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Room-Temperature $B(OAc)_3$-Promoted Diels–Alder Reaction of Juglone with Styrenes: Total Syntheses of Tetrangulol and Anhydrolandomycinone

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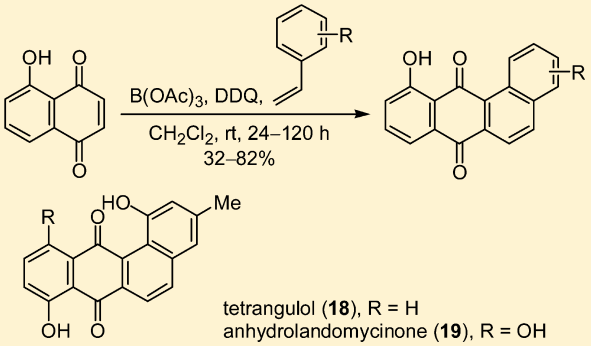
Supporting Information

ABSTRACT: The Diels–Alder reaction of juglone with various styrenes in the presence of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was promoted by $B(OAc)_3$ at room temperature. The reaction proceeded smoothly and gave the products in a good yield and with excellent regioselectivity. This strategy was applied to the total syntheses of tetrangulol and anhydrolandomycinone.



INTRODUCTION

Angucyclinones are a large group of naturally occurring quinones that have a benz[*a*]anthracenequinone framework (Figure 1) and

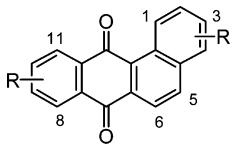


Figure 1. Structure of angucyclinones.

exhibit a broad range of biological activities.[1] Owing to the biological importance of angucyclinones, considerable attention has been focused on the development of methods that facilitate the efficient and rapid syntheses of these compounds. Thus far, many synthetic methods have been developed for the synthesis of this class of compounds.[2] Among them, the most straightforward strategy is the Diels–Alder reaction of naphthoquinones with styrenes and an oxidant such as chloranil.[3] However, these reactions require harsh conditions and a long time for completion because styrenes typically act as dienophiles rather than dienes, especially in the Diels–Alder reaction. Further, the product yield and regioselectivity of these reactions are poor. Therefore, although these reactions have been studied for over three decades, their applications in organic synthesis are limited.

The Lewis-acid-promoted Diels–Alder reaction of juglone (5-hydroxy-1,4-naphthoquinone)[4] and its derivatives[5] with dienes is well-known; however, similar reactions with styrenes are rare.[3a,c] Lewis acids increase not only the reactivity but also the regioselectivity of the substrate.[4a,b] Boron reagents are the most commonly used Lewis acids for reactions involving juglone and its derivatives,[4,5] and this motivated us to use a boron Lewis acid in the Diels–Alder reaction of juglone with styrenes. Herein, we report the reaction conditions that aid the rapid construction of the angucyclinone skeleton at low temperatures with high yield and regioselectivity.

RESULTS AND DISCUSSION

(a). Cycloaddition of Juglone and Styrene. At the outset, styrene (**2a**) was used to examine the reaction conditions (Table 1). First, juglone (1 equiv) and $B(OAc)_3$[6] (1.1 equiv) were mixed in dichloromethane at room temperature for 10 min and then, styrene (4 equiv) and DDQ (3 equiv) were added. DDQ was chosen as the oxidant because we expected the reaction to proceed at room temperature in the presence of such a strong oxidant.[7] To our delight, the desired product **3a** was formed under these conditions; however, the reaction was not completed even after 24 h probably because of the polymerization of styrene under Lewis acid conditions.[8] Therefore, additional amounts of $B(OAc)_3$ (1.1 equiv), styrene (4 equiv), and DDQ (3 equiv) were added to the reaction mixture after 24 h, and this addition was repeated every 24 h until juglone was completely consumed. Finally, the reaction was completed after 72 h, and a single product **3a** was obtained in 81% yield (entry 1). The structure of **3a** was confirmed by comparing its spectral data with those reported in the literature.[3b] The reaction with other Lewis acids was also examined under the same conditions. A strong Lewis acid only resulted in the polymerization of styrene (entries 2–6), whereas a weak Lewis acid resulted in the recovery of juglone and styrene (entry 7). When chloranil was used as the oxidant, a trace amount of **3a** was

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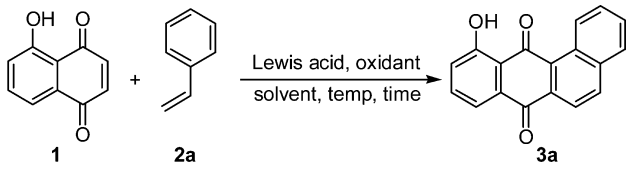
Table 1. Various Lewis-acid-promoted Diels–Alder Reactions of Juglone with Styrene in the Presence of an Oxidant



entry	Lewis acid	oxidant	solvent	temp	time (h)	yield[a]
1	$B(OAc)_3$	DDQ	CH_2Cl_2	rt	72	81%
2	$BF_3{\cdot}OEt_2$	DDQ	CH_2Cl_2	rt	2	–[b]
3	$TiCl_4$	DDQ	CH_2Cl_2	rt	2	–[b]
4	$FeCl_3$	DDQ	CH_2Cl_2	rt	2	–[b]
5	$AlCl_3$	DDQ	CH_2Cl_2	rt	2	–[b]
6	$MgBr_2$	DDQ	CH_2Cl_2	rt	72	–[c]
7	$B(OAc)_3$	chloranil	CH_2Cl_2	rt	72	trace[c]
8	$B(OAc)_3$	DDQ	$ClCH_2CH_2Cl$	reflux	3.5	46%
9	$B(OAc)_3$	chloranil	$ClCH_2CH_2Cl$	reflux	18	38%

[a]Isolated yield. [b]Polymerization of styrene. [c]Recovery of starting materials.

obtained along with the starting materials. Attempts to reduce the reaction time by increasing the reaction temperature resulted in lower yields (entries 8–9). Thus, the best yield was observed when the reaction was carried out at room temperature with $B(OAc)_3$ and DDQ.

