 1186, 1119, 1111, 1092, 1076, 1034, 1014, 993, 943, 791, 752, 742 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 382 (3.74). MS (EI, 70 eV, 200 °C): *m*/*z* (%) = 394 (12) [M$^+$], 310 (100), 295 (64), 252 (5), 167 (10), 149 (22), 113 (5), 85 (20), 57 (65), 43 (8). HRMS (EI, 70 eV): $C_{23}H_{22}O_6$ calcd. for 394.14164: found 394.14191. $C_{23}H_{22}O_6$ (394.42): calcd. C 70.04, H 5.62; found C 69.57, H 5.30.

1-Hydroxy-8-methoxy-3-methyl-2-(4-methyl-3-oxohexanoyl)anthracene-9,10-dione (12): A solution of the phenol ester **11** (341 mg, 0.94 mmol) in THF (20 mL) was treated at 0 °C with LiH (10 mmol, 80 mg) and the suspension was refluxed for 20 h (TLC monitoring). The mixture was carefully neutralized at 0 °C by addition of HCl (2 mol/L, 2 mL), reduced to one fifth of its volume under reduced pressure, and diluted with dichloromethane (100 mL). The organic phase was washed successively with HCl (2 mol/L, 2 × 40 mL) and water (40 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure to afford the diketone **12** (215 mg, mmol, 97%, m.p. 155 °C) as yellow crystals after crystallization from dichloromethane/ethanol (1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ (enol) = 0.98 (t, $J_{5',6'}$ = 7.5 Hz, 3 H, 6′-H), 1.23 (d, $J_{4',7'}$ = 6.8 Hz, 3 H, 7′-H), 1.56 (m, 1 H, 5_α′-H), 1.75 (m, 1 H, 5_β′-H), 2.39 (m, 1 H, 4′-H), 2.47 (s, 3 H, CH_3), 4.09 (s, 3 H, OCH_3), 5.84 (s, 1 H, 2′-H), 7.40 (d, $J_{6,7}$ = 8.3 Hz, 1 H, 7-H), 7.64 (s, 1 H, 4-H), 7.78 (dd, $J_{5,6}$ = 7.7 Hz, $J_{6,7}$ = 8.3 Hz, 1 H, 6-H), 7.98 (dd, $J_{5,6}$ = 7.7 Hz, $J_{5,7}$ = 0.8 Hz, 1 H, 5-H), 13.34 (s, 1 H, OH), 15.63 (br. s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ (enol) = 11.7 (q, C-6′), 16.9 (q, C-7′), 20.5 (q, C-1′′), 27.1 (t, C-5′, CH_2), 44.0 (d, C-4′), 56.7 (q, OCH_3), 101.9 (d, C-2′), 115.3 (s, C-9a), 118.4 (d, C-7), 120.2 (d, C-5), 120.5 (d, C-4), 120.8 (s, C-8a), 132.3 (s, C-2), 132.5 (s, C-4a), 135.6 (s, C-10a), 135.8 (d, C-6), 145.3 (s, C-3), 160.0 (s, C-1), 161.0 (s, C-8), 182.5 (s, C-10), 185.8 (s, C-1′), 188.4 (s, C-9), 198.5 (s, C-3′) ppm. IR (KBr): $\tilde{\nu}$ = 3446, 2966, 2929, 2875, 1674, 1653, 1626, 1585, 1558, 1491, 1473, 1466, 1456, 1446, 1437, 1352, 1277, 1240, 1186, 1066, 1039, 976, 858, 796, 752 cm^{-1}. UV (MeOH): λ_{max} (lg ε) = 418 (5.08). MS (EI, 70 eV): *m*/*z* (%) = 394 (22) [M$^+$], 379 (8), 337 (8), 310 (50), 295 (100), 252 (10), 57 (12). HRMS (EI, 70 eV): $C_{23}H_{22}O_6$ calcd. for 394.14164; found 394.14314. $C_{23}H_{22}O_6$ (394.42): calcd. C 70.04, H 5.62; found C 69.74, H 5.74.

2-*sec*-Butyl-11-methoxy-5-methyl-4*H*-naphtho[2,3-*h*]chromene-4,7,12-trione (13): Trifluoroacetic acid (5 mL) was added to the diketone **12** (45 mg, 0.114 mmol) and the solution was stirred at room temperature for 1 h. Dichloromethane (15 mL) was then added and the solvent was removed under reduced pressure. The procedure was repeated twice to remove the trifluoroacetic acid. The crude product was dissolved in dichloromethane (50 mL) and successively washed with saturated $NaHCO_3$ solution (20 mL), dilute HCl (2 mol/L, 20 mL), water (20 L), and brine (30 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure.

