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Synthesis of Macrosporin and Related 9,10-Anthraquinones by Biomimetic Polyketide Aromatization and Cyclization of 6-Benzylresorcylates

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This paper describes the synthesis of an array of 9,10-anthraquinones **2** by initial preparation of 6-benzylresorcylates **3** from oxo-dioxinone precursors **4** and their subsequent conversion to anthrones by cyclization and oxidation. Resorcylates **3** were obtained by an improved two-step procedure from oxo ester **5** and acyl chlorides **6**. These methods were applied in a seven-step synthesis of the fungal natural product macrosporin (**1**).

Introduction

9,10-Anthraquinones[1] are an important class of natural products that show various biological activities.[2] In 1957, Suemitsu et al. reported the first isolation of the 9,10-anthraquinone macrosporin (**1**, Figure 1) from the plant pathogen fungus[3] *Macrosporium porri*,[4] followed by its structure determination by degradation.[5] Over the years, macrosporin (**1**) has been isolated from a number of other phytopathogenic fungi[6] and shown to inhibit several protein kinases[6j] as well as having antiproliferative[6h,7] and antibacterial activities.[6f,8]

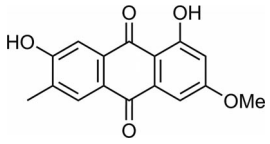
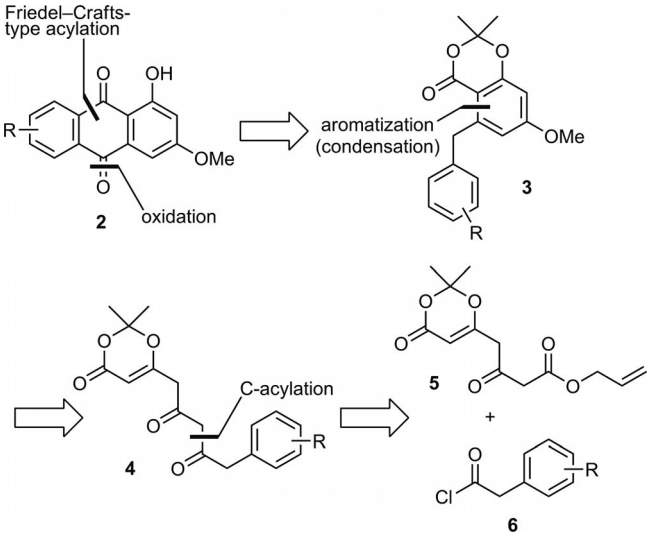


Figure 1. Macrosporin (**1**).

Although the biosynthesis of **1** proceeds through the octaketide pathway,[9,10] the only reported total synthesis of **1** utilized a Diels–Alder reaction of a 1,4-naphthoquinone and a diene[11] to introduce the 9,10-anthaquinone unit.[12] Building on our recent biomimetic syntheses of resorcylate natural products,[13,14] we sought to explore an alternative synthesis of 9,10-anthraquinones including **1** that utilizes a polyketide-like construction of one of the arenes, with subsequent intramolecular Friedel–Crafts acylation to close the tricyclic array. This retrosynthetic analysis is outlined in Scheme 1. We envisioned that key resorcylate **3** should be available by biomimetic cyclization of dioxo-dioxinone **4**, which in turn should be available from known oxo ester **5**[14] and acyl chloride **6** by Claisen reaction. The strategy in Scheme 1 should easily allow the preparation of 1,3-dihydroxy-9,10-anthraquinones with diverse substitution patterns and therefore should be of general utility.



Scheme 1. Retrosynthetic analysis of macrosporin-like 9,10-anthraquinones **2**.

Results and Discussion

Selective Claisen condensation of acyl chlorides **6a**–**g**[15] with dioxinone oxo ester **5**[14] gave dioxinone dioxo esters **7**, which were subjected directly to $Pd(PPh_3)_4$-catalyzed deallylation and decarboxylation (Table 1). In this reaction, morpholine was used both as a π-allyl scavenger[16] as well as a base to catalyze cyclization of the resultant dioxo-dioxinones **4** to generate 6-benzylresorcylates **8a**–**g** in a one-pot reaction in high yield (61–74% over two steps). This is a