(b). Cycloaddition of Juglone and Styrene Derivatives. Under the same reaction conditions mentioned earlier, we examined the substrate scope of the substituted styrenes. The results are listed in Table 2. We found that a variety of styrenes could afford the cycloaddition products **3b–l** in moderate to good yields with complete regiocontrol. Most of these reactions were completed in 24 h and yielded a single regioisomer 11-hydroxybenz[*a*]anthracene-7,12-dione **3**. When styrenes with an electron-donating group were used, the reactions were completed within 24 h (entries 1–8), whereas when styrenes with an electron-withdrawing substituent were used, the reactions were slow and the desired products were obtained in moderate yields (entries 9–11). Attempts to improve the yields by changing the reaction temperatures or by using other Lewis acids were unsuccessful. It should be mentioned that juglone was completely consumed in all cases. However, in several cases, the cycloadducts were obtained in moderate yields, probably because the reaction also generated intractable materials that were insoluble or did not elute on silica gel. In the case of entry 2, two regioisomers **3c** and **3c′** were obtained in a 2:1 ratio and they could not be separated by column chromatography. The **3c**:**3c′** ratio was determined by ^{1}H NMR analysis. However, the pure major isomer **3c** could be obtained by recrystallization. **3c′** was obtained as the minor product probably because of the steric clash between the methyl and carbonyl groups. A similar result was also observed for styrene **2f** (entry 5). In the case of entry 4, the yield of **3e** decreased owing to the formation of an additional byproduct **4e**. Attempts to suppress the formation of this byproduct by using other Lewis acids or by changing the reaction temperatures were unsuccessful. It is noteworthy that the cycloadduct **3i** (entry 8) was formed in 24 h at room temperature in 44% yield. In an earlier study, this compound was prepared using the same starting materials—juglone and styrene **2i**—in refluxing toluene, but the reaction required 6 days and provided 37% yield.[9] Although the yields from both the strategies were similar, our strategy was easy to handle and required mild reaction conditions and a shorter reaction time. It should be mentioned that DDQ can also be used as a dienophile[10] in the cycloaddition; however, we did not observe any cycloadducts from DDQ and styrenes under these conditions. This was probably because the reactivity of juglone was activated by $B(OAc)_3$, which could react with styrenes more rapidly than DDQ.

Under the same conditions, the styrenes **5–9**[11] bearing an electron-withdrawing group or electron-donating group at the β position did not yield any cycloadducts and only the starting materials were recovered (Figure 2).

The structure of **3** was elucidated by carrying out IR, ^{1}H and ^{13}C NMR, and low- and high-resolution mass spectral analyses. The position of the hydroxyl group in **3** was determined by performing an HMBC experiment. The HMBC spectra of **3** revealed two cross-peaks between one carbonyl group and hydrogen atom but no cross-peak between the other carbonyl group and hydrogen atom (Figure 3).

(c). Mechanism and Structural Effects of Diels–Alder Reaction. The mechanism of the Diels–Alder reaction of juglone and styrenes is proposed on the basis of the above results and is depicted in Schemes 2 and 3. First, juglone and $B(OAc)_3$ formed a boroacetate complex **10**,[4a] which activated the C-2 position of juglone. Then, the β carbon of the styrenes facilitated addition at this position, and a benzylic carbocation intermediate **11** was formed (Scheme 1). Subsequent cyclization formed **12**, which was further transformed into **13** via tautomerization and double bond isomerization. Finally, oxidation with DDQ yielded the cycloadducts **3**. Thus, the cycloaddition reaction proceeded fast with an electron-rich styrene, whereas it proceeded slowly or did not proceed at all with an electron-deficient styrene.

The lone pair on the oxygen atom at the para-position in styrene could stabilize the benzylic carbocation intermediate **14** through resonance (Scheme 2). Consequently, the tautomerization of **15** and the subsequent oxidation of the tautomeric form **16** by DDQ may proceed more easily than cyclization and result in the formation of naphthoquinone **17**. Finally, acetate may attack the benzylic position in **17** to form naphthoquinone **4e**.

(d). Total Syntheses of Tetrangulol and Anhydrolandomycinone. After the efficient regiocontrolled synthesis of angucyclinones, we decided to apply our strategy to the total syntheses of tetrangulol and anhydrolandomycinone. Tetrangulol, which was isolated from *Streptomyces rimosus*,[12] is the first member of the family of naturally occurring angucyclinones. Anhydrolandomycinone was isolated from *Streptomyces cyanogenus* S-136 in 2011;[13] however, in 1990, it was identified as the

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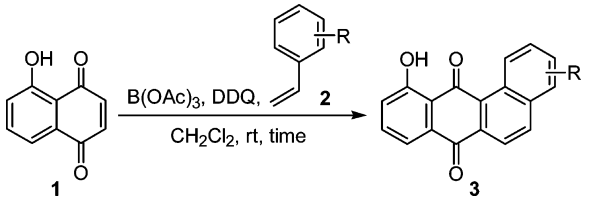
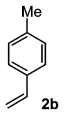
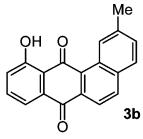
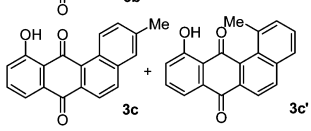
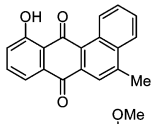
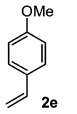
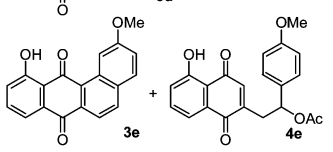
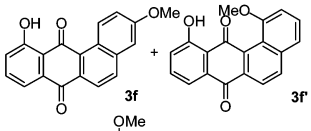
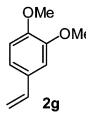
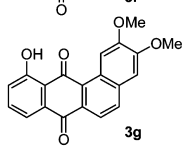
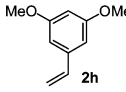
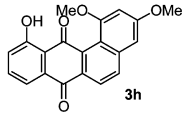
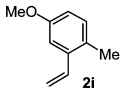
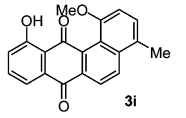
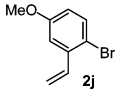
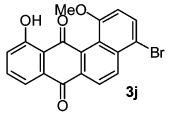
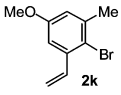
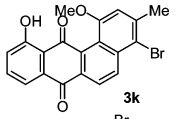
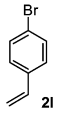
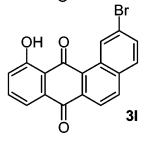
Table 2. Yields for $B(OAc)_3$-promoted Diels–Alder Reaction of Juglone with Various Styrenes in the Presence of DDQ at Room Temperature



1	 2b	24 h	 3b	70%
2	 2c	24 h	 3c + 3c'	75% (2:1)
3	 2d	24 h	 3d	60%
4	 2e	24 h	 3e + 4e	39% + 16%
5	 2f	24 h	 3f + 3f'	82% (2:1)
6	 2g	24 h	 3g	61%
7	 2h	24 h	 3h	72%
8	 2i	24 h	 3i	44%
9	 2j	48 h	 3j	59%
10	 2k	24 h	 3k	32%
11	 2l	120 h	 3l	40%

[a]Isolated yield.

dehydration product of landomycinone.[14] Anhydrolandomycinone shows cytotoxicity against both the human breast cancer cell lines MCF-7 and MAD-231.[13]

Our retrosynthetic analysis is summarized in Scheme 3. Tetrangulol and anhydrolandomycinone could be obtained

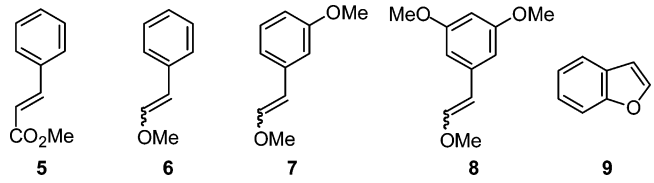


Figure 2. Styrenes not yielding any cycloadducts.