Crystallization (toluene/ethanol) afforded the product as yellow crystals (32 mg, 75%, m.p. 219 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (t, $J_{2',3'}$ = 7.6 Hz, 3 H, 3′-H), 1.43 (d, $J_{1',4'}$ = 7.1 Hz, 3 H, 4′-H), 1.78 (m, 1 H, 2_α′-H), 1.96 (m, 1 H, 2_β′-H), 2.77 (m, 1 H, 1′-H), 2.98 (s, 3 H, CH_3), 4.06 (s, 3 H, OCH_3), 6.23 (s, 1 H, 3-H), 7.37 (dd, $J_{9,10}$ = 8.3 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 10-H), 7.70 (dd, $J_{8,9}$ = 7.7 Hz, $J_{9,10}$ = 8.3 Hz, 1 H, 9-H), 7.88 (dd, $J_{8,9}$ = 7.7 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 8-H), 7.92 (s, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.6 (q, C-3′), 17.9 (q, C-4′), 23.9 (q, CH_3), 27.3 (t, C-2′), 40.2 (d, C-1′), 56.8 (q, OCH_3), 110.8 (d, C-3), 118.5 (d, C-10), 119.3 (d, C-8), 122.6 (s, C-12a), 123.6 (s, C-11a), 124.4 (d, C-6), 126.5 (s, C-4a), 134.4 (d, C-9), 134.5 (s, C-7a), 135.0 (s, C-6a), 147.2 (s, C-5), 156.0 (s, C-12b), 159.7 (s, C-11), 173.2 (s, C-2), 179.6 (s, C-12), 180.5 (s, C-4), 183.2 (s, C-7) ppm. IR (KBr): $\tilde{\nu}$ = 3431, 2968, 2925, 2877, 1676, 1653, 1647, 1628, 1587, 1466, 1446, 1387, 1281, 1227, 1076, 1039, 947, 752 cm^{-1}. UV (MeOH): λ_{max} (lgε) = 386 (4.10). MS (EI, 70 eV): *m*/*z* (%) = 376 (100) [M$^+$], 359 (32), 347 (8), 330 (15), 310 (48), 295 (78), 279 (15), 266 (20), 252 (12), 205 (9), 167 (22), 149 (43), 139 (11), 97 (13), 85 (16), 57 (62), 43 (28). HRMS (EI, 70 eV): $C_{23}H_{20}O_5$ calcd. for 376.13107; found 376.13116. $C_{23}H_{20}O_5$ (376.40): calcd. C 73.39, H 5.36; found C 72.83, H 4.84.

2-*sec*-Butyl-11-hydroxy-5-methyl-4*H*-naphtho[2,3-*h*]chromen-4,7,12-trione (14): A solution of boron trichloride in dichloromethane (1.7 mL, 1 mol/L) was added dropwise under argon at –70 °C to a solution of the methoxy compound **13** (24 mg) in dry dichloromethane (5 mL). The temperature was allowed to rise to –20 °C during 1 h (TLC monitoring). The mixture was diluted with dichloromethane, the organic phase washed with saturated sodium hydrogen carbonate, water, dried with anhydrous $MgSO_4$, and the solvent was removed under reduced pressure to afford phenol **14** (20 mg, 86%, m.p. 186–188 °C). ^{1}H NMR (500 MHz, $CDCl_3$.): δ = 0.98 (t, $J_{2',3'}$ = 7.6 Hz, 3 H, 3′-H), 1.43 (d, $J_{1',4'}$ = 7.1 Hz, 3 H, 4′-H), 1.78 (m, 1 H, 2α′-H), 1.96 (m, 1 H, 2β′-H), 2.74 (m, 1 H, 1′-H), 3.01 (s, 3 H, CH_3), 6.24 (s, 1 H, 3-H), 7.35 (dd, $J_{9,10}$ = 8.3 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 10-H), 7.70 (dd, $J_{8,9}$ = 7.7 Hz, $J_{9,10}$ = 8.3 Hz, 1 H, 9-H), 7.82 (dd, $J_{8,9}$ = 7.7 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 8-H), 8.04 (s, 1 H, 6-H), 13.64 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.7 (q, C-3′), 17.8 (q, C-4′), 24.2 (q, C-1′′), 27.3 (t, C-2′), 40.5 (d, C-1′), 111.3 (d, C-3), 116.8 (s, C-11a), 119.2 (s, C-12a), 119.5 (d, C-8), 125.3 (d, C-10), 125.5 (d, C-6), 126.6 (s, C-4a), 132.3 (s, C-7a) 136.2 (d, C-9), 139.5 (s, C-6a), 149.8 (s, C-5), 156.8 (s, C-1a), 162.6 (s, C-11), 172.9 (s, C-2), 179.3 (s, C-4), 182.0 (s, C-7), 187.2 (s, C-12) ppm. IR (KBr): $\tilde{\nu}$ = 3847, 3431, 3064, 2966, 2924, 2352, 1650, 1647, 1580, 1460, 1373, 1352, 1319, 1265, 1221, 1074, 1010, 906, 829 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 362 (18) [M$^+$], 307 (2), 279 (20), 243 (19), 198 (3), 167 (48),149 (100), 85 (38), 57 (78), 43 (50), 28 (38). HRMS (EI, 70 eV): calcd. for $C_{22}H_{18}O_5$ 362.1154; found 362.1144.

