Pergamon

Tetrahedron 56 (2000) 4753–4758

TETRAHEDRON

Total Synthesis of Angucyclines. Part 15:[1] A Short Synthesis of (±)-6-Deoxybrasiliquinone B

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Received 27 March 2000; accepted 15 May 2000

Abstract—The 6-deoxybrasiliquinones **2** and **14a** were prepared by a boron triacetate mediated Diels–Alder reaction of juglone (**9**) with the crude mixture of ethoxy dienes **6** and **7**. The primary non-aromatic Diels–Alder product **10** was isolated after reaction of the dienol **8** with **9**. Dimethyldioxirane oxidation of **10** afforded the epoxide **11**. © 2000 Published by Elsevier Science Ltd.

Introduction

The brasiliquinones were isolated from the actinomycete *Nocardia brasiliensis*.[2] They represent the first angucyclinones[3,4] with an ethyl side chain instead of the usual methyl group at C-3 on ring A of the benzo[*a*]anthraquinone skeleton as shown in ochromycinone (**3**) (Fig. 1). Thus, their polyketide biosynthesis probably involves a propionate starter unit, similar as postulated for the majority of the anthracycline antitumor antibiotics.[5,6] The brasiliquinones show activity against Gram-positive bacteria including *Mycobacterium* sp. and are also active against multiple drug-resistant P388/ADR tumor cells.

Recently, two syntheses of brasiliquinones B (**1**) were published which were both based on disconnection 'a' as shown in Fig. 1. In the approach of Deshpande et al.[7] a Friedel–Crafts type reaction was used, whereas Mal and Roy[8] employed the anionic Michael type anellation strategy. We now disclose a very short synthesis via disconnection 'b', using the Diels–Alder reaction of juglone (**9**) with the 1-ethoxy diene (**8**). In addition, we wanted to study the possibility to arrive at non-aromatic derivatives of **1** for further functional group manipulations.

Results and Discussion

For the construction of diene **7**, a Heck reaction of a vinyl halide and vinyl ethyl ether was envisaged. The required 5-ethyl-1,3-cyclohexanedione (**4**)[9] was prepared by condensation of acetoacetate with ethyl 2-pentenoate analogous to a procedure of Szychowski and MacLean.[10] Conversion of **4** to the vinyl bromide **5** was best achieved by treatment with oxalyl bromide according to a protocol of Mewshaw[11] (Scheme 1). Anderson and Hallberg have previously investigated the palladium-catalyzed vinylation of alkyl vinyl ethers with enol triflates and vinyl bromides.[12] In most cases, the 2-alkoxy 1,3-dienes were the major products. By contrast, with bromocyclohexanones similar to **5**, the β-addition products such as **7** predominated over

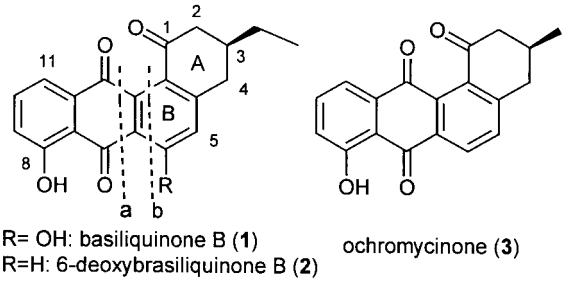
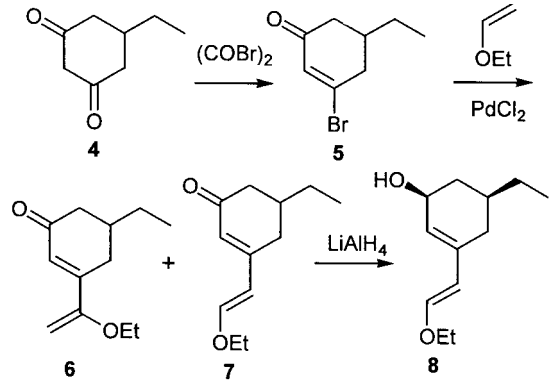


Figure 1. Structures of brasiliquinones **1** and **2** and ochromycinone (**3**).



Scheme 1. Synthesis of the cyclic dienes **6**–**8** for the Diels–Alder reaction with juglone (**9**).

Keywords: Diels–Alder reaction; boron triacetate; angucycline antibiotics; brasiliquinones; dimethyldioxirane oxidation.