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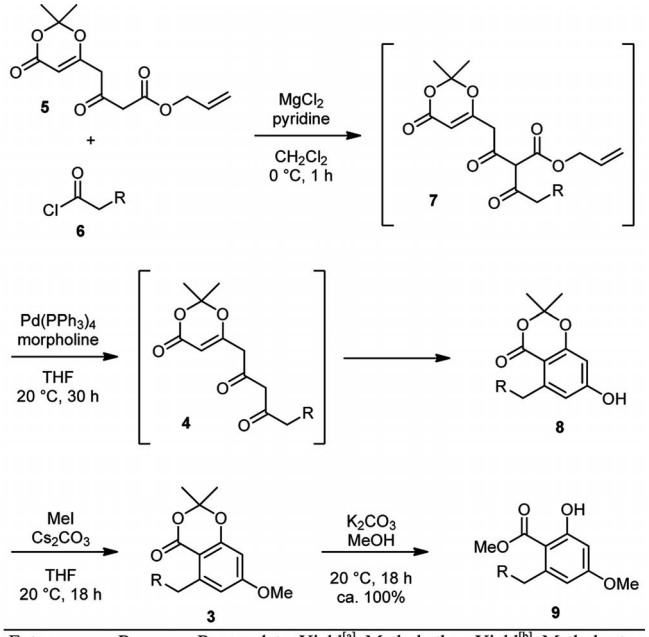
significant improvement to previously reported multistep methods.[13b–13d,14] Phenol methylation of **8a**–**g** was carried out by using iodomethane and cesium carbonate to afford the corresponding ethers (91–96%). Attempts to cyclize benzylresorcylates **3** directly to anthrones **10** were not successful, probably due to side reactions with the by-product acetone. Thus, resorcylates **3a**–**g** were transesterified to provide methyl esters **9a**–**g** by using methanolic potassium carbonate in quantitative yields.

Table 1. Synthesis of 6-benzylresorcylates **9a**–**g**.

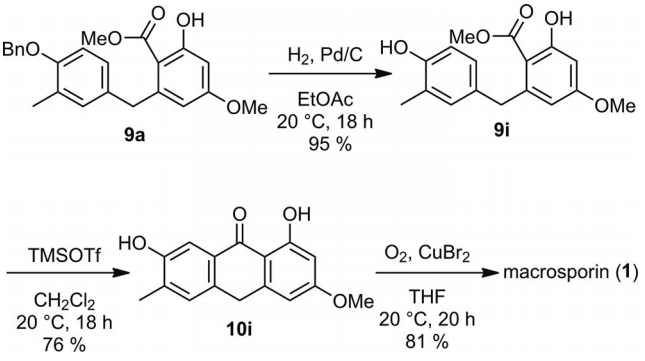


Entry	R	Resorcylate	Yield[a]	Methyl ether	Yield[b]	Methyl ester
1	BnO	**8a**[c]	72 %	**3a**	95 %	**9a**
2	MeO	**8b**	68 %	**3b**	95 %	**9b**
3	MeO	**8c**	74 %	**3c**	94 %	**9c**
4	OMe	**8d**	73 %	**3d**	91 %	**9d**
5	MeO, MeO	**8e**	74 %	**3e**	93 %	**9e**
6	OMe, OMe	**8f**	61 %	**3f**	96 %	**9f**
7	OMe, MeO	**8g**	62 %	**3g**	93 %	**9g**

[a] Isolated yield over two steps from **5**. [b] Isolated yield. [c] Acyl chloride **6a** was prepared as described in ref.[15]

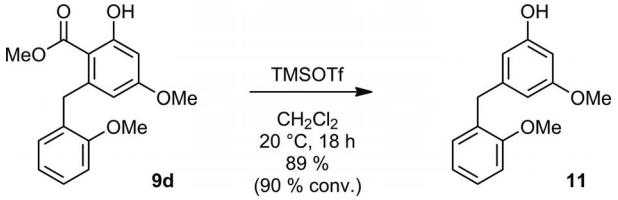
Initial attempts to cyclize resorcylates **9** to anthrones **10** catalyzed by Lewis acids were unsuccessful, as was the reaction in concentrated sulfuric acid. However, heating in polyphosphoric acid (PPA)[17] gave anthrones **10b**–**h** in moderate yields (42–63%, Table 2). As could be expected for a Friedel–Crafts-type reaction, yields were significantly higher for substrates with electron-donating substituents in positions *ortho* and/or *para* to the reacting arene carbon atom. Finally, oxidation with cerium ammonium nitrate (CAN)[17] gave 9,10-anthraquinones **2** in good yields (74–88%).

The cyclization of 6-benzylresorcylates to anthrones in PPA worked well for methyl-protected phenols. It failed, however, for benzyl-protected phenol **9a** and led instead only to decomposition. Deprotection by hydrogenation using Pd/C gave phenol **9i** (95%, Scheme 2). Attempts to form anthrone **10i** from this compound by heating in PPA were again unsuccessful. To solve this problem, we examined other methods of cyclization and found that trimethylsilyl triflate in dichloromethane also catalyzed the desired *C*-acylation. These slightly milder reaction conditions gave anthrone **10i** in 76% yield. With PPA, phenol phosphorylation is likely to occur, while we assume that trimethylsilyl triflate gave an intermediate aryl trimethylsilyl ether, which appears to be beneficial for the reaction. Although resorcylates **9b**–**g** also contain unprotected phenol units, these seem to be less reactive, presumably due to hydrogen bonding with the adjacent carbonyl group. To our disappointment, attempted oxidation of anthrone **10i** with CAN to generate the corresponding 9,10-anthraquinone **1** gave intractable mixtures of products, again most likely due to side reactions involving the unprotected phenol on C-7. This problem was solved by the use of cupric bromide and oxygen instead,[18] giving macrosporin **1** in 81% yield. The analytical data for synthetically produced **1** are in full agreement with reported values for the isolated natural product.[4a,6,9a,9b]