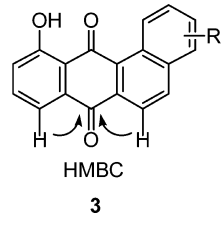
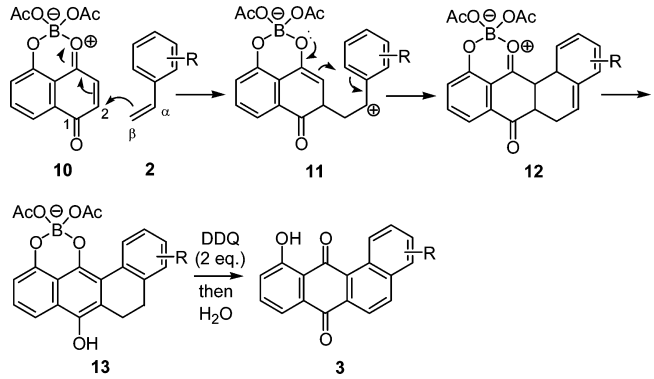
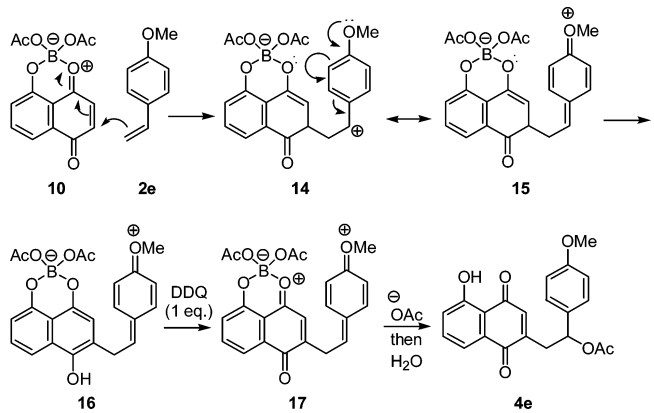


Figure 3. Key HMBC correlations to establish structure of **3**.

Scheme 1. Plausible Mechanism to Form 3



Scheme 2. Plausible Mechanism to Form 4e



from the same intermediate **20**. This common intermediate **20** was synthesized using our proposed strategy, that is, the Diels–Alder reaction of *O*-methylnaphthazarin **21** and bromostyrene **2k**.

The bromostyrene **2k** was prepared from **22**[15] via a benzylic oxidation followed by the Wittig reaction (Scheme 4). The role of bromine in **2k** was set to control the orientation of the Diels–Alder reaction with **21**. Two regioisomers might be obtained in the Diels–Alder reaction without bromine in **2k**.

With bromostyrene **2k** in hand, the tetracyclic compound **20** was obtained as a single isomer in 63% yield from the regiocontrolled intermolecular Diels–Alder reaction of **21**[16] with **2k** in the presence of $B(OAc)_3$ and DDQ (Scheme 5). The next step in the synthesis of tetrangulol was the removal of

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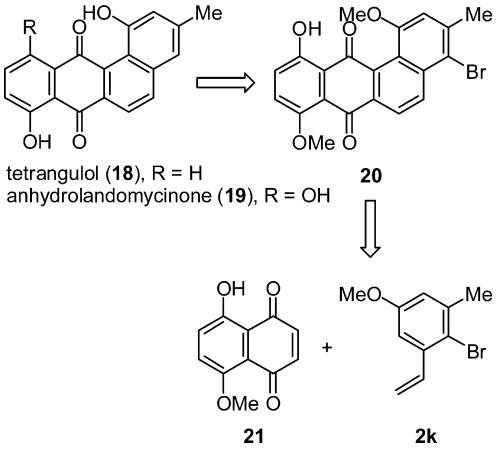
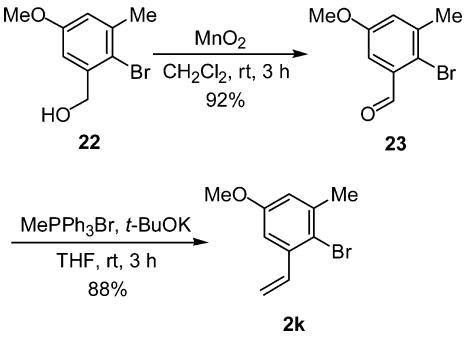
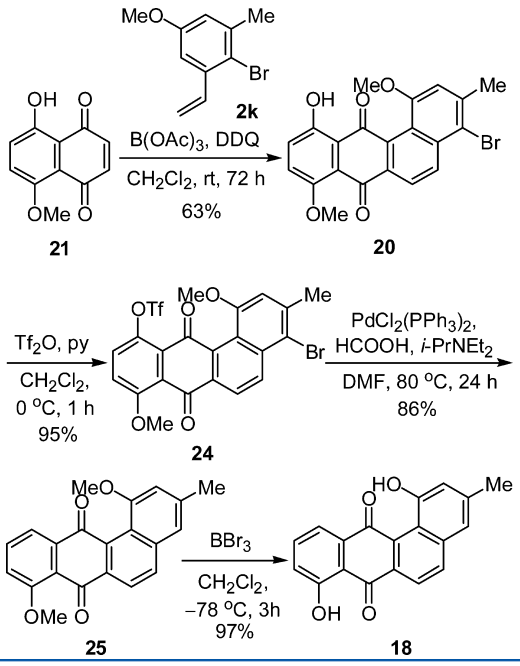
Scheme 3. Retrosynthetic Analysis



Scheme 4. Preparation of Bromostyrene 2k



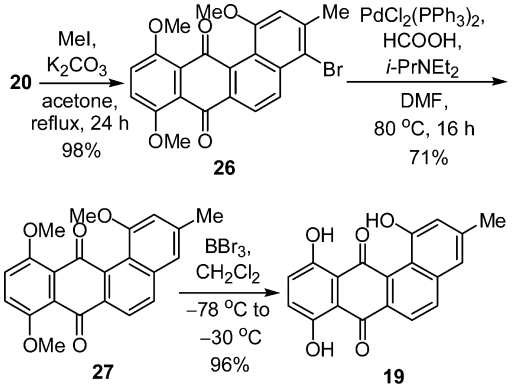
Scheme 5. Total Synthesis of Tetrangulol



the hydroxyl group and bromine. For this purpose, the deoxygenation and debromination of **20** were carried out by the conversion of **20** to triflate **24** and by palladium-catalyzed formate reduction.[17] Finally, deprotection of the methyl ethers in **25** by BBr_3 gave tetrangulol (**18**).[18]