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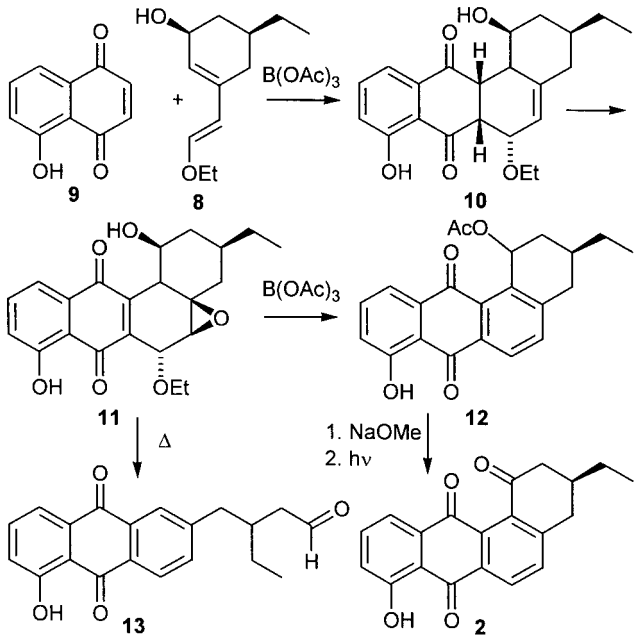
PII: S0040-4020(00)00398-7



Scheme 2. Diels–Alder reaction of juglone (**9**) with hydroxy diene (**8**) and functional group transformations of adduct **10**.

the 2-ethoxy dienes **6** (ratio **7**:**6** ca. 6:1).[12] The pure *E*-isomer of **7** could be isolated after chromatographic separation from **6** as deduced from the large coupling constant of 12.8 Hz in the ^{1}H NMR spectrum. The allylic alcohol **8**, which was also required for Diels–Alder reactions, could be prepared by LAH reduction of **7** to afford stereoselectively the 1,5-*cis* alcohol **8**.

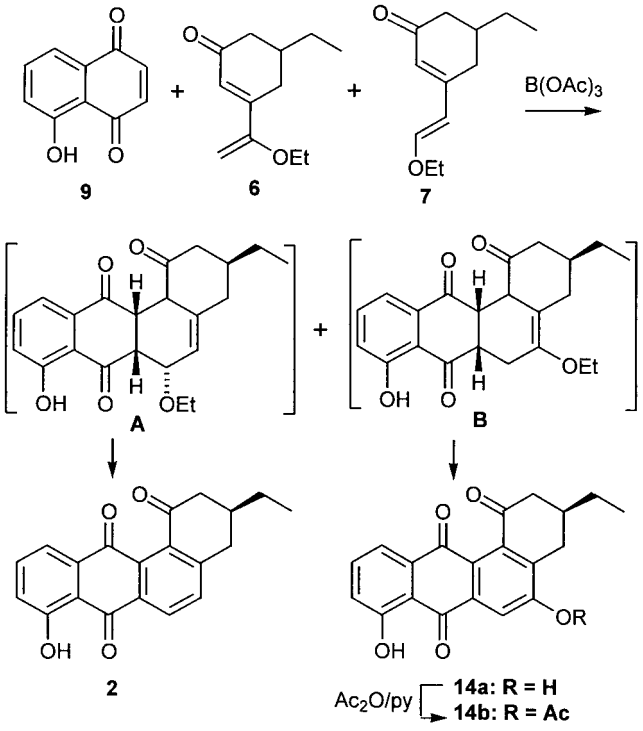
The reaction of the electron-rich diene **8** with juglone **9** was studied first. Larsen et al.[13,14] and also Sulikowski et al.[15] previously used similar hydroxy dienes. In subsequent steps, the hydroxyl group at C-1 in the products was then oxidized to a carbonyl group present in most angucyclines. The boron triacetate catalyzed reaction of **8** with juglone **9** proceeded at 0°C in a short time to afford the non-aromatic adduct **10** in 71% yield (Scheme 2). The olefin **10** was selectively converted to the all-*cis* epoxide **11** by treatment at 0°C with dimethyldioxirane. The quinoide double bond was not attacked under these mild conditions. Both derivatives **10** and **11** are thus easily accessible starting materials for non-aromatic angucyclines.[16]

In the present study, we also wanted to investigate the thermal and chemical stability of the epoxide **11**. Treatment of **11** with the mild Lewis acid boron triacetate afforded the aromatized acetate **12** in modest (23%) yield. Interestingly, in addition to elimination, the acetylation of the benzylic hydroxyl group in the presence of boron triacetate had occurred. The intermediate alcohol obtained by saponification of **12** was then converted to 6-deoxybrasiliquinone (**2**) by photoxidation with diffuse sunlight. This remarkably mild oxidation reaction was discovered in our laboratory during the synthesis of a daunomycinone/rabelomycinone hydride[17] (compare[18]) and is now frequently used as a reaction in the last step of angucycline syntheses.[8,19–21]

Another interesting reaction was discovered by heating the epoxide **11** to 150°C. A ring opening to the aldehyde **13** was observed to occur in 57% yield. At least three bonds are broken in this reaction which was also observed by Larsen et al. in a related case.[14] Tricyclic rearrangement products have also been found to occur with natural products such as aquayamycin.[22]