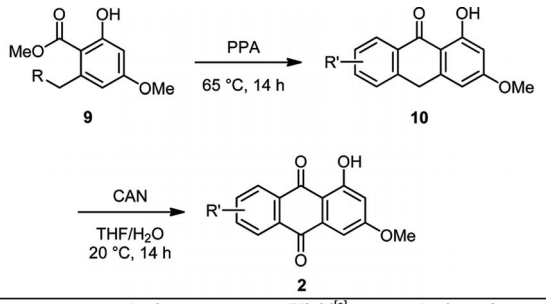
Scheme 2. Synthesis of macrosporin (**1**).

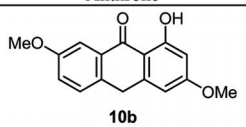
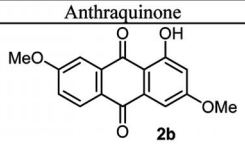
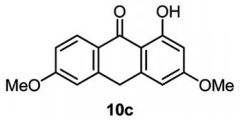
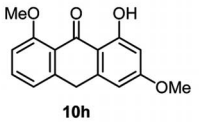
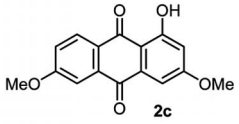
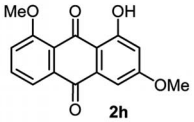
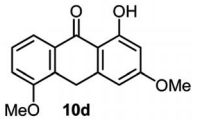
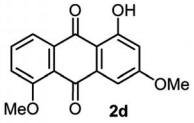
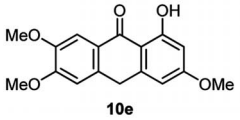
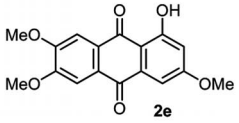
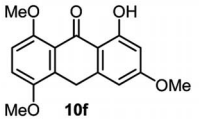
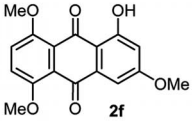
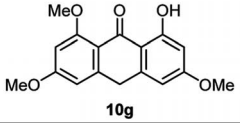
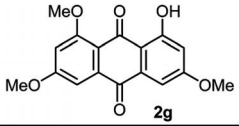
Interestingly, an attempt to apply the reaction conditions used for the cyclization of resorcylate **9i** to yield anthrone **10i** to substrate **9d** failed to afford anticipated anthrone **10d**.



Scheme 3. Reaction of resorcylate **9d** with trimethylsilyl triflate.

Table 2. Synthesis of 9,10-anthraquinones **2b**–**h**.



Entry	Methyl ester	Anthrone	Yield[a]	Anthraquinone	Yield[a]
1	**9b**	 **10b**	45 %	 **2b**	80 %
2	**9c**	 **10c** +  **10h**	50 %[b] + 11 %[b]	 **2c** +  **2h**	87 % + 85 %
3	**9d**	 **10d**	38 %	 **2d**	71 %
4	**9e**	 **10e**	63 %	 **2e**	88 %
5	**9f**	 **10f**	60 %	 **2f**	79 %
6	**9g**	 **10g**	58 %	 **2g**	74 %

[a] Isolated yield. [b] Reaction of **9c** gave a mixture of anthrones **10c** and **10h**, which were isolated and oxidized separately to anthraquinones **2c** and **2h** respectively.

In this case, a selective but incomplete deprotection and decarboxylation of the ester was observed, yielding benzylbenzene **11** (Scheme 3). Although trimethylsilyl triflate worked well on substrate **9i**, it seems to be even more substrate-sensitive than PPA, which in this case, gave 38% of cyclization product **10d**. Consequently, these two conditions complement each other, PPA being the appropriate reagent for most anthrones, and trimethylsilyl triflate being superior for electron-rich phenols.

Conclusions

We describe a versatile method for the synthesis of 6-benzylresorcylates and their transformation into 9,10-anthraquinones by intramolecular Friedel–Crafts acylation and oxidation. This strategy was applied in a seven-step synthesis of the fungal natural product macrosporin (**1**) in 40% overall yield.

Experimental Section

General Methods: All reactions were carried out in oven-dried glassware under argon by using commercially supplied solvents and reagents unless otherwise stated. Polyphosphoric acid (PPA) was bought from Sigma–Aldrich ($H_{n+2}P_nO_{3n+1}$, 115% H_3PO_4 basis). THF was redistilled from Na/Ph_2CO. Hexanes refers to petroleum spirit of boiling range 40–60 °C. Column chromatography was carried out on silica gel by using flash techniques (eluents are given in parentheses). Analytical TLC was performed with precoated sil-

ica gel F_{254} aluminum plates with visualization under UV light or by staining with acidic vanillin or anisaldehyde spray reagents. Melting points were measured with a hot stage apparatus. IR spectra were recorded neat. ^{1}H NMR spectra were recorded at 400 or 500 MHz, whereas ^{13}C NMR spectra were recorded at 100 or 125 MHz. Chemical shifts (δ) are quoted in ppm.