Next, we focused on the synthesis of anhydrolandomycinone through the removal of the bromine moiety in **20** by palladium-catalyzed formate reduction; however, the reaction was not successful. The reaction was not completed even after the addition of an excess amount of reagents or a considerable extension of the reaction time. However, this issue was resolved by converting the phenolic hydroxyl group to methyl ether before the reduction, and then, the desired debromination product **27** was obtained in good yield (Scheme 6). Global deprotection of the

Scheme 6. Total Synthesis of Anhydrolandomycinone



methyl ether with BBr_3 gave the target molecule anhydrolandomycinone (**19**). The spectral data were in good agreement with those reported in the literature.[14]

CONCLUSION

In summary, we developed a simple strategy for the synthesis of angucyclinones; $B(OAc)_3$ was used as a Lewis acid to promote the Diels–Alder reaction of juglone with various styrenes in the presence of DDQ at room temperature. We successfully applied this strategy to the total syntheses of tetrangulol and anhydrolandomycinone from *O*-methylnaphthazarin **21** and styrene **2k**.

EXPERIMENTAL SECTION

General Information. Unless stated otherwise, reagents were obtained from commercial sources and used without further purification. All reactions were performed under a nitrogen atmosphere in anhydrous solvents, which were dried prior to use following standard procedures. Reactions were monitored by thin-layer chromatography on 0.25 mm E. Merck silica gel plates (60F-254) using 7% ethanolic phosphomolybdic acid as developing agent. Merck silica gel 60 (particle size 0.04–0.063 mm) was employed for flash chromatography. Melting points are uncorrected. IR spectra were recorded as films on KBr plates. ^1H NMR spectra were obtained in $CDCl_3$ unless otherwise noted at 400 or 500 MHz. ^{13}C NMR spectra were obtained at 100 or 125 MHz. Chemical shifts were reported in δ (ppm) using solvent resonance as the internal reference.

General Procedure for the Diels–Alder Reaction of Juglone and Styrenes. A mixture of juglone (**1**) (187 mg, 1 mmol) and $B(OAc)_3$ (206 mg, 1.1 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min and then styrene derivative (4 mmol) and DDQ (680 mg, 3 mmol) were added to the reaction mixture. After stirred at room temperature for 24 h, additional $B(OAc)_3$ (206 mg, 1.1 mmol), styrene derivatives (4 mmol), and DDQ (680 mg, 3 mmol) were added to the reaction mixture, and this addition was repeated every 24 h until juglone was completely consumed. The reaction was quenched with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic extracts were washed successively with water, brine, dried over $MgSO_4$, filtered and concentrated. The crude product was recrystallizd from CH_3CN to give **3**. The filtrate was further purified by flash silica-gel chromatography (hexanes/CH_2Cl_2) to give additional **3**. Analytically pure **3** was obtained by crystallization from CH_2Cl_2–hexane.

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11-Hydroxybenz[*a*]anthracene-7,12-dione (3a). Red solid; mp 202−204 °C; IR (neat) ν 1664, 1631, 1459, 1381, 1297, 1226, 1209, 1075, 852, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.83 (s, 1H), 9.76 (d, J = 9.0 Hz, 1H), 8.36 (d, J = 8.5 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.80−7.75 (m, 2H), 7.68−7.63 (m, 2H), 7.32 (dd, J = 8.5, 1.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 182.3, 162.2, 136.7, 136.2, 136.1, 134.4, 132.3, 130.5, 130.2, 129.0, 128.8, 128.5, 128.4, 124.9, 122.6, 119.0, 117.1; MS (EI) m/z (% base peak) 274 (M$^+$, 100), 246 (27), 218 (34), 189 (81), 163 (16), 137 (5), 126 (7), 109 (9), 94 (17); HRMS (EI) calcd for $C_{18}H_{10}O_3$ 274.0630, Found 274.0626. Anal. Calcd for $C_{18}H_{10}O_3$: C, 78.82; H, 3.67. Found: C, 79.02; H, 4.03.

11-Hydroxy-2-methylbenz[*a*]anthracene-7,12-dione (3b). Red solid; mp 180−182 °C; IR (neat) ν 1663, 1631, 1586, 1461, 1367, 1295, 1230, 1205, 859, 792, 740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.81 (s, 1H), 9.48 (s, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.75−7.73 (m, 2H), 7.61 (dd, J = 8.5, 8.5 Hz, 1H), 7.44 (dd, J = 8.5, 1.0 Hz, 1H), 7.28 (dd, J = 8.5, 1.0 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 183.4, 162.2, 140.7, 136.0, 135.9, 135.1, 134.5, 132.4, 131.0, 130.8, 128.8, 127.8, 127.4, 124.8, 121.7, 118.9, 117.1, 22.6; MS (EI) m/z (% base peak) 288 (M$^+$, 100), 273 (31), 260 (7), 231 (9), 202 (17), 189 (13), 144 (6), 101 (4); HRMS (EI) calcd for $C_{19}H_{12}O_3$ 288.0786, Found 288.0783.

11-Hydroxy-3-methylbenz[*a*]anthracene-7,12-dione (3c) and 11-Hydroxy-1-methylbenz[*a*]anthracene-7,12-dione (3c′). Red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.82 (s, 1H), 11.84 (s, 1H), 9.62 (d, J = 9.2 Hz, 1H), 8.31 (d, J = 8.8 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 7.79−7.55 (m, 9H), 7.33−7.29 (m, 2H), 2.59 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 189.8, 183.3, 183.2, 162.3, 160.6, 141.2, 139.2, 137.6, 137.4, 137.2, 136.1, 136.0, 135.7, 135.5, 133.9, 133.8, 132.8, 132.6, 132.4, 128.8, 128.7, 128.5, 128.2, 128.1, 127.7, 126.7, 126.6, 124.7, 124.3, 122.7, 121.5, 119.0, 118.9, 117.3, 117.2, 21.9, 21.5.