In a second Diels–Alder reaction, the mixture of the keto dienes **6** and **7** was treated with juglone (**9**). Both the diene and the dienophile are electron-deficient and such reactions are known to proceed very sluggishly. High pressure conditions are the normal solution to the problem due to the negative activation volume of Diels–Alder reactions. However, Guingant and Barreto found that boron triacetate also effectively catalyzes this reaction in related cases.[23] Under the boron triacetate catalyzed conditions, the primary Diels–Alder adduct **A** cannot be isolated but undergoes rapid elimination of ethanol followed by isomerization and air oxidation to the 1-keto quinone **2** (6-deoxbrasiliquinone, 50% yield, Scheme 3). In addition, a polar minor product **14a** of very low solubility resulting from reaction of juglone (**9**) with the 2-ethoxy diene **6** via intermediate **B** was isolated in 7% yield. A non-chelated phenolic group was easily established in **14a** by analysis of the mass spectrum and selective mono-acetylation to **14b** inducing the expected lowfield shift of the 6-H signal in the ^{1}H NMR spectrum.

The remaining question was the location of the chelated phenolic hydroxyl group in **14a** at C-8 or C-11. Experimental evidence in uncatalized reactions of juglone with 2-alkoxysubstituted dienes[24–27] and also theoretical frontier orbital considerations[28] suggested the formation of an 11-hydroxy angucyclinone. However, using the carbonyl



Scheme 3. Diels–Alder reaction of juglone (**9**) with the keto dienes **6** and **7** to yield the brasiliquinones **2** and **14a**.

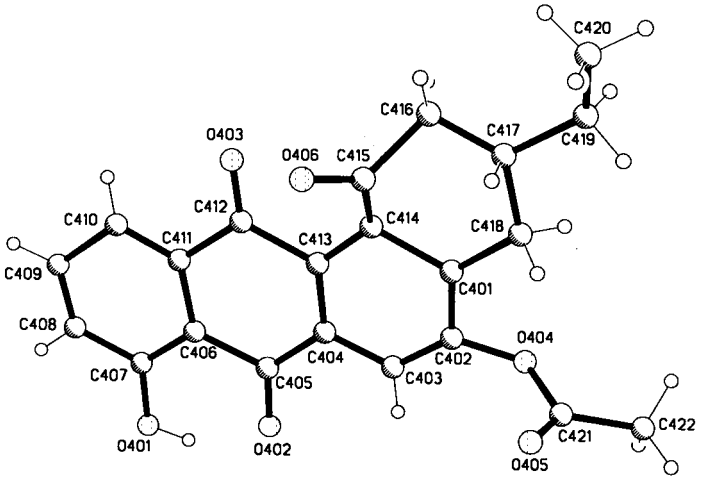


Figure 2. Crystal structure of **14b**.

substituted 2-ethoxy diene **6** in a boron triactetate-catalyzed reaction, the 5,8-dihydroxybenzonaphthacene **14a** was formed, as proven by X-ray analysis[29] of the acetate **14b** shown in Fig. 2. The phenol **14a** represents the first synthetic angucyclinone hydroxylated at C-5 and has analogy to the naturally occurring 5,6-dihydroxylated fridamycinone C.[30]

The biological activities of the 6-deoxybrasiliquinones **2** and **14a** as well as the non-aromatic products **10** and **11** are presently under investigation.

In summary, the 6-deoxybrasiliquinones **2** and **14a** are prepared in only four steps starting from cyclohexadione **4** and juglone (**9**). Aromatization of ring B can be prevented by reaction of the dienol **8** with **9**. Dimethyldioxirane is an excellent reagent for selective epoxidation of allylic ethers such as **10**.

Experimental

For general methods and instrumentation see Ref. 31. NMR assignments are verified by two dimensional spectra.

5-Ethylcyclohexane-1,3-dione (4). Methyl 2-pentenoate (11.2 g, 87.5 mmol) and ethyl acetoacetate (11.4 g, 87.5 mmol) were added to a solution of sodium ethoxide (2.0 g of sodium, 87.0 mmol) in dry ethanol (40 ml). The solution was refluxed under nitrogen for 4 h, the solvent removed under reduced pressure, and the residue dissolved in water (120 ml). The solution was treated with KOH (10.0 g, 178.6 mmol) and refluxed for 20 min. The mixture was acidified to pH 2 by careful addition of 4N H_2SO_4 and again refluxed until the evolution of gas ceased (ca. 1 h). Most of the ethanol was also distilled off this way. The residue was stored for 18 h in the refrigerator and the crystals were filtered off and recrystallized from acetone/water, 1:1, to afford the dione **4** (12.2 g, 48%) as colorless crystals; mp: 60°C.