Synthesis of 9,10-Anthraquinones 2b–h and the Macrosporin Precursor 9a

General Procedure for the Synthesis of 5-Benzyl-7-hydroxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]-dioxin-4-ones 8a–g from Dioxinone Oxo Ester 5 and Acyl chlorides 6a–g: Pyridine (0.90 mL, 11.2 mmol, 3.0 equiv.) and $MgCl_2$ (355 mg, 3.73 mmol, 1.0 equiv.) were added with stirring to **5**[14] (1.00 g, 3.73 mmol, 1.0 equiv.) in CH_2Cl_2 (15 mL) at 0 °C. After 15 min, **6a**–**g**[15] (4.85 mmol, 1.3 equiv.) was added dropwise, and the resulting mixture was stirred at 0 °C for 1 h. Aqueous HCl (1 M; 40 mL) and CH_2Cl_2 (50 mL) were added and the phases separated. The aqueous layer was extracted with CH_2Cl_2 (2× 50 mL), and the combined organic layers were dried ($MgSO_4$) and the volatiles rotary-evaporated. The resultant **7a**–**g** was dissolved in THF (19 mL), and morpholine (0.97 mL, 11.2 mmol, 3.0 equiv.) was added. The solution was degassed by purging with argon for 15 min. $Pd(PPh_3)_4$ (86 mg, 74 μmol, 0.02 equiv.) was added at 20 °C, and, after 30 h, HCl (1 M; 40 mL) and CH_2Cl_2 (50 mL) were added and the phases separated. The aqueous layer was further extracted with Et_2O (3× 50 mL), and the combined organic layers were dried ($MgSO_4$) and the volatiles rotary-evaporated. The crude product was chromatographed (hexanes/THF, 19:1 → 9:1 → 6:1 → 4:1) to afford **8a**–**g**.

5-[4-(Benzyloxy)-3-methylbenzyl]-7-hydroxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (8a): White solid, 72% over 2 steps. R_f = 0.44 (hexanes/Et_2O, 1:1). M.p. 170–172 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1687, 1614, 1580, 1506, 1291, 1256, 1227, 1200, 1172 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.26 (s, 1 H, OH), 7.44 (d, J = 7.4 Hz, 2 H, 2 Ar-*H*), 7.34 (t, J = 7.3 Hz, 2 H, 2 Ar-*H*), 7.26 (t, J = 7.3 Hz, 1 H, Ar-*H*), 7.00 (d, J = 1.9 Hz, 1 H, Ar-*H*), 6.97 (dd, J = 8.3, 2.0 Hz, 1 H, Ar-*H*), 6.86 (d, J = 8.3 Hz, 1 H, Ar-*H*), 6.18 (d, J = 2.3 Hz, 1 H, Ar-*H*), 6.17 (d, J = 2.3 Hz, 1 H, Ar-*H*), 5.05 (s, 2 H, Ph-CH_2-OAr), 4.34 (s, 2 H, Ar-CH_2-Ar′), 2.21 (s, 3 H, Ar-CH_3), 1.61 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.2, 159.8 (2 C), 156.2, 149.7, 138.7, 133.0, 132.3, 128.9 (2 C), 128.3, 128.1, 127.7 (2 C), 127.0, 113.7, 111.8, 104.9, 104.7, 101.8, 70.3, 39.2, 25.5 (2 C), 16.4 ppm. HR-MS (ESI): calcd. for $C_{25}H_{25}O_5$ [M + H]$^+$ 405.1702; found 405.1703. $C_{25}H_{24}O_5$ (404.46): calcd. C 74.24, H 5.98; found C 74.24, H 5.97.

7-Hydroxy-5-(4-methoxybenzyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (8b): White solid, 68% over 2 steps. R_f = 0.32 (hexanes/Et_2O, 1:3). M.p. 122–124 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1687, 1611, 1577, 1281, 1268, 1241, 1204, 1167, 1054, 1039, 838 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.19 (s, 1 H, OH), 7.10 (d, J = 8.6 Hz, 2 H, 2 Ar-*H*), 6.80 (d, J = 8.7 Hz, 2 H, 2 Ar-*H*), 6.17 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.16 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.35 (s, 2 H, Ar-CH_2-Ar′), 3.73 (s, 3 H, OMe), 1.61 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.2, 159.9, 159.7, 159.1, 149.6, 133.0, 130.9 (2 C), 114.2 (2 C), 113.7, 104.9, 104.7, 101.8, 55.1, 39.1, 25.5 (2 C) ppm. HR-MS (ESI): calcd. for $C_{18}H_{19}O_5$ [M + H]$^+$: 315.1232; found 315.1235. $C_{18}H_{18}O_5$ (314.33): calcd. C 68.78, H 5.77; found C 68.69, H 5.74.