10-Bromo-2-*sec*-butyl-11-hydroxy-5-methyl-4*H*-naphtho[2,3-*h*]chromene-4,7,12-trione (15): 60 mg of **13** (0.16 mmol) was treated as described for **14** but with boron tribromide instead of boron trichloride to yield the phenol **14** (23 mg, 40%) and the bromophenol **15** (39 mg, 56%, m.p. 210 °C). ^{1}H NMR (500 MHz, $CDCl_3$.): δ = 0.98 (t, $J_{2',3'}$ = 7.6 Hz, 3 H, 3′-H), 1.43 (d, $J_{1',4'}$ = 7.1 Hz, 3 H, 4′-H), 1.77 (m, 1 H, 2α′-H), 1.96 (m, 1 H, 2β′-H), 2.73 (m, 1 H, 1′-H), 3.01 (s, 3 H, CH_3), 6.25 (s, 1 H, 3-H), 7.67 (d, $J_{8,9}$ = 8 Hz, 1 H, 9-H), 7.94 (d, $J_{8,9}$ = 8 Hz, 1 H, 8-H), 8.02 (s, 1 H, 6-H), 13.64 (s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.7 (q, C-3′), 17.8 (q, C-4′), 24.2 (q, C-1′′), 27.3 (t, C-2′), 40.4 (d, C-1′), 111.4 (d, C-3), 117.1 (s, C-11a), 119.4 (s, C-12a), 119.5 (d, C-8), 120.3 (d, C-10), 125.5 (d, C-6), 126.6 (s, C-4a),131.3 (s, C-7a) 135.7 (d, C-9), 139.5 (s, C-6a), 150 (s, C-5), 156.8 (s, C-1a), 159.0 (s, C-11), 172.9 (s, C-2), 179.1 (s, C-4), 181.4 (s, C-7), 187.0 (s, C-12) ppm. IR (KBr): $\tilde{\nu}$ = 3853, 3423, 3075, 2972, 2924, 2874, 2363, 2331, 1661, 1580, 1460, 1416, 1378, 1335, 1313, 1264, 1210, 1106, 1068, 932, 840, 742 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 440 (100) [M$^+$], 362 (72), 281 (30), 243 (12), 196 (8), 167 (12), 139 (18), 85 (10), 57 (26), 43 (50), 28 (30). HRMS (EI, 70 eV): calcd. for $C_{22}H_{17}BrO_5$ 440.0259; found 440.0259.

11-Acetoxy-2-*sec*-butyl-5-methyl-4*H*-naphtho[2,3-*h*]chromene-4,7,12-trione (16): The phenol **14** (15.0 mg, 0.04 mmol) was treated at room temperature under argon for 2 h with acetic anhydride (0.3 mL), pyridine (0.3 mL), and a catalytic amount of DMAP (5 mg). After addition of water, the mixture was extracted with dichloromethane, the combined organic phases were washed with saturated sodium hydrogen carbonate, dilute hydrochloric acid, and brine, and dried with anhydrous magnesium sulfate. The solvents were removed under reduced pressure and the crude product purified by preparative TLC (dichloromethane) to afford the acetate **16** as an orange solid (17.6 mg, 95%, m.p. 191 °C). ^{1}H NMR (500 MHz, $CDCl_3$.): δ = 0.98 (t, $J_{2',3'}$ = 7.6 Hz, 3 H, 3′-H), 1.41 (d, $J_{1',4'}$ = 7.1 Hz, 3 H, 4′-H), 1.76 (m, 1 H, 2α′-H), 1.97 (m, 1 H, 2β′-H), 2.67 (s, 3 H, CH_3), 2.71 (m, 1 H, 1′-H), 3.01 (s, 3 H, CH_3), 6.24 (s, 1 H, 3-H), 7.45 (dd, $J_{9,10}$ = 8.3 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 10-H), 7.76 (dd, $J_{8,9}$ = 7.7 Hz, $J_{9,10}$ = 8.3 Hz, 1 H, 9-H), 7.98 (dd, $J_{8,9}$ = 7.7 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 8-H), 8.21 (s, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.7 (q, C-3′), 17.6 (q, C-4′), 20.7 (q, CH_3), 23.9 (q, CH_3), 27.3 (t, C-2′), 40.5 (d, C-1′), 111.2 (d, C-3), 121.6 (s, C-12a), 124.64 (d, C-6), 125.2 (s, C-11a), 126.5 (s, C-4a), 130.2 (d, C-8), 134.0 (s, C-7a), 134 (d, C-9) 135.0 (s, C-6a), 148.32 (s, C-5), 156.8 (s, C-1a), 161.2 (s, C-11), 169.1 (q, CH_3), 169.5 (q, CH_3), 172.6 (s, C-2), 179.4 (s, C-4), 182.3 (s, C-7), 205.3 (s, C-12) ppm. IR (KBr): $\tilde{\nu}$ = 3423, 3059, 2966, 2924, 2352, 1764, 1647, 1585, 1466, 1384, 1308, 1280, 1215, 1025, 911, 753 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 404 (70) [M$^+$], 362 (100), 334 (19), 281 (50), 243 (12), 202 (16), 168 (14), 149 (130), 85 (30), 58 (53), 43 (60), 28 (16). HRMS (EI, 70 eV): calcd. for $C_{24}H_{20}O_5$ 404.1260; found 404.1255.