3-Bromo-5-ethyl-2-cyclohexenone (5). A solution of dione **4** (1.26 g, 9.00 mmol) and DMF (1 ml) in dry CH_2Cl_2 (25 ml) was treated at 0°C within 5 min with oxalyl bromide (1.00 ml, 2.33 g, 10.80 mmol). The solution was allowed to warm to 20°C and stirring was continued for 40 min. The mixture was then dissolved in diethyl ether (100 ml) and washed with water (40 ml). The organic phase was separated, dried ($MgSO_4$), and concentrated at reduced pressure. The residue was purified by flash chromatography on silica gel (CH_2Cl_2) to yield the vinyl bromide **5** (1.63 g, 89%) as a colorless oil which cystallized on standing in the refrigerator, mp: 116°C (pentane/diethyl ether). ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.98 (t, J=7.3 Hz; 3H, $CHCH_2CH_3$), 1.47 (quint, J=7.3 Hz; 2H, $CHCH_2CH_3$), 2.08–2.23 (m; 2H), 2.48–2.65 (m; 2H), 2.91 (m; 1H), 6.48 (s; 1H, 2-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.42 (q, CH_2CH_3), 28.47 (t, CH_2CH_3), 37.54 (d, C-5), 42.83 (t), 43.03 (t), 132.73 (d, C-2), 150.10 (s, C-3), 197.07 (s, C-1).

(*E*)-3-(2-Ethoxyvinyl)-5-ethylcyclohex-2-enone (7). A solution of the vinyl bromide **5** (1.20 g, 5.91 mmol), Et_3N (1.2 ml, 0.87 g, 8.61 mmol), vinyl diethyl ether (2.9 ml, 2.18 g, 30.21 mmol), and $Pd(OAc)_2$ (0.13 g, 0.58 mmol) in dry toluene (6 ml) was kept under argon for 5 h at 90°C (TLC monitoring).[12] The dark reaction mixture was then dissolved in diethyl ether (100 ml), washed with water (2×30 ml), dried ($MgSO_4$), and concentrated at reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2) to afford the dienone **7** (0.88 g, 77%) as a colorless oil. For one experiment, the crude mixture of **6** and **7** was used in a Diels–Alder reaction (see below). ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.99 (t, J=7.3 Hz; 3H, $CHCH_2CH_3$), 1.37 (t, J=7.0 Hz; 3H, OCH_2CH_3), 1.43–1.51 (quin, J=7.0 Hz; 2H, $CHCH_2CH_3$), 2.04–2.17 (m; 3H), 2.51–2.60 (m; 2H), 3.96 (q, J=7.0 Hz; 2H, OCH_2CH_3), 5.70 (d, $J_{1',2'}$=12.8 Hz; 1H, 1′-H), 5.85 (s; 1H, 2-H), 7.03 (d, $J_{2',1'}$=12.8 Hz; 1H, 2′-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.56 (q, CH_2CH_3), 15.11 (q, OCH_2CH_3), 29.03 (t, CH_2CH_3), 31.89 (t), 36.76 (d, C-5), 43.94 (t), 66.86 (t, OCH_2CH_3), 108.16 (d, C-1′), 124.09 (d, C-2′), 153.90 (d, C-2), 157.09 (s, C-3), 200.22 (s, C-1).

(*E*,1*R,5*R**)-3-(2-Ethoxyvinyl)-5-ethyl-2-cyclohexenol (8).** A solution of the dienone **7** (0.80 g, 4.12 mmol) in dry THF (1 ml) was added dropwise at −78°C to a suspension

of LAH (0.30 g, 7.92 mmol) in dry THF (10 ml). The mixture was stirred for 0.5 h at −78°C and was then allowed to warm to 20°C overnight. Aqueous NaOH (6 N, ca. 0.5 ml) was then added dropwise. After stirring for 30 min, $MgSO_4$ was added and the mixture was filtered over a batch of Celite (diethyl ether). The filtrate was concentrated at reduced pressure to yield the alcohol **8** (0.61 g, 76%) as a yellow oil that was used for the next reaction without further purification. ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.97 (t, J=7.3 Hz; 3H, CH_2CH_3), 1.31 (t, J=7.0 Hz; 3H, OCH_2CH_3), 1.43–2.19 (m; 7H, 4-H_2, 5-H, 6-H_2, CH_2CH_3), 3.80 (q, J=7.0 Hz; 2H, OCH_2CH_3), 4.35 (m; 1H, 1-H), 5.48 (s; 1H, 2-H), 5.58 (d, $J_{1',2'}$=12.9 Hz; 1H, 1′-H), 6.55 (d, $J_{2',1'}$=12.9 Hz; 1H, 2′-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.66 (q, CH_2CH_3), 15.24 (q, OCH_2CH_3), 29.70 (t, CH_2CH_3), 31.69 (t), 34.89 (d, C-5), 39.69 (t), 65.82 (t, OCH_2CH_3), 69.07 (d, C-1), 109.13 (d, C-1′), 127.11 (d, C-2′), 135.37 (s, C-3), 147.35 (d, C-2).