7-Hydroxy-5-(3-methoxybenzyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (8c): White solid, 74% over 2 steps. R_f = 0.37 (hexanes/Et_2O, 1:1). M.p. 124–126 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1692, 1611, 1583, 1489, 1449, 1390, 1355, 1296, 1265, 1209, 1168, 1052 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.23 (s, 1 H, OH), 7.14 (t, J = 7.8 Hz, 1 H, Ar-*H*), 6.79 (m$_c$, 1 H, Ar-*H*), 6.75 (d, J = 7.6 Hz, 1 H, Ar-*H*), 6.72 (dd, J = 2.4, 8.3 Hz, 1 H, Ar-*H*), 6.20 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.18 (d, J = 2.3 Hz, 1 H, Ar-*H*), 4.40 (s, 2 H, Ar-CH_2-Ar′), 3.72 (s, 3 H, OMe), 1.62 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.2, 160.8, 159.8 (2 C), 148.8, 142.7, 129.7, 122.2, 115.7, 113.8, 112.0, 105.0, 104.8, 102.0, 55.0, 40.0, 25.5 (2 C) ppm. HR-MS (ESI): calcd. for $C_{18}H_{19}O_5$ [M + H]$^+$ 315.1232; found 315.1230. $C_{18}H_{18}O_5$ (314.33): calcd. C 68.78, H 5.77; found C 68.65, H 5.78.

7-Hydroxy-5-(2-methoxybenzyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (8d): White solid, 73% over 2 steps. R_f = 0.22 (hexanes/THF, 3:1). M.p. 182–184 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1724, 1692, 1611, 1584, 1493, 1447, 1284, 1268, 1243, 1205, 1165, 1107, 104 8, 1027, 832, 752, 718, 680 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.12 (s, 1 H, OH), 7.17 (ddd, J = 1.7, 8.1, 8.2 Hz, 1 H, Ar-*H*), 7.05 (dd, J = 1.6, 7.4 Hz, 1 H, Ar-*H*), 6.92 (d, J = 8.2 Hz, 1 H, Ar-*H*), 6.83 (ddd, J = 1.0, 7.6, 7.8 Hz, 1 H, Ar-*H*), 6.15 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.07 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4. (s, 2 H, Ar-CH_2-Ar′), 3.75 (s, 3 H, OMe), 1.64 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.1, 159.8, 159.7, 158.6, 149.0, 131.3, 129.5, 128.1, 120.9, 113.0, 111.0, 105.0, 104.8, 101.7, 55.4, 34.4, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{18}H_{19}O_5$ [M + H]$^+$ 315.1232; found 315.1233. $C_{18}H_{18}O_5$ (314.33): calcd. C 68.78, H 5.77; found C 68.83, H 5.79.

5-(3,4-Dimethoxybenzyl)-7-hydroxy-2,2-dimethyl-4*H*-benzo[*d*]-[1,3]dioxin-4-one (8e): White solid, 74% over 2 steps. R_f = 0.29 (hexanes/Et_2O/CH_2Cl_2, 2:1:1). M.p. 150–152 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1722, 1695, 1613, 1586, 1514, 1448, 1291, 1263, 1208, 1168, 1140, 1028 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.20 (s, 1 H, OH), 6.81 (s, 1 H, Ar-*H*), 6.80 (d, J = 8.0 Hz, 1 H, Ar-*H*), 6.70 (dd, J = 1.9, 8.2 Hz, 1 H, Ar-*H*), 6.16 (s, 2 H, 2 Ar-*H*), 4.35 (s, 2 H, Ar-CH_2-Ar′), 3.74 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 1.62 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.2, 159.8 (2 C), 150.5, 149.7, 149.0, 133.6, 122.0, 114.4, 113.5, 112.8, 104.9, 104.7, 101.8, 56.0, 55.9, 39.6, 25.5 (2 C) ppm. HR-MS (ESI): calcd. for $C_{19}H_{21}O_6$ [M + H]$^+$ 345.1338; found 345.1354. $C_{19}H_{20}O_6$ (344.36): calcd. C 66.27, H 5.85; found C 66.17, H 5.78.