Bromination of Anthrapyranone 13: A solution of the anthrapyranone **13** (15 mg, 0.040 mmol) in moist CCl_4 (10 mL) was treated with a solution of Br_2 in CCl_4 (0.08 mmol, 0.08 mmol/mL, 1 mL). The solution was irradiated under nitrogen (normal 100-W daylight lamp) until the starting material was almost consumed (ca. 95%, TLC monitoring, 1–2 h). The solvent was removed under reduced pressure and the crude products were separated by column chromatography on silica gel (CH_2Cl_2) to afford the bromide **17** from the less polar fraction (6 mg, 33%, m.p. 192 °C) and the alcohol **20** from the polar fraction (6 mg, 38%).

2-(1-Bromo-1-methylpropyl)-11-methoxy-5-methyl-4*H*-naphtho-[2,3-*h*]chromene-4,7,12-trione (17): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.11 (t, $J_{2',3'}$ = 7.3 Hz, 3 H, 3′-H), 2.25 (s, 3 H, 4′-H), 2.59–2.66 (m, 2 H, 2′-H), 2.98 (d, $J_{6,1''}$ = 0.7 Hz, 3 H, CH_3), 4.08 (s, 3 H, OCH_3), 6.61 (s, 1 H, 3-H), 7.45 (dd, $J_{9,10}$ = 8.3 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 10-H), 7.76 (dd, $J_{8,9}$ = 7.7 Hz, $J_{9,10}$ = 8.3 Hz, 1 H, 9-H), 7.90 (dd, $J_{8,9}$ = 7.7 Hz, $J_{8,10}$ = 1.0 Hz, 1 H, 8-H), 8.00 (d, $J_{6,1''}$ = 0.7 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.2 (q, C-3′), 23.5 (q, C-1′′), 27.8 (q, C-4′), 36.0 (t, C-4′), 56.7 (q, OCH_3), 63.1 (s, C-1′), 110.4 (d, C-3), 118.9 (d, C-8/10), 119.0 (d, C-8/10), 123.3 (s, C-12a), 123.7 (s, C-11a), 124.5 (d, C-6), 126.1 (s, C-4a), 134.5 (d, C-9), 135.4 (s, C-6a, C-7a), 146.9 (s, C-5), 155.6 (s, C-12b), 159.9 (s, C-11), 167.9 (s, C-2), 176.5 (s, C-12), 179.5 (s, C-4), 183.0 (s, C-7) ppm. IR (KBr): $\tilde{\nu}$ = 2966, 2924, 1670, 1647, 1585, 1462, 1452, 1363, 1329, 1277, 1228, 1101, 1036, 951 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 454 (4) [M$^+$], 376 (100), 359 (38), 330 (12), 295 (38), 266

(26), 152 (8), 80 (24) [Br], 57 (6). HRMS (EI, 70 eV): $C_{23}H_{19}BrO_5$ calcd. for 454.04159; found 454.04400.