(1*R,3*R**,6*R**,6a*S**,12a*S**,12b*R**)-1,8-Dihydroxy-6-ethoxy-3-ethyl-1,2,3,4,6,6a,12a,12b-octahydrobenz[*a*]anthracene-7,12-dione (10).** A solution of the dienol **8** (0.60 g, 3.06 mmol) was added slowly at 0°C to a solution of juglone (**9**) (0.44 g, 2.55 mmol) and boron triacetate (0.48 g, 2.55 mmol) in dry CH_2Cl_2 (40 ml). The solution was stirred for 10 min at 0°C and then poured into water (50 ml). The mixture was extracted with CH_2Cl_2 (2×50 ml), the combined organic phases were washed with water (3×50 ml), dried ($MgSO_4$), and concentrated at reduced pressure to ca. 20 ml. The solution was diluted with ether (200 ml), again concentrated at reduced ca. 50 ml, and left in the refrigerator overnight. The Diels–Alder product **11** (0.67 g, 71%) crystallized as faint yellow needles, mp: 141–143°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.63 (t, J=7.0 Hz; 3H, CH_2CH_3), 0.96 (t, J=7.3 Hz; 3H, OCH_2CH_3), 1.09 (m; 1H, 2-H_a), 1.28–1.42 (m; 2H, CH_2CH_3), 1.49–1.82 (m; 2H, 3-H_a, 4-H_a), 2.03 (m; 1H, 2-H_e), 2.11–2.26 (m; 2H, 12b-H, 1-OH), 2.42 (m; 1H, 4-H_e), 3.04 (m; 1H, OCH_2CH_3), 3.18 (m; 1H, 12a-H), 3.40 (m; 1H, OCH_2CH_3), 3.76 (m; 1H, 6a-H), 4.12 (m; 1H, 6-H), 4.94 (m; 1H, 1-H), 5.73 (br. s; 1H, 5-H), 7.18 (d, $J_{9,10}$=8.3 Hz; 1H, 9-H), 7.40 (d, $J_{11,10}$=8.3 Hz; 1H, 10-H), 7.60 (t, $J_{10,9}$=$J_{10,11}$=8.3 Hz; 1H, 10-H), 12.09 (s; 1H, 8-OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.72 (q, CH_2CH_3), 14.93 (q, OCH_2CH_3), 29.71 (t, CH_2CH_3), 36.18 (d, C-3), 40.63 (t), 42.36 (t), 43.98 (d, C-12b), 47.69 (d, C-12a), 55.00 (d, C-6a), 65.31 (t, OCH_2CH_3), 70.01 (d, C-1), 72.69 (d, C-6), 116.97 (d, C-5), 119.02 (s), 119.74 (d, C-9), 122.30 (d, C-11), 136.91 (d, C-10), 139.95 (s), 141.86 (s), 161.58 (s, C-8), 197.13 (s, C-12), 205.80 (C-7). MS (EI, 70 eV), *m/z* (%): 370 (3) [M^+], 324 (100) [M^+−EtOH], 278 (90), 263 (45), 214 (44), 195 (58), 165 (51), 134 (69). IR (KBr): $\tilde{\nu}$=3487 cm^{-1} (OH), 1698 (C=O), 1620 (C=O). Anal. Calcd for $C_{22}H_{26}O_5$ (370.18) C 71.32, H 7.08; Found: C 71.12, H 6.89.

(1*R,3*R**,4a*S**,5*R**,6*S**,12b*S**)-1,8-Dihydroxy-4a,5-epoxy-6-ethoxy-3-ethyl-1,2,3,4,6,6a,12a,12b-octahydrobenz-[*a*]anthracene-7,12-dione (11).** A solution of the Diels–Alder product **10** (250 mg, 0.675 mmol) in CH_2Cl_2 (50 ml) was treated at 0°C with a ca. 0.08 M solution of dimethyldioxirane in acetone (25 ml, ca. 2 mmol).[32] The solution was kept for 15 h at 0°C and then concentrated at reduced pressure. The residue was crystallized from CH_2Cl_2/diethyl ether to afford the epoxide **11** (215 mg, 83%) as a yellow solid, mp: 145°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.97 (t, J=7.2 Hz; 3H, CH_2CH_3), 1.24 (t, J=6.9 Hz; 3H, OCH_2CH_3), 1.34–1.75 (m; 6H, 2-H_2, 3-H, 4-H_a, CH_2CH_3), 2.19–2.29 (m; 2H, 4-H_e, 1-OH), 3.32 (m; 1H, 5-H), 3.39–3.44 (m; 1H, 12b-H), 3.67–3.87 (m; 3H, 1-H, OCH_2CH_3), 5.18 (s; 1H, 6-H), 7.28 (d, $J_{9,10}$=7.2 Hz; 1H, 9-H), 7.57–7.67 (m; 2H, 10-H, 11-H), 12.06 (s; 1H, 8-OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.71 (q, CH_2CH_3), 16.21 (q, OCH_2CH_3), 29.41 (t, CH_2CH_3), 35.03 (d, C-3), 38.74 (t), 42.92 (t), 45.03 (d, C-12b), 58.11 (d, C-5), 58.89 (s, C-4a), 67.59 (t, OCH_2CH_3), 68.66 (d, C-1), 76.00 (d, C-6), 115.12 (s), 120.05 (d, C-9), 125.06 (d, C-11), 132.33 (s), 136.68 (d, C-10), 139.71 (s), 145.80 (s), 161.78 (s, C-8), 186.29 (s, C-12), 189.69 (C-7). UV (CH_2Cl_2): λ_{max} (log ϵ)=276 nm (3.70), 428 (2.02). MS (EI, 70 eV), *m/z* (%): 384 (82) [M^+], 338 (40) [M^+−EtOH], 310 (36) [M^+−EtOH−CO], 294 (38) [M^+−EtOH−CO−O], 258 (100), 229 (29). IR (KBr): $\tilde{\nu}$=3445 cm^{-1} (OH), 1673 (C=O), 1645 (C=O), 1614 (C=C), 1449, 1275, 1237, 1085. Anal. Calcd for $C_{22}H_{24}O_6$ (384.16) C 68.72, H 6.30; Found: C 68.56, H 6.13.