5-(2,5-Dimethoxybenzyl)-7-hydroxy-2,2-dimethyl-4*H*-benzo[*d*]-[1,3]dioxin-4-one (8f): White solid, 61% over 2 steps. R_f = 0.48 (hexanes/Et_2O/CH_2Cl_2, 2:1:1). M.p. 197–199 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1724, 1692, 1611, 1584, 1498, 1447, 1432, 1269, 1224, 1166, 1046, 1027, 857, 805, 715 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.12 (s, 1 H, OH), 6.83 (d, J = 8.7 Hz, 1 H, Ar-*H*), 6.72 (dd, J = 3.1, 8.6 Hz, 1 H, Ar-*H*), 6.69 (d, J = 3.0 Hz, 1 H, Ar-*H*), 6.15 (d, J = 2.3 Hz, 1 H, Ar-*H*), 6.09 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.38 (s, 2 H, Ar-CH_2-Ar′), 3.70 (s, 3 H, OMe), 3.67 (s, 3 H, OMe), 1.64 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.1, 159.8, 159.7, 154.7, 152.8, 148.9, 130.5, 117.5, 113.0, 112.2, 111.9, 105.0, 104.9, 101.7, 55.9, 55.4, 34.4, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{19}H_{21}O_6$ [M + H]$^+$ 345.1338; found 345.1343. $C_{19}H_{20}O_6$ (344.36): calcd. C 66.27, H 5.85; found C 66.18, H 5.91.

5-(3,5-Dimethoxybenzyl)-7-hydroxy-2,2-dimethyl-4*H*-benzo[*d*]-[1,3]dioxin-4-one (8g): White solid, 62% over 2 steps. R_f = 0.36 (hexanes/Et_2O, 1:1). M.p. 154–156 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1694, 1610, 1594, 1459, 1353, 1290, 1205, 1157, 1059, 839 cm^{-1}. ^{1}H NMR (400 MHz, [D$_8$]THF, 25 °C): δ = 9.21 (s, 1 H, OH), 6.38 (d, J = 2.3 Hz, 2 H, 2 Ar-*H*), 6.30 (t, J = 2.3 Hz, 1 H, Ar-*H*), 6.20 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.17 (d, J = 2.3 Hz, 1 H, Ar-*H*), 4.36 (s, 2 H, Ar-CH_2-Ar′), 3.70 (s, 6 H, 2 OMe), 1.63 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, [D$_8$]THF, 25 °C): δ = 164.2, 161.9 (2 C), 159.8 (2 C), 148.8, 143.2, 113.6, 108.0 (2 C), 105.0, 104.8, 101.9, 98.7, 55.1 (2 C), 40.2, 25.5 (2 C) ppm. HR-MS (ESI): calcd. for $C_{19}H_{21}O_6$ [M

+ H]$^+$ 345.1338; found 345.1339. $C_{19}H_{20}O_6$ (344.36): calcd. C 66.27, H 5.85; found C 66.19, H 5.92.

General Procedure for the Synthesis of 5-Benzyl-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]-dioxin-4-ones 3a–g from 5-Benzyl-7-hydroxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]-dioxin-4-ones 8a–g: Cs_2CO_3 (2.15 g, 6.60 mmol, 3.0 equiv.) and MeI (0.41 mL, 6.60 mmol, 3.0 equiv.) were added with stirring to **8a**–**g** (2.20 mmol, 1.0 equiv.) in THF (22 mL) at 20 °C. After 18 h, aqueous HCl (1 M: 40 mL) and Et_2O (50 mL) were added and the phases separated. The aqueous layer was further extracted with Et_2O (2× 50 mL), and the combined organic layers were dried ($MgSO_4$) and the volatiles rotary-evaporated. The crude product was chromatographed on silica (hexanes/Et_2O, 3:1) to obtain **3a**–**g**.

5-[4-(Benzyloxy)-3-methylbenzyl]-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3a): Colorless oil, 95%. R_f = 0.62 (hexanes/Et_2O, 1:1). IR: $\tilde{\nu}$ = 1726, 1610, 1577, 1503, 1279, 1156, 1132, 1059 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.44 (d, J = 7.3 Hz, 2 H, 2 Ar-*H*), 7.38 (pt, J = 7.4 Hz, 2 H, 2 Ar-*H*), 7.31 (tt, J = 2.4, 7.2 Hz, 1 H, Ar-*H*), 7.00 (d, J = 1.8 Hz, 1 H, Ar-*H*), 6.97 (dd, J = 1.9, 8.3 Hz, 1 H, Ar-*H*), 6.80 (d, J = 8.2 Hz, 1 H, Ar-*H*), 6.37 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.31 (d, J = 2.5 Hz, 1 H, Ar-*H*), 5.05 (s, 2 H, Ph-CH_2-OAr), 4.39 (s, 2 H, Ar-CH_2-Ar′), 3.77 (s, 3 H, OMe), 2.24 (s, 3 H, Ar-CH_3), 1.68 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 164.8, 160.2, 159.1, 155.3, 148.7, 137.6, 132.0, 131.6, 128.4 (2 C), 127.7, 127.3, 127.1 (2 C), 126.9, 112.9, 111.4, 104.9 (2 C), 99.2, 69.9, 55.5, 38.8, 25.6 (2 C), 16.4 ppm. HR-MS (ESI): calcd. for $C_{26}H_{27}O_5$ [M + H]$^+$ 419.1858; found 419.1868. $C_{26}H_{26}O_5$ (418.48): calcd. C 74.62, H 6.26; found C 74.58, H 6.33.