2-(1-Hydroxy-1-methylpropyl)-11-methoxy-5-methyl-4*H*-naphtho-[2,3-*h*]chromene-4,7,12-trione (20): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (t, J = 7.2 Hz, 3 H, 3′-H), 1.67 (s, 3 H, 4′-H), 1.98 and 2.11 (2 dd, J = 14.4 Hz, J = 7.6 Hz, 2 H, 2′-H), 2.99 (s, 3 H, 1′′-H), 4.05 (s, 3 H, OCH_3), 6.48 (s, 1 H, 3-H), 7.37 (m, 1 H, 8-H or 10-H), 7.71 (dd, J = 8.3 Hz, J = 7.7 Hz, 1 H, 9-H), 7.90 (dd, J = 7.6 Hz, J = 1.0 Hz, 1 H, 10-H or 8-H), 7.97 (d, J = 0.9 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.1 (q, C-3′), 23.8 (q, C-1′′), 25.8 (q, C-4′), 33.8 (t, C-2′), 56.8 (q, O*C*H$_3$), 74.1 (s, C-1′), 109.4 (d, C-3), 118.7 and 119.4 (2d, C-8, C-10), 123.3 (s), 124.7 (d, C-6), 126.3 (s), 134.5 (s), 134.6 (d, C-9), 147.6 (s), 152.9 and 155.5 (2s), 159.9 (s), 171.6 (s), 179.6 and 180.7 (2s) ppm. IR (KBr): $\tilde{\nu}$ = 3379, 2925, 2854, 1738, 1720, 1682, 1651, 1587, 1464, 1446, 1379, 1333, 1306, 1273, 1230, 1188, 1097, 1038, 951 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 392 (40) [M$^+$], 376 (30), 363 (100), 344 (30), 333 (10), 319 (10), 295 (32), 266 (12), 252 (10), 152 (10), 125 (10), 97 (22), 57 (34). HRMS (EI, 70 eV): $C_{23}H_{20}O_6$ calcd. for 392.12599; found 392.12612.

Procedure B: The acetate **21** (4.3 mg, 0.01 mmol) was dissolved in dry methanol, 10 mg potassium carbonate was added, and the mixture was stirred at 21 °C until the starting material was consumed (ca. 10 h, TLC monitoring). The solution was filtered and the solvent removed under reduced pressure to afford the alcohol **20** (3.9 mg, quantitative) as a yellow solid.

5-Bromomethyl-2-(1-bromo-1-methylpropyl)-11-methoxy-1-oxabenz-[*a*]anthracene-4,7,12-trione (18): In a related bromination, the anthrapyranone **13** (75.2 mg, 0.2 mmol) was brominated in dry tetrachloromethane with an excess of 6 equiv. of bromine. The irradiation was continued until the starting material was consumed (TLC monitoring). In addition to 41 mg (45%) of monobromide **17**, the dibromide **18** (33.5 mg, 32%) and the tribromide **19** (16 mg, 13%) were isolated after chromatographic separation. M.p. 150 °C (decomposition). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (s, 3 H, 3′-H), 2.21 (s, 3 H, 4′-H), 2.57 (qd, J = 7.2 Hz, J = 1.5 Hz, 2 H, 2′-H), 4.05 (s, 3 H, OCH_3), 5.33 (dd, J = 11.3 Hz, J = 0.4 Hz, 1 H, 1′′-H), 5.35 (dd, J = 11.3 Hz, J = 0.4 Hz, 1 H, 1′′-H), 6.70 (s, 1 H, 3-H), 7.39 (dd, J = 8.2 Hz, J = 1.0 Hz, 1 H, 8-H or 10-H), 7.73 (dd, J = 8.2 Hz, J = 7.7 Hz, 1 H, 9-H), 7.90 (dd, J = 7.7 Hz, J = 1.0 Hz, 1 H, 10-H or 8-H), 8.23 (s, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.4 (q, C-3′), 28.4 (q, C-4′), 29.7 (t, C-1′′), 31.0 (t, C-2′), 56.9 (q, OCH_3), 62.6 (s, C-1′), 111.0 (d, C-3), 118.9 and 119.5 (2d, C-8, C-10), 123.4 and 124.6 (2s, C-11a, C-12a), 124.8 (s, C-4a), 125.2 (d, C-6), 134.3 and 136.1 (2s, C-6a, C-7a), 134.8 (d, C-9), 144.4 (s, C-5), 155.5 (s, C-11), 159.8 (s, C-12b), 168.7 (s, C-2), 178.8, 179.8 and 182.3 (3s, C-4, C-7, C-12) ppm. IR (KBr): $\tilde{\nu}$ = 2924, 2852, 1676, 1653, 1647, 1637, 1278 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 534 (5) [M$^+$], 454 (8), 374 (42), 362 (80), 310 (22), 281 (72), 133 (28), 79 (100), 57 (77). HRMS calcd. for $C_{23}H_{17}{}^{79}Br^{81}BrO_5$ 533.9501; found 533.9498.