11-Hydroxy-3-methylbenz[*a*]anthracene-7,12-dione (3c). Red solid; mp 219−221 °C; IR (neat) ν 1663, 1624, 1587, 1469, 1296, 1216, 1036, 851, 781, 740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.84 (s, 1H), 9.63 (d, J = 9.0 Hz, 1H), 8.32 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.79 (dd, J = 7.8, 1.3 Hz, 1H), 7.67 (br s, 1H), 7.64 (dd, J = 8.3, 7.8 Hz, 1H), 7.58 (dd, J = 9.0, 1.5 Hz, 1H), 7.31 (dd, J = 8.3, 1.3 Hz, 1H), 2.55 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.2, 183.3, 162.2, 139.1, 137.1, 136.1, 135.5, 133.7, 132.6, 132.4, 128.6, 128.5, 128.2, 128.0, 124.7, 122.7, 118.9, 117.1, 21.6; MS (EI) m/z (% base peak) 288 (M$^+$, 100), 273 (27), 260 (20), 232 (16), 202 (28), 189 (20), 163 (4), 139 (6), 101 (9); HRMS (EI) calcd for $C_{19}H_{12}O_3$ 288.0786, Found 288.0779. Anal. Calcd for $C_{19}H_{12}O_3$: C, 79.16; H, 4.20. Found: C, 79.12; H, 4.62.

11-Hydroxy-5-methylbenz[*a*]anthracene-7,12-dione (3d). Red solid; mp 243−245 °C; IR (neat) ν 1667, 1628, 1586, 1460, 1371, 1294, 1214, 1078, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.88 (s, 1H), 9.80 (d, J = 9.0 Hz, 1H), 8.20 (s, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.78−7.68 (m, 3H), 7.63 (dd, J = 8.5, 8.0 Hz, 1H), 7.31 (dd, J = 8.5, 0.5 Hz, 1H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9, 183.5, 162.2, 143.9, 135.9, 135.8, 133.9, 132.3, 130.7, 129.7, 129.0, 128.7, 127.1, 124.9, 124.7, 123.4, 118.8, 117.1, 20.7; MS (EI) m/z (% base peak) 288 (M$^+$, 100), 273 (10), 260 (13), 231 (14), 202 (20), 189 (8), 139 (4), 101 (7); HRMS (EI) calcd for $C_{19}H_{12}O_3$ 288.0786, Found 288.0793.

11-Hydroxy-2-methoxybenz[*a*]anthracene-7,12-dione (3e). Red solid; mp 208−210 °C; IR (neat) ν 1665, 1633, 1580, 1466, 1352, 1296, 1224, 1201, 1073, 1042, 854, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.95 (s, 1H), 9.25 (d, J = 2.0 Hz, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.80−7.77 (m, 2H), 7.63 (dd, J = 8.0, 8.0 Hz, 1H), 7.32−7.29 (m, 2H), 4.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.2, 183.4, 162.3, 161.5, 136.0, 135.9, 134.9, 132.6, 132.5, 132.4, 130.4, 126.7, 124.8, 121.7, 120.7, 118.9, 117.2, 106.4, 55.6; MS (EI) m/z (% base peak) 304 (M$^+$, 100), 275 (15), 261 (11), 233 (16), 205 (6), 176 (11), 152 (6), 111 (4), 97 (6); HRMS (EI) calcd for $C_{19}H_{12}O_4$ 304.0736, Found 304.0734.

Acetic acid 2-(5-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)-1-(4-methoxyphenyl)ethyl ester (4e). Orange solid; mp 145−147 °C; IR (neat) ν 1728, 1645, 1610, 1513, 1456, 1366, 1236, 1175, 1027, 760 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.89 (s, 1H), 7.65−7.60 (m, 2H), 7.31 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 8.5 Hz, 2H), 6.70 (s, 1H), 5.99 (dd, J = 9.0, 5.0 Hz, 1H), 3.78 (s, 3H), 3.14 (dd, J = 14.0, 5.0 Hz, 1H), 2.98 (dd, J = 14.0, 9.0 Hz, 1H), 2.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.9, 183.9, 170.1, 161.2, 159.6, 148.3, 136.5, 136.3, 131.9, 131.4, 127.8, 124.3, 119.5, 115.0, 114.0, 73.4, 55.2, 37.0, 21.1; MS (EI) m/z (% base peak) 366 (M$^+$, 3), 324 (29), 306 (21), 291 (5), 247 (4), 218 (4), 188 (14), 137 (100), 109 (15) 92 (20); HRMS (EI) calcd for $C_{21}H_{18}O_6$ 366.1103, Found 366.1105.

11-Hydroxy-3-methoxybenz[*a*]anthracene-7,12-dione (3f) and 11-Hydroxy-1-methoxybenz[*a*]anthracene-7,12-dione (3f′). Red solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.83 (s, 1H), 11.64 (s, 1H), 9.71 (d, J = 9.5 Hz, 1H), 8.36 (d, J = 8.5 Hz, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.66−7.59 (m, 4H), 7.51 (d, J = 8.0 Hz, 1H), 7.41 (dd, J = 9.5, 3.0 Hz, 1H), 7.33−7.30 (m, 2H), 7.20 (d, J = 3.0 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 4.01 (s, 3H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 188.8, 183.0, 182.8, 162.2, 160.0, 159.5, 157.5, 139.0, 138.1, 136.1, 135.2, 134.6, 134.2, 134.1, 132.5, 132.4, 132.0, 130.1, 130.0, 128.6, 127.5, 127.2, 125.6, 124.6, 123.8, 123.5, 123.3, 122.6, 122.3, 120.7, 118.8, 117.0, 109.6, 106.9, 106.4, 56.0, 55.4.

11-Hydroxy-3-methoxybenz[*a*]anthracene-7,12-dione (3f). Red solid; mp 216−218 °C; IR (neat) ν 1662, 1632, 1469, 1296, 1214, 852, 780, 741 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.82 (s, 1H), 9.67 (d, J = 9.5 Hz, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.08 (d, J = 8.8 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.64 (dd, J = 8.0, 7.5 Hz, 1H), 7.39 (d, J = 9.5 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.18 (s, 1H), 3.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.3, 183.1, 162.2, 159.5, 139.0, 136.1, 134.6, 132.5, 132.4, 130.2, 128.7, 125.7, 124.6, 123.4, 122.7, 118.9, 117.1, 106.9, 55.4; MS (EI) m/z (% base peak) 304 (M$^+$, 0.1), 288 (100), 273 (23), 260 (16), 245 (4), 232 (12), 202 (17), 189 (13), 176 (4), 139 (4), 101 (8); HRMS (EI) calcd for $C_{19}H_{12}O_4$ 304.0736, Found 304.0734.