7-Methoxy-5-(4-methoxybenzyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3b): White solid, 95%. R_f = 0.65 (hexanes/Et_2O, 1:1). M.p. 72–74 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1727, 1611, 1577, 1512, 1435, 1389, 1280, 1247, 1204, 1157, 1059, 1041 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.12 (d, J = 8.6 Hz, 2 H, 2 Ar-*H*), 6.82 (d, J = 8.7 Hz, 2 H, 2 Ar-*H*), 6.35 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.30 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.41 (s, 2 H, Ar-CH_2-Ar′), 3.78 (s, 3 H, OMe), 3.77 (s, 3 H, OMe), 1.67 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 164.8, 160.2, 159.2, 158.0, 148.6, 132.1 (2 C), 130.2, 113.8 (2 C), 112.8, 104.9, 104.8, 99.3, 55.5, 55.2, 38.8, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{19}H_{21}O_5$ [M + H]$^+$ 329.1389; found 329.1404. $C_{19}H_{20}O_5$ (328.36): calcd. C 69.50, H 6.14; found C 69.48, H 6.23.

7-Methoxy-5-(3-methoxybenzyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3c): Colourless oil, 94%. R_f = 0.24 (hexanes/Et_2O, 3:1). IR: $\tilde{\nu}$ = 1723, 1609, 1576, 1488, 1433, 1389, 1329, 1277, 1261, 1203, 1155, 1056 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.19 (t, J = 7.8 Hz, 1 H, Ar-*H*), 6.80–6.73 (m, 3 H, Ar-*H*), 6.38 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.32 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.46 (s, 2 H, Ar-CH_2-Ar′), 3.77 (s, 6 H, 2 OMe), 1.68 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 164.8, 160.2, 159.6, 159.2, 147.7, 141.6, 129.3, 121.6, 114.9, 113.0, 111.5, 104.9 (2 C), 99.4, 55.5, 55.1, 39.6, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{19}H_{21}O_5$ [M + H]$^+$ 329.1389; found 329.1377. $C_{19}H_{20}O_5$ (328.36): calcd. C 69.50, H 6.14; found C 69.41, H 6.05.

7-Methoxy-5-(2-methoxybenzyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3d): White solid, 91%. R_f = 0.71 (hexanes/Et_2O, 1:1). M.p. 118–120 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1723, 1610, 1576, 1493, 1434, 1279, 1243, 1202, 1154, 1057, 1029, 754 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.21 (ddd, J = 1.7, 7.9, 7.9 Hz, 1 H, Ar-*H*), 7.05 (dd, J = 1.4, 7.7 Hz, 1 H, Ar-*H*), 6.89–6.85 (m, 2 H, 2 Ar-*H*), 6.30–6.29 (m, 2 H, 2 Ar-*H*), 4.48 (s, 2 H, Ar-CH_2-Ar′), 3.79 (s, 3 H, OMe), 3.73 (s, 3 H, OMe), 1.71 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 164.7, 160.2, 158.9, 157.5, 148.1, 130.4, 128.5, 127.6, 120.5, 112.2, 110.4, 105.1, 104.7, 99.1, 55.3 (2 C), 33.8, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{19}H_{21}O_5$ [M + H]$^+$ 329.1389; found 329.1384. $C_{19}H_{20}O_5$ (328.36): calcd. C 69.50, H 6.14; found C 69.38, H 6.16.

5-(3,4-Dimethoxybenzyl)-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3e): White solid, 93%. R_f = 0.32 (hexanes/Et_2O, 1:1). M.p. 108–110 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1720, 1609, 1575, 1278, 1258, 1202, 1153, 1139, 1057, 1043, 1026, 727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 6.79 (d, J = 1.3 Hz, 1 H, Ar-*H*), 6.78 (d, J = 7.0 Hz, 1 H, Ar-*H*), 6.72 (dd, J = 1.9, 8.3 Hz, 1 H, Ar-*H*), 6.36 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.30 (d, J = 2.6 Hz, 1 H, Ar-*H*), 4.41 (s, 2 H, Ar-CH_2-Ar′), 3.84 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 1.68 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9, 160.2, 159.2, 148.8, 148.3, 147.4, 132.6, 121.1, 112.8, 112.7, 111.1, 104.9, 104.8, 99.3, 55.83, 55.79, 55.5, 39.2, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{20}H_{23}O_6$ [M + H]$^+$ 359.1495; found 359.1483. $C_{20}H_{22}O_6$ (358.39): calcd. C 67.03, H 6.19; found C 66.94, H 6.16.