2-(1-Bromo-1-methylpropyl)-5-dibromomethyl-11-methoxy-1-oxabenz[*a*]anthracene-4,7,12-trione (19): M.p. 174–176 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.2 Hz, 3 H, 3′-H), 2.21 (s, 3 H, 4′-H), 2.56 (q, J = 7.2 Hz, 2 H, 2′-H), 4.05 (s, 3 H, OCH_3), 6.71 (s, 1 H, 3-H), 7.40 (m, 1 H, 10-H), 7.74 (m, 1 H, 9-H), 7.93 (m, 1 H, 8-H), 8.78 (s, 1 H, 1′′-H), 8.97 (s, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.4 (q, C-3′), 28.4 (q, C-4′), 36.1 (t, C-2′), 36.9 (d, C-1′′), 56.9 (q, OCH_3), 62.3 (s, C-1′), 111.0 (d, C-3), 119.0 (d, C-10), 119.6 (d, C-8), 121.3 (s, C-4a), 123.3 (s, C-11a), 125.0 (s, C-6a/C-12a), 125.7 (d, C-6), 134.2 (s, C-7a), 134.9 (d, C-9), 136.6 (s, C-12a/C-6a), 147.6 (s, C-5), 154.2 (s, C-12b), 159.9 (s, C-11), 169.0 (s, C-2), 179.1 (s, C-4), 179.5 (s, C-12), 181.8 (s, C-7) ppm. IR (KBr): $\tilde{\nu}$ = 2924, 2852, 1683, 1653, 1636, 1617, 1457, 1276 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 614 (1) [M$^+$], 612 (1) [M$^+$], 548 (2), 502 (1), 453 (1), 412 (16), 368 (10), 167 (29), 82 (98), 80 (100). HRMS calcd. for $C_{23}H_{17}{}^{79}Br_2{}^{81}BrO_5$ 611.8605; found 611.8605.

1-(11-Methoxy-5-methyl-4,7,12-trioxo-1,4,7,12-tetrahydrobenz[*a*]-anthracen-2-yl)-1-methylpropyl Acetate (21): The monobromide **17** (9.1 mg, 0.02 mmol) was dissolved in dry dimethylformamide (1 mL), and silver acetate (20 mg) was added under argon at room temperature. The mixture was stirred overnight at room temperature, the silver salts were filtered off and washed with dichloromethane, and the solvents were removed under reduced pressure. Purification by preparative TLC (dichloromethane/diethyl ether, 95:5) afforded the acetate **21** (7.4 mg, 85%) as an orange solid with m.p. 225–227 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.97 (t, J = 7.6 Hz, 3 H, 3′-H), 1.89 and 2.20 (2s, each 3 H, 4′-H, $COCH_3$), 2.22 (m, 2 H, 2′-H), 2.97 (d, J = 1.0 Hz, 3 H, 1′′-H), 4.02 (s, 3 H, OCH_3), 7.35 (dd, J = 8.5 Hz, J = 1.1 Hz, 1 H, 8-H or 10-H), 7.69 (dd, J = 8.5 Hz, J = 7.7 Hz, 1 H, 9-H), 7.88 (dd, J = 7.7 Hz, J = 1.1 Hz, 1 H, 10-H or 8-H), 7.94 (m, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.9 (q, C-3′), 21.6 and 22.4 (2q, C-4′, CO*C*H$_3$), 23.8 (q, C-1′′), 56.6 (q, OCH_3), 81.2 (s, C-1′), 109.9 (d, C-3), 118.6 and 119.3 (2d, C-8, C-10), 122.8 (s), 123.7 (s), 124.6 (d, C-6), 126.4 (s), 134.4 (d, C-9), 134.5, 135.2, 147.2, 155.2, 159.2, 169.1, 169.9, 179.3, 180.3 and 183.1 (3s, C-4, C-7, C-12) ppm. IR (KBr): $\tilde{\nu}$ = 2923, 2851, 1740, 1674, 1645, 1587, 1465, 1446, 1331, 1305, 1247, 1227, 949 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 434 (100) [M$^+$], 392 (60), 363 (80), 359 (64), 295 (58), 266 (22), 57 (22). HRMS calcd. for $C_{25}H_{22}O_7$ 434.1366; found 434.1365.