11-Hydroxy-2,3-dimethoxybenz[*a*]anthracene-7,12-dione (3g). Red solid; mp 268−270 °C; IR (neat) ν 1659, 1627, 1585, 1485, 1430, 1368, 1303, 1262, 1215, 1075, 1040, 870, 741 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.97 (s, 1H), 9.31 (s, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.05 (d, J = 8.5 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.64 (dd, J = 8.5, 7.5 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 7.16 (s, 1H), 4.15 (s, 3H), 4.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.5, 183.3, 162.3, 153.1, 151.3, 136.0, 134.2, 134.1, 132.9, 132.7, 127.1, 126.6, 124.6, 121.7, 118.8, 117.3, 107.0, 106.9, 56.2, 56.0; MS (EI) m/z (% base peak) 334 (M$^+$,100), 291 (23), 263 (9), 248 (4), 220 (14), 205 (2), 192 (6), 163 (11), 138 (3), 88 (3); HRMS (EI) calcd for $C_{20}H_{14}O_5$ 334.0841, Found 334.0847. Anal. Calcd for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22. Found: C, 71.60; H, 4.30.

11-Hydroxy-1,3-dimethoxybenz[*a*]anthracene-7,12-dione (3h). Red solid; mp 183−185 °C; IR (neat) ν 1662, 1639, 1608, 1451, 1276, 1212, 1164, 1078, 741 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.60 (s, 1H), 8.20 (d, J = 8.5 Hz, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.60 (dd, J = 8.0, 7.5 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 6.81 (d, J = 2.0 Hz, 1H), 6.74 (d, J = 2.0 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.1, 182.7, 161.3, 160.0, 158.6, 139.5, 135.3, 134.4, 133.1, 132.5, 132.3, 123.6, 123.2, 118.8, 118.0, 117.0, 102.2, 99.3, 56.0, 55.7; MS (EI) m/z (% base peak) 334 (M$^+$, 100), 316 (71), 287 (19), 273 (12), 245 (11), 220 (13), 192 (9), 176 (11), 163 (14), 150 (4), 88 (8); HRMS (EI) calcd for $C_{20}H_{14}O_5$ 334.0841, Found 334.0838. Anal. Calcd for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22. Found: C, 71.43; H, 4.35.

11-Hydroxy-1-methoxy-4-methylbenz[*a*]anthracene-7,12-dione (3i). Red solid; mp 180−182 °C; IR (neat) ν 1666, 1631, 1579, 1456, 1349, 1291, 1219, 1202, 1076, 1031, 858, 739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.61 (s, 1H), 8.25 (d, J = 8.5 Hz, 1H), 8.22 (d, J = 8.5 Hz, 1H), 7.75 (dd, J = 7.5, 1.0 Hz, 1H), 7.60 (dd, J = 8.5, 7.5 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.29 (dd, J = 8.5, 1.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 3.96 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.0, 182.9, 160.0, 155.9, 136.9, 135.2, 134.4, 133.6,

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132.4, 130.6, 130.5, 126.7, 123.8, 122.1, 121.4, 118.8, 118.0, 109.3, 55.9, 18.9; MS (EI) *m/z* (% base peak) 318 (M^+, 95), 300 (100), 287 (22), 275 (14), 247 (5), 218 (5), 202 (10), 189 (13), 159 (8), 127 (6), 101 (6); HRMS (EI) calcd for $C_{20}H_{14}O_4$ 318.0892, Found 318.0885. Anal. Calcd for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.48; H, 5.18.

4-Bromo-11-hydroxy-1-methoxybenz[*a*]anthracene-7,12-dione (3j). Red solid; mp 243−245 °C; IR (neat) ν 1666, 1638, 1600, 1579, 1448, 1347, 1291, 980, 848, 744 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.53 (s, 1H), 8.50 (d, J = 9.0 Hz, 1H), 8.33 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.64 (dd, J = 8.0, 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 182.5, 160.2, 157.2, 135.9, 135.5, 134.3, 133.6, 133.4, 132.3, 124.1, 123.7, 122.7, 119.0, 117.8, 114.8, 113.7, 110.0, 56.1; MS (EI) *m/z* (% base peak) 384 (90), 382 (M^+, 90), 366 (100), 364 (99), 353 (20), 351 (19), 313 (11), 280 (13), 260 (8), 204 (35), 176 (36), 151(14), 88 (19); HRMS (EI) calcd for $C_{19}H_{11}{}^{79}BrO_4$ 381.9841, Found 381.9847.

4-Bromo-11-hydroxy-1-methoxy-3-methylbenz[*a*]-anthracene-7,12-dione (3k). Red solid; mp 268−270 °C; IR (neat) ν 1665, 1643, 1602, 1578, 1443, 1360, 1292, 1206, 1078, 846, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.55 (s, 1H), 8.58 (d, J = 8.5 Hz, 1H), 8.30 (d, J = 8.5 Hz, 1H), 7.77 (d, J = 7.0 Hz, 1H), 7.63 (dd, J = 8.5, 7.0 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 7.00 (s, 1H), 3.98 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.6, 182.6, 160.1, 156.4, 140.8, 136.4, 135.4, 134.2, 133.6, 133.3, 132.4, 124.0, 123.7, 121.2, 118.9, 117.9, 115.4, 112.3, 56.1, 24.7; MS (EI) *m/z* (% base peak) 398 (77), 396 (M^+, 78), 380 (100), 378 (98), 367 (15), 274 (16), 218 (27), 189 (63), 163 (16), 101 (13), 94 (16); HRMS (EI) calcd for $C_{20}H_{13}{}^{79}BrO_4$ 395.9997, Found 396.0006.

2-Bromo-11-hydroxybenz[*a*]anthracene-7,12-dione (3l). Red solid; mp 218−220 °C; IR (neat) ν 1666, 1631, 1580, 1455, 1292, 1201, 859, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 12.68 (s, 1H), 9.95 (d, J = 0.5 Hz, 1H), 8.33 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 8.3 Hz, 1H), 7.77−7.70 (m, 3H), 7.64 (dd, J = 8.5, 8.0 Hz, 1H), 7.31 (dd, J = 8.5, 1.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.4, 182.8, 162.4, 136.3, 136.0, 135.0, 134.9, 132.2, 132.1, 131.2, 130.7, 130.2, 127.3, 125.4, 125.1, 123.0, 119.1, 116.9; MS (EI) *m/z* (% base peak) 354 (88), 352 (M^+, 89), 324 (10), 296 (8), 274 (16), 245 (12), 217 (36), 189 (32), 163 (18), 136 (11), 94 (25); HRMS (EI) calcd for $C_{18}H_9{}^{79}BrO_3$ 351.9735, Found 351.9742. Anal. Calcd for $C_{18}H_9BrO_3$: C, 61.22; H, 2.57. Found: C, 60.95; H, 3.06.