(1*R,3*R**)-1-Acetoxy-3-ethyl-8-hydroxy-1,2,3,4-tetrahydrobenz[*a*]anthracene-7,12-dione (12).** A solution of the epoxide **11** (100 mg, 0.260 mmol) in dry THF (10 ml) was treated with boron triacetate (1.5 g) and the mixture was stirred at 20°C for 15 h. The solution was then poured into 1N HCl (100 ml) and extracted with CH_2Cl_2 (3×30 ml). The combined organic phases were washed with water (3×50 ml), dried ($MgSO_4$), and concentrated at reduced pressure. The residue was purified by chromatography on silica (diethyl ether/petroleum ether, 1:4) to afford the aromatic monoacetate **12** (22 mg, 23%) as a yellow solid; mp: 145–147°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.03 (t, J=7.2 Hz; 3H, CH_2CH_3), 1.32–1.61 (m; 3H, 2-H_a CH_2CH_3), 1.89–2.03 (m; 1H, 3-H), 2.08 (s; 3H, Ac), 2.40–2.59 (m; 2H, 2-H_e, 4-H_a), 3.13 (m; 1H, 4-H_e), 6.80 (m; 1H, 1-H), 7.28 (d, $J_{9,10}$=8.1 Hz; 1H, 9-H), 7.50–7.78 (m; 3H, 5-H, 10-H, 11-H), 8.27 (d, $J_{6,5}$=8.1 Hz; 1H, 6-H), 12.45 (s; 1H, 8-OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.54 (q, CH_2CH_3), 21.60 (q, Ac), 29.36 (t, CH_2CH_3), 29.70 (d, C-3), 35.22 (t), 37.92 (t), 68.11 (d, C-1), 115.64 (s), 120.20 (d, C-9), 123.68 (d, C-11), 127.67 (d, C-5), 132.16 (s), 133.73 (s), 135.17 (d, C-10), 135.70 (s), 136.00 (s), 137.17 (d, C-6), 147.69 (s), 162.12 (s, C-8), 170.78 (s, Ac), 184.01 (s, C-12), 188.63 (s, C-7). UV (CH_2Cl_2): λ_{max} (log ϵ)=272 nm (4.26), 284 (3.51), 354 (1.14), 405 (1.82). MS (EI, 70 eV), *m/z* (%): 364 (4) [M^+], 321 (100) [M^+−Ac], 275 (40). IR (KBr): $\tilde{\nu}$=3439 cm^{-1} (OH), 1743 (C=O), 1634 (C=O), 1460, 1368, 1270, 1237. HRMS: Calcd for $C_{22}H_{20}O_5$: 364.1311; Found: 364.1311±3 ppm.

***rac*-3-Ethyl-8-hydroxy-3,4-dihydro-2*H*-benz[*a*]anthracene-1,7,12-trione (2) (6-deoxybrasiliquinone B).** *Method A:* A solution of the acetate **12** (20 mg, 0.055 mmol) in THF (2 ml) was treated with NaOMe in methanol (2N, 2 ml). The mixture was stirred for 15 min at 20°C, the alkaline solution was acidified by addition of 0.5N HCl (10 ml) and the product extracted with ethyl acetate (3×10 ml). The combined organic phases were washed with water (3 ml), dried ($MgSO_4$), and the solvent was removed at