11-Acetoxy-2-(1-bromo-1-methylpropyl)-5-methyl-4*H*-naphtho-[2,3-*h*]chromene-4,7,12-trione (24): A dilute solution of bromine in carbon tetrachloride (1 mL, 0.04 mmol, 0.04 mol/L) was added to a solution of the acetate (7.0 mg, 0.02 mmol) in carbon tetrachloride (3 mL). The solution was irradiated for 2 h under argon, at room temperature with a 100-W daylight lamp. The solvent was removed under reduced pressure. Purification by preparative TLC on silica gel (dichloromethane/diethyl ether, 95:5) afforded the monobromide **24** (2.0 mg, 20%) and the alcohol **23** (2.0 mg, 24%) in addition to 3.2 mg of starting material **21**. M.p. 192 °C. ^{1}H NMR (500 MHz, $CDCl_3$.): δ = 1.07 (t, J = 7.6 Hz, 3 H, 3′-H), 2.17 (s, 3 H, 4′-H), 2.48 (s, 3 H, $COCH_3$), 2.54 (q, J = 7.4 Hz, 2 H, 2′-H), 2.99 (s, 3 H, 1′′-H), 6.60 (s, 1 H, 3-H), 7.46 (dd, J = 7.8 Hz, J = 1.3 Hz, 1 H, 8-H or 10-H), 7.78 (dd, J = 7.8 Hz, 1 H, 9-H), 8.00 (m, 1 H, 6-H), 8.20 (dd, J = 7.8 Hz, J = 1.3 Hz, 1 H, 10-H or 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.4 (q, C-3′), 21.1 (q, CO*C*H$_3$), 23.8 (q, C-1′′), 28.0 (q, C-4′), 36.0 (t, C-2′), 62.4 (s, C-1′), 110.7 (d, C-3), 120.3 (s, C-12a), 121.5 (s, C-6a), 125.0 (d, C-6), 125.2, 129.6 (2d, C-8, C-10), 126.1 (s, C-4a), 126.5 (s, C-11a), 133.9 (s, C-7a), 134.4 (d, C-9), 148.3 (s, C-5), 149.8 (s, C-11), 155.6 (s, C-12b), 168.1 (s, C-2), 169.5 (s, *C*OCH$_3$), 179.6 (s, C-34), 180.0 (s, C-12), 182.1 (s, C-7) ppm. IR (KBr): $\tilde{\nu}$ = 2924, 2852, 1683, 1676, 1653, 1647, 1636, 1458, 1182, 625, 582 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 484 (10) [M$^+$], 482 (10) [M$^+$], 442 (9), 440 (9), 404 (16), 402 (16), 362 (58), 361 (46), 349 (14), 281 (100), 149 (18), 111 (22), 97 (34), 83 (38), 71 (45), 57 (78). HRMS (EI, 70 eV): calcd. for $C_{24}H_{19}{}^{79}BrO_6$ 482.0365, found 482.0370, calcd. for $C_{24}H_{19}{}^{81}BrO_6$ 484.0344; found 484.0335.

11-Acetoxy-2-(1-hydroxy-1-methylpropyl)-5-methyl-4*H*-naphtho-[2,3-*h*]chromene-4,7,12-trione (23): ^{1}H NMR (500 MHz, $CDCl_3$.): δ = 0.97 (t, J = 7.5 Hz, 3 H, 3′-H), 1.66 (s, 3 H, 4′-H), 1.94 (dq, J = 13.9 Hz, J = 7.5 Hz, 1 H, 2′-H), 2.08 (dq, J = 13.9 Hz, J = 7.5 Hz,

1 H, 2′-H), 2.48 (s, 3 H, $COCH_3$), 3.00 (s, 3 H, 1′′-H), 6.49 (s, 1 H, 3-H), 7.46 (dd, J = 7.9 Hz, J = 1.2 Hz, 1 H, 8-H or 10-H), 7.79 (d, J = 7.8 Hz, 1 H, 9-H), 8.00 (m, 1 H, 6-H), 8.22 (dd, J = 7.7 Hz, J = 1.2 Hz, 1 H, 10-H or 8-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.0 (q, C-3′), 21.2 (t, $COCH_3$), 23.9 (q, C-1′′), 25.8 (q, C-4′), 33.8 (t, C-2′), 74.1 (s, C-1′), 109.5 (d, C-3), 124.0, 125.4 (2d), 130.3 (d), 134.6 (d) ppm. IR (NaCl, film): $\tilde{\nu}$ = 2955, 2923, 2853, 1678, 1650, 1640, 1463, 1370, 1306, 1267 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 420 (72) [M^+], 349 (99), 281 (82), 236 (16), 197 (10), 167 (32), 149 (58), 83 (55), 57 (100). HRMS (EI, 70 eV): calcd. for $C_{24}H_{20}O_7$ 420.1209; found 420.1206.

γ-Indomycinon (*rac*-3): A solution of the alcohol **23** (2.0 mg) in dry methanol (1 mL) was stirred at room temperature with 5 mg of potassium carbonate. The reaction was monitored by TLC and after consumption of the starting material the suspension was filtered and the solvent removed at reduced pressure. Comparison with an authentic sample proved the identity with natural γ-indomycinon.