2-Bromo-5-methoxy-3-methylbenzaldehyde (23). A mixture of (2-Bromo-5-methoxy-3-methylphenyl)methanol (**22**) (2 g, 8.7 mmol) and MnO_2 (15 g, 173 mmol) in CH_2Cl_2 was stirred at room temperature for 3 h. Filtration and concentration in vacuo gave **23** (1.84 g, 92%) as a white solid. Mp 84−85 °C; IR (neat) ν 3016, 2978, 2938, 2841, 1679, 1589, 1464, 1388, 1315, 1160, 1076, 939, 869, 757, 614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.40 (s, 1H), 7.25 (d, J = 2.8 Hz, 1H), 7.05 (d, J = 2.8 Hz, 1H), 3.82 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 158.6, 140.6, 134.4, 123.7, 120.8, 110.3, 55.6, 22.8; MS (EI) *m/z* (% base peak) 230 (99), 228 (M^+, 100), 200 (30), 199 (20), 169 (5), 148 (8), 120 (19), 105 (14), 91 (36); HRMS (EI) calcd for $C_9H_9{}^{79}BrO_2$ 227.9786, Found 227.9780. Anal. Calcd for $C_9H_9BrO_2$: C, 47.19; H, 3.96. Found: C, 47.13; H, 4.19.

2-Bromo-5-methoxy-1-methyl-3-vinylbenzene (2k). To a suspension of methyltriphenylphosphonium bromide (5.6 g, 15.7 mmol) in THF (20 mL) at 0 °C was added *t*-BuOK (1.76 g, 15.7 mmol). After stirred for 1 h, aldehyde **23** (3 g, 13.1 mmol) in THF (15 mL) was added, and stirred at room temperature for another 3 h. The reaction mixture was quenched with water and the solvent was evaporated. The residue was dissolved in CH_2Cl_2 and washed successively with water, brine and dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/EtOAc = 3:1) to give **2k** (2.64 g, 88%) as a yellowish oil. IR (neat) ν 2958, 1578, 1460, 1398, 1314, 1161, 1018, 916 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, J = 17.4, 10.9 Hz, 1H), 6.92 (d, J = 3.0 Hz, 1H), 6.75 (d, J = 3.0 Hz, 1H), 5.64 (dd, J = 17.4, 1.2 Hz, 1H), 5.33 (dd, J = 10.9, 1.2 Hz, 1H), 3.80 (s, 3H). 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 139.5, 138.8, 136.9, 117.1, 116.5, 116.1, 109.6, 55.4, 24.0; MS (EI) *m/z* (% base peak) 228 (100), 226 (M^+, 99), 213 (6), 211 (5), 185 (18), 183 (19), 147 (39), 132 (19), 115 (22), 104 (25), 77 (20); HRMS (EI) calcd for $C_{10}H_{11}{}^{79}BrO$ 225.9993, Found 225.9996.

4-Bromo-11-hydroxy-1,8-dimethoxy-3-methylbenz[*a*]-anthracene-7,12-dione (20). A mixture of **21** (204 mg, 1 mmol) and $B(OAc)_3$ (206 mg, 1.1 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min and then **2k** (907 mg, 4 mmol) and DDQ (680 mg, 3 mmol) were added to the reaction mixture. After stirred at room temperature for 24 h, additional $B(OAc)_3$ (206 mg, 1.1 mmol), **2k** (907 mg, 4 mmol), and DDQ (680 mg, 3 mmol) were added to the reaction mixture, and this addition was repeated every 24 h until **21** was completely consumed. The reaction was quenched with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic extracts were washed successively with water, brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:3) to give **20** (270 mg, 63%) as a red solid. Analytically pure **20** was obtained by crystallization from CH_2Cl_2−hexane: mp 244−246 °C; IR (neat) ν 1661, 1637, 1580, 1458, 1435, 1360, 1251, 1175, 1021, 832, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.51 (s, 1H), 8.57 (d, J = 9.0 Hz, 1H), 8.32 (d, J = 9.0 Hz, 1H), 7.31 (m, 2H), 6.99 (s, 1H), 4.02 (s, 3H), 3.97 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.5, 181.4, 156.2, 154.2, 153.7, 140.4, 135.9, 134.5, 133.3, 133.0, 125.6, 123.8, 121.5, 120.6, 118.8, 117.9, 115.4, 112.2, 56.9, 56.0, 24.7; MS (EI) *m/z* (% base peak) 428 (100), 426 (M^+, 99), 409(15), 393 (44), 391 (42), 379 (16), 364 (13), 347 (12), 302 (14), 300 (16), 261 (8), 233 (4), 176 (11), 151 (13), 88 (9); HRMS (EI) calcd for $C_{21}H_{15}{}^{79}BrO_5$ 426.0103, Found 426.0101.

Trifluoromethanesulfonic Acid 4-Bromo-1,8-dimethoxy-3-methyl-7,12-dioxo-7,12-dihydrobenz[*a*]-anthracen-11-yl Ester (24). To a stirred solution of **20** (120 mg, 0.28 mmol) in CH_2Cl_2 (15 mL) at 0 °C were added Tf_2O (172 mg, 0.56 mmol) and pyridine (0.5 mL). After stirred at 0 °C for 1 h, the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:3) to give **24** (150 mg, 95%) as an orange red solid. Analytically pure **24** was obtained by crystallization from EtOAc: mp 283−285 °C; IR (neat) ν 1666, 1604, 1472, 1432, 1227, 1204, 1138, 1011, 970, 818, 745 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J = 9.0 Hz, 1H), 8.25 (d, J = 9.0 Hz, 1H), 7.56 (d, J = 9.0 Hz, 1H), 7.26 (d, J = 9.0 Hz, 1H), 6.98 (s, 1H), 4.06 (s, 3H), 4.01 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.3, 180.6, 158.7, 155.9, 141.0, 138.7, 135.8, 135.4, 133.2, 132.4, 132.2, 128.5, 123.5, 121.8, 120.4, 118.9 (q, J = 319 Hz), 116.8, 115.2, 111.9, 56.9, 56.0, 24.9; MS (EI) *m/z* (% base peak) 560 (94), 558 (M^+, 89), 427 (12), 425 (12), 368 (26), 366 (26), 318 (100), 303 (33), 213 (12), 176 (7), 150 (3); HRMS (EI) calcd for $C_{22}H_{14}{}^{79}BrF_3O_7S$ 557.9596, Found 557.9600.

1,8-Dimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (25). A mixture of **24** (30 mg, 0.05 mmol), *i*-PrNEt$_2$ (58 mg, 0.5 mmol), HCO_2H (14 mg, 0.3 mmol), and $Pd(PPh_3)_2Cl_2$ (4 mg, 0.005 mmol) in dry DMF (6 mL) under Ar atmosphere was heated to 80 °C for 24 h. After cooled to room temperature, the mixture was diluted with CH_2Cl_2 and washed successively with NH_4Cl, brine, and dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:2) to give **25** (15.3 mg, 86%) as an orange-yellow solid. Mp 191−193 °C; IR (neat) ν 1664, 1619, 1588, 1470, 1444, 1137, 1009, 947, 839, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.69−7.67 (m, 2H), 7.25−7.24 (m, 2H), 6.89 (s, 1H), 4.04 (s, 3H), 3.98 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 182.2, 159.4, 157.0, 140.3, 139.4, 137.7, 135.2, 134.9, 133.9, 132.5, 122.6, 120.7, 120.1, 119.1, 118.5, 116.3, 111.2, 56.4, 56.0, 22.1; MS (EI) *m/z* (% base peak) 332 (M^+, 100), 315 (56), 285 (17), 273 (9), 257 (5), 231 (6), 215 (11), 202 (17), 189 (13), 163 (3), 139 (3), 107 (5), 101 (10); HRMS (EI) calcd for $C_{21}H_{16}O_4$ 332.1049, Found 332.1053.