reduced pressure. The residue was redissolved in CH_2Cl_2 (12 ml) and exposed to diffuse sunlight for 12 h in 4 NMR tubes. The combined solutions were concentrated at reduced pressure and purified by preparative TLC on silica gel (CH_2Cl_2) to afford 6-deoxybrasiliquinone B (**2**), (9 mg, 52%), mp: 143–144°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.12 (t, J=7.2 Hz; 3H, CH_2CH_3), 1.46–1.75 (q; 2H, CH_2CH_3), 2.35–2.56 (m; 1H, 3-H), 2.59–2.71 (m; 2H, 2-H_a, 4-H_a), 2.93–3.10 (m; 2H, 2-H_e, 4-H_e), 7.27 (d, $J_{9,10}$=7.6 Hz; 1H, 9-H), 7.56 (d, $J_{5,6}$=8.0 Hz, 1H, 5-H), 7.61–7.73 (m; 2H, 10-H, 11-H), 8.28 (d, $J_{6,5}$=8.0 Hz; 1H, 6-H), 12.28 (s; 1H, 8-OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.80 (q, CH_2CH_3), 29.96 (t, CH_2CH_3), 31.72 (d, C-3), 38.72 (t, C-4), 43.05 (t, C-2), 115.13 (s), 119.28 (d, C-9), 123.21 (d, C-11), 128.98 (d, C-5), 129.54 (s), 133.28 (s), 134.74 (s), 134.97 (d, C-10), 135.88 (s), 136.73 (d, C-6), 147.17 (s), 161.56 (s, C-8), 184.22 (s, C=O), 187.09 (s, C=O), 197.63 (s, C-1). UV (CH_2Cl_2): λ_{max} (log ϵ)=265 nm (4.31), 405 (3.43). MS (EI, 70 eV), *m/z* (%): 320 (31) [M^+], 292 (59) [M^+-CO], 279 (100), 262 (35), 250(55). IR (KBr): $\tilde{\nu}$=3446 cm^{-1} (OH), 1702 (C=O), 1668 (C=O), 1638 (C=O), 1458, 1366, 1272, 1228. HRMS: Calcd for $C_{20}H_{16}O_4$: 320.1049; Found: 320.1049±3 ppm. Anal. Calcd for $C_{20}H_{16}O_4$: 320.34: C 74.99, H 5.03; Found: C 74,37, H 4.77.

***rac*-4-(5-Hydroxy-9,10-dioxo-9,10-dihydroanthracen-2-ylmethyl)-3-pentanal (13).** The finely ground epoxide **11** (35 mg, 0.091 mmol) was sublimed at 0.8 Torr by external heating with hot air. The sublimate was purified by TLC chromatography on silica gel (CH_2Cl_2) to yield the open chain aldehyde **13** as a yellow solid (17 mg, 57%); mp: 95–96°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.99 (t, J=7.2 Hz; 3H, CH_2CH_3), 1.38–1.44 (m; 2H, CH_2CH_3), 2.36–2.53 (m; 3H, 2-H_2, 3-H), 2.72–2.94 (m; 2H, 4-H_2), 7.34 (d, $J_{6',7'}$=8.3 Hz; 1H, 6′-H), 7.63–7.75 (m; 2H, 4′-H, 7′-H), 7.86 (d, $J_{8',7'}$=7.5 Hz; 1H, 8′-H), 8.11 (s; 1H, 1′-H), 8.28 (d, $J_{4',3'}$=8.0 Hz; 1H, 3′-H), 9.77 (m; 1H, 1-H), 12.68 (s; 1H, 8-OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.48 (q, CH_2CH_3), 26.82 (t, CH_2CH_3), 36.59 (d, C-3), 40.84 (t, C-4), 47.75 (t, C-2), 116.54 (s), 119.99 (d, C-6′), 124.86 (d, C-8′), 127.74 (d, C-1′), 128.26 (d, C-4′), 131.92 (s), 133.91 (s), 134.03 (s), 135.54 (d, C-3′), 137.08 (d, C-7′), 148.75 (s, C-2′), 162.95 (s, C-5′), 183.09 (s, C-9′), 188.91 (s, C-10′), 202.36 (d, C-1). UV (CH_2Cl_2): λ_{max} (log ϵ)=248 nm (4.19), 338 (1.09), 405 (1.85). MS (EI, 70 eV), *m/z* (%): 322 (31) [M^+], 278 (100) [M^+-CH_3CHO], 263 (33) [M^+-CH_3CHO–Me], 149 (32). IR (KBr): $\tilde{\nu}$=3467 cm^{-1} (OH), 1721 (C=O), 1672 (C=O), 1634 (C=O), 1590 (C=C), 1449, 1357, 1291, 1264. HRMS: Calcd for $C_{20}H_{18}O_4$: 322.1205; Found: 322.1205±3 ppm.

***rac*-3-Ethyl-8-hydroxy-3,4-dihydro-2*H*-benz[*a*]anthracene-1,7,12-trione (2) (*rac*-6-deoxybrasiliquinone B).** *Method B:* A solution of juglone (**9**) (503 mg, 0.29 mmol), the crude mixture of the dienes **6** and **7** (ratio ca. 1:6, 600 mg, ca. 0.25 mmol by NMR) and boron triacetate (0.56 g, 30 mmol) in CH_2Cl_2 (20 ml) was stirred at 20°C for 15 h. The mixture was washed with water (2×20 ml), the organic phase was dried ($MgSO_4$), and the solvent was removed at reduced pressure. Column chromatography of the residue on silica gel (CH_2Cl_2) afforded from the major nonpolar fraction 6-deoxybrasiliquinone B (**2**) (417 mg, 50%), and from the polar fraction, the phenol **14a** (56 mg, 7%), mp: 256°C.