Acknowledgments

We thank Prof. H. Laatsch (Univ. of Göttingen) for a sample of natural γ-indomycinone, the Deutsche Forschungsgemeinschaft (DFG) (Project KR 595/10-4) for financial support and the BASF AG, Ludwigshafen, for a gift of chemicals.

[1] R. W. Schumacher, B. S. Davidson, D. A. Montenegro, V. S. Bernan, *J. Nat. Prod.* **1995**, *58*, 613–617.
[2] K. Eckardt, *Quinones and Other Carbocyclic Antitumor Antibiotics* in *Antitumor Compounds of Natural Origin: Chemistry and Biochemistry* (Ed.: A. Aszalos), vol. II, CRC Press, Boca Raton **1981**.
[3] U. Séquin, *The Antibiotics of the Pluramycin Group (4H-Anthra[1,2-b]pyran Antibiotics)* in *Prog. Chem. Org. Nat. Prod.* (Ed.: L. Zechmeister), vol. 50, Springer, Wien, New York, **1986**, pp. 58–122.
[4] M. R. Hansen, L. H. Hurley, *Acc. Chem. Res.* **1996**, *29*, 249–258.
[5] K. Nakatani, A. Okamoto, I. Saito, *Angew. Chem.* **1999**, *111*, 3581–3583.
[6] M. Hansen, L. Hurley, *J. Am. Chem. Soc.* **1995**, *117*, 2421–2429.
[7] H. Brockmann, *Angew. Chem.* **1968**, *80*, 493; *Angew. Chem. Int. Ed. Engl.* **1968**, *39*, 481.
[8] M. A. F. Biabani, H. Laatsch, E. Helmke, H. Weyland, *J. Antibiot.* **1997**, *50*, 874–877.
[9] F. M. Hauser, R. P. Rhee, *J. Org. Chem.* **1980**, *45*, 3061–3068.
[10] M. Uyeda, K. Yokomizo, A. Ito, K. Nakayama, H. Watanabe, Y. Kido, *J. Antibiot.* **1997**, *50*, 828–832.
[11] J. S. Kim, K. Shin-Ya, J. Eishima, K. Furihata, H. Seto, *J. Antibiot.* **1996**, *49*, 947–948.
[12] K. Krohn, J. Vitz, *Eur. J. Org. Chem.* **2004**, 209–219.
[13] H. Uno, K. Sakamoto, E. Honda, N. Ono, *Chem. Commun.* **1999**, 1005–1106.
[14] H. Uno, K. Sakamoto, E. Honda, K. Fukuhara, N. Ono, J. Tanaka, M. Sakanaka, *J. Chem. Soc. Perkin Trans. 1* **2001**, 229–238.
[15] Z. Fei, F. E. McDonald, *Org. Lett.* **2005**, *7*, 3617–3620.
[16] L. F. Tietze, K. M. Gericke, R. S. Singidi, *Angew. Chem.* **2006**, *118*, 7146–7150; *Angew. Chem. Int. Ed.* **2006**, *45*, 6990–6993.
[17] L. F. Tietze, R. R. Singidi, K. M. Gericke, *Org. Lett.* **2007**, *8*, 5873–5876.
[18] K. Krohn, A. Vidal, J. Vitz, B. Westermann, M. Abbas, I. Green, *Tetrahedron: Asymmetry* **2007**, *18*, 3051–3057.
[19] K. Krohn, E. Roemer, M. Top, *Liebigs Ann.* **1996**, 271–277.
[20] R. Leimu, *Ber. Dtsch. Chem. Ges.* **1937**, *70*, 1040–1053.
[21] A. V. Kalinin, V. Snieckus, *Tetrahedron Lett.* **1998**, *39*, 4999–5002.
[22] K. Furuta, Y. Miwa, K. Iwanaga, H. Yamamoto, *J. Am. Chem. Soc.* **1988**, *110*, 6254–6255.
[23] R. L. Hannan, R. B. Barber, H. Rapoport, *J. Org. Chem.* **1979**, *44*, 2153–2158.
[24] A sample of natural γ-indomycinone was kindly provided by Prof. H. Laatsch (Univ. of Göttingen). No melting points are given for the naturally occurring γ-indomycinone[1] or the synthetic product.[17] In our hands, all 1′-hydroxylated products (**3**, **20**, **23**) decomposed around 250 °C, depending upon the speed of heating.
[25] K. Krohn, D. Gehle, O. Kamp, T. van Ree, *J. Carbohydr. Chem.* **2003**, *22*, 377–383.

Received: January 8, 2007
Published Online: February 28, 2007