Tetrangulol (18). To a stirred solution of **25** (8 mg, 0.024 mmol) in CH_2Cl_2 (2 mL) was added BBr_3 (0.06 mL, 0.06 mmol) at −78 °C.

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After stirred at −78 °C for 3 h, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was washed successively with water, brine and dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:1) to give **18** (7 mg, 97%) as a brown solid. Mp 199−201 °C; IR (neat) ν 1637, 1616, 1577, 1543, 1499, 1477, 1453, 1412, 1374, 1292, 1254, 1157, 1080, 793, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 12.24 (s, 1H), 11.27 (s, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.12 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 7.2 Hz, 1H), 7.68 (dd, J = 8.0, 7.2 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 1.6 Hz, 1H), 7.13 (d, J = 1.6 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6, 187.8, 161.6, 155.2, 142.0, 139.1, 137.7, 136.9, 134.78, 134.77, 132.3, 124.7, 121.8, 121.3, 121.2, 120.1, 120.0, 114.6, 21.2; MS (EI) m/z (% base peak) 304 (M^+, 100), 287 (5), 275 (7), 247 (7), 231 (3), 202 (5), 189 (6), 176 (2), 152 (4), 101 (4); HRMS (EI) calcd for $C_{19}H_{12}O_4$ 304.0736, Found 304.0730.

4-Bromo-1,8,11-trimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (26). A mixture of **20** (42 mg, 0.098 mmol), MeI (30 mg, 0.2 mmol), and K_2CO_3 (20 mg, 0.15 mmol) in acetone (3 mL) was heated to reflux for 24 h. After cooled to room temperature, the mixture was quenched with water and extracted with CH_2Cl_2. The combined organic extracts were washed with brine and dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:5) to give **26** (43 mg, 98%) as a yellow solid. Analytically pure **26** was obtained by crystallization from CH_2Cl_2−hexane: mp 221−223 °C; IR (neat) ν 1675, 1658, 1577, 1409, 1362, 1271, 1230, 1138, 1057, 1010, 800 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 8.8 Hz, 1H), 8.21 (d, J = 8.8 Hz, 1H), 7.26 (d, J = 9.3 Hz, 1H), 7.18 (d, J = 9.3 Hz, 1H), 6.92 (s, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.98 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.9, 182.2, 155.8, 153.3, 150.8, 140.3, 137.5, 135.7, 132.9, 130.9, 127.8, 123.6, 122.2, 120.5, 119.6, 117.3, 115.3, 111.5, 57.3, 56.8, 56.2, 24.8; MS (EI) m/z (% base peak) 442 (100), 440 (M^+, 100), 425 (33), 423 (30), 393 (14), 381 (8), 343 (10), 315 (5), 288 (3), 221(5), 176 (5), 158(4), 101 (3); HRMS (EI) calcd for $C_{22}H_{17}{}^{79}BrO_5$ 440.0259, Found 440.0253.

1,8,11-Trimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (27). A mixture of **26** (21 mg, 0.05 mmol), *i*-PrNEt$_2$ (58 mg, 0.5 mmol), HCO_2H (14 mg, 0.3 mmol), and $Pd(PPh_3)_2Cl_2$ (4 mg, 0.005 mmol) in dry DMF (3 mL) under Ar atmosphere was heated to 80 °C for 16 h. After cooled to room temperature, the mixture was diluted with CH_2Cl_2 and washed successively with NH_4Cl, brine, and dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:3) to give **27** (12.2 mg, 71%) as an orange red solid. Mp >250 °C (dec.); IR (neat) ν 1660, 1622, 1574, 1486, 1417, 1275, 1233, 1137, 1056, 1011, 960, 852, 810 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.24 (d, J = 9.5 Hz, 1H), 7.23 (s, 1H), 7.16 (d, J = 9.5 Hz, 1H), 6.85 (s, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.97 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.2, 182.6, 156.6, 153.2, 150.8, 140.3, 137.6, 137.4, 132.7, 131.3, 128.0 122.3, 122.2, 120.0, 119.6, 118.7, 117.1, 110.7, 57.4, 56.8, 56.0, 22.1; MS (EI) m/z (% base peak) 362 (M^+, 68), 345 (53), 315 (34), 289 (26), 273 (29), 261 (32), 215 (54), 202 (90), 189 (87), 163 (60), 139 (68), 127 (27), 101 (15), 57 (100); HRMS (EI) calcd for $C_{22}H_{18}O_5$ 362.1154, Found 362.1150.

Anhydrolandomycinone (19). To a stirred solution of **27** (20 mg, 0.055 mmol) in CH_2Cl_2 (3 mL) was added BBr_3 (1.5 mL, 1.5 mmol) at −78 °C. After stirred at −78 °C for 1 h, the reaction mixture was warmed to −30 °C and stirred at this temperature for another 3 h. The mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was washed successively with water, brine and dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash silica-gel chromatography (hexanes/CH_2Cl_2 = 1:1) to give **19** (17 mg, 96%) as a brown-black solid. Analytically pure **19** was obtained by crystallization from CH_2Cl_2−pentane: mp 214−216 °C; IR (neat) ν 1609, 1584, 1554, 1505, 1453, 1262, 1185, 835, 816, 793, 709 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 12.89 (s, 1H), 12.39 (s, 1H), 10.98 (s, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.29 (d, J = 9.5 Hz, 1H), 7.27 (d, J = 9.5 Hz, 1H), 7.25 (s, 1H), 7.08 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 190.2, 185.5, 158.1, 157.3, 154.2, 141.3, 138.4, 137.5, 135.0, 130.8, 129.7, 129.5, 121.0, 120.8, 119.7, 119.1, 113.0, 110.5, 20.2; MS (EI) m/z (% base peak) 320 (M^+, 100), 302 (22), 291 (9), 261 (7), 217 (6), 189 (18), 163 (13), 152 (13), 128 (10), 109 (5); HRMS (EI) calcd for $C_{19}H_{12}O_5$ 320.0685, Found 320.0692.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H and ^{13}C NMR for compounds **2k**, **3**, **4e**, **18**−**20**, and **23**−**27**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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