***rac*-3-Ethyl-5,8-dihydroxy-3,4-dihydro-2*H*-benzo[*a*]-anthracene-1,7,12-trione (14a).** Mp: 256°C (decomp.). ^{1}H NMR (200 MHz, D_6-acetone): δ=1.06 (t, J=7.4 Hz; 3H, CH_2CH_3), 1.62 (q; 2H, CH_2CH_3), 2.2 (m; 1H, 3-H), 2.41–2.67 (m; 2H, 2-H_a, 2-H_a), 2.9 (m; 1H, 4-H_e), −3.27 (dd, 1H, 4-H_e), 7.30 (d, $J_{9,10}$=8.3 Hz; 1H, 10-H), 7.59 (d, $J_{8,9}$=7.7 Hz, 1H, 8-H), 7.78 (s, 1H, 6-H), 7.81 (t; 1H, 9-H), 12.29 (s; 1H, 11-OH). UV (CH_2Cl_2): λ_{max} (log ϵ)=283 nm (4,13), 329 (3.47), 389 (3.60). IR (KBr): $\tilde{\nu}$=3391 cm^{-1} (OH), 1701 (C=O), 1654 (C=O), 1575 (C=C), 1456, 1363, 1285. MS (EI, 70 eV), *m/z* (%): 336.1 (78) [M^+], 308.1 (62), 281.0 (76), 280.0 (100), 279.1 (78), 252.0 (31), 224.1 (24), 168.1 (56), 139.1 (68); Anal. Calcd for $C_{20}H_{16}O_5$: 336.34: C 71.42, H 4.79; Found: 71.22, H 4.68.

***rac*-5-Acetoxy-3-ethyl-8-hydroxy-3,4-dihydro-2*H*-benzo[*a*]anthracene-1,7,12-trione (14b).** A suspension of the phenol **14a** (17 mg, 0.05 mmol) in CH_2Cl_2 (2 ml) was treated with 0.2 ml of acetic anhydride and 0.1 ml of pyridine. After 20 min stirring at 20°C, the phenol was dissolved and the reaction quenched by addition of 2N HCl (1 ml). Excess acetic anhydride was hydrolyzed by stirring the mixture for 30 min. The phases were separated, the organic phase was dried ($MgSO_4$), and the solvent removed at reduced pressure. The residue was purified by filtration through a short column of silica gel (2 g, CH_2Cl_2) and the acetate was isolated from the nonpolar fraction and crystallized from diethyl ether to yield yellow plates of **14b** (20 mg, 96%); mp: 148°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.05 (t, J=7.4 Hz; 3H, CH_2CH_3), 1.59 (q; 2H, CH_2CH_3), 2.2 (m; 1H, 3-H), 2,45 (s, 3H, $COCH_3$), 2.4–2.7 (m; 2H, 2-H_a, 4-H_a), 2.95–3.12 (m; 2H, 2-H_e), −3.27 (dd, 1H, 4-H_e), 7.30 (t, $J_{9,10}$=8.3 Hz; 1H, 10-H), 7.66–7.74 (m, 2H, 8-H, 9-H), 7.88 (s, 1H, 6-H), 7.81 (t; 1H, 9-H), 12.29 (s; 1H, 11-OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ=11.52 (q, CH_2CH_3), 21.22 (q, $COCH_3$), 29.42 (t, CH_2CH_3), 31.90 (4-CH_2), 37.25 (d, C-3), 45.39 (t, 2-CH_2), 115.82 (s, C-5), 120.23 (d, C-8), 122.54 (s, C-6), 124.17 (d, C-10), 133.68, 134,74, 135.32, 137.66 (s, C-9), 139.10 (s, C-4a), 143.30 (s, C-12b), 151.95 (s, C-5), 162.35 (s, C-11), 168.61(s, ester C=O), 182.40 (s, C=O), 187.17 (s, C=O), 199.23 (s, C-1). UV (CH_2Cl_2): λ_{max} (log ϵ)=283 nm (4,13), 329 (3.47), 389 (3.60). IR (KBr): $\tilde{\nu}$=3447 cm^{-1} (OH), 1768 (ester C=O), 1702 (C=O), 1653 (C=O), 1636 (C=O), 1592 (C=C), 1472, 1359, 1214, 1188. MS (EI, 70 eV), *m/z* (%): 378.1 (69) [M^+], 350.1 (42), 336.1 (66), 308.1 (76), 280.0 (100), 251.0 (26), 224.0 (22), 196.0 24), 168.1 (41), 139.1 (77); Anal. Calcd for $C_{22}H_{18}O_6$: (378.38): C 69.83, H 4.79; Found: C 69.75, H 4.51.

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