5-(2,5-Dimethoxybenzyl)-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3f): Colorless oil, 96%. R_f = 0.60 (hexanes/Et_2O, 1:1). IR: $\tilde{\nu}$ = 1726, 1611, 1577, 1499, 1434, 1389, 1280, 1226, 1157, 1056, 855, 715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 6.80 (d, J = 8.8 Hz, 1 H, Ar-*H*), 6.72 (dd, J = 3.1, 8.8 Hz, 1 H, Ar-*H*), 6.63 (d, J = 3.0 Hz, 1 H, Ar-*H*), 6.31 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.29 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.44 (s, 2 H, Ar-CH_2-Ar′), 3.75 (s, 3 H, OMe), 3.73 (s, 3 H, OMe), 3.71 (s, 3 H, OMe), 1.70 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 164.8, 160.2, 158.9, 153.5, 151.9, 147.7, 129.8, 116.7, 112.4, 111.5 (2 C), 105.1, 104.8, 99.2, 56.1, 55.6, 55.3, 33.9, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{20}H_{23}O_6$ [M + H]$^+$ 359.1495; found 359.1500. $C_{20}H_{22}O_6$ (358.39): calcd. C 67.03, H 6.19; found C 66.93, H 6.21.

5-(3,5-Dimethoxybenzyl)-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (3g): White solid, 93%. R_f = 0.53 (hexanes/Et_2O, 1:1). M.p. 100–102 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1725, 1608, 1577, 1459, 1430, 1328, 1280, 1203, 1155, 1059 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 6.38 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.36 (d, J = 2.2 Hz, 2 H, 2 Ar-*H*), 6.32–6.30 (m, 2 H, 2 Ar-*H*), 4.41 (s, 2 H, Ar-CH_2-Ar′), 3.77 (s, 3 H, OMe), 3.75 (s, 6 H, 2 OMe), 1.68 [s, 6 H, C(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 164.8, 160.7 (2 C), 160.2, 159.1, 147.4, 142.4, 113.0, 107.3 (2 C), 104.9, 104.8, 99.4, 98.1, 55.5, 55.2 (2 C), 39.7, 25.6 (2 C) ppm. HR-MS (ESI): calcd. for $C_{20}H_{23}O_6$ [M + H]$^+$ 359.1495; found 359.1513. $C_{20}H_{22}O_6$ (358.39): calcd. C 67.03, H 6.19; found C 66.93, H 6.21.

General Procedure for the Synthesis of Methyl 6-Benzyl-2-hydroxy-4-methoxybenzoates 9a–g from 5-Benzyl-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]-dioxin-4-ones 3a–g: K_2CO_3 (829 mg, 6.00 mmol, 3.0 equiv.) was added with stirring to **3a**–**g** (2.00 mmol, 1.0 equiv.) in dry MeOH (20 mL) at 20 °C. After 18 h, the solvent was evaporated, and Et_2O (60 mL) and HCl (1 M; 40 mL) were added to the resultant solid. The phases were separated, and the aqueous layer was further extracted with Et_2O (3× 50 mL). The combined organic extracts were dried ($MgSO_4$) and the volatiles rotary-evaporated to obtain **9a**–**g** in quantitative yields.

5-[4-(Benzyloxy)-3-methylbenzyl]-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (9a): White solid. R_f = 0.61 (hexanes/Et_2O, 3:1). M.p. 76–78 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1650, 1615, 1576, 1503, 1434, 1327, 1252, 1204, 1158, 1131 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.85 (s, 1 H, OH), 7.50 (d, J = 7.3 Hz, 2 H, 2 Ar-*H*), 7.43 (pt, J = 7.3 Hz, 2 H, 2 Ar-*H*), 7.36 (t, J = 7.2 Hz, 1 H, Ar-*H*), 6.96 (d, J = 1.7 Hz, 1 H, Ar-*H*), 6.90 (dd, J = 2.0, 8.3 Hz, 1 H, Ar-*H*), 6.84 (d, J = 8.3 Hz, 1 H, Ar-*H*), 6.45

(d, J = 2.6 Hz, 1 H, Ar-*H*), 6.33 (d, J = 2.6 Hz, 1 H, Ar-*H*), 5.09 (s, 2 H, Ph-CH_2-OAr), 4.23 (s, 2 H, Ar-CH_2-Ar′), 3.84 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 2.32 (s, 3 H, H, Ar-CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.6, 165.7, 163.9, 155.0, 145.5, 137.5, 132.6, 130.9, 128.3 (2 C), 127.6, 127.0 (2 C), 126.7, 126.4, 111.9, 111.3, 104.9, 98.9, 69.8, 55.1, 51.6, 41.1, 16.3 ppm. HR-MS (ESI): calcd. for $C_{24}H_{25}O_5$ $[M + H]^+$ 393.1702; found 393.1708. $C_{24}H_{24}O_5$ (392.44): calcd. C 73.45, H 6.16; found C 73.36, H 6.18.

Methyl 2-Hydroxy-4-methoxy-6-(4-methoxybenzyl)benzoate (9b): White solid. R_f = 0.45 (hexanes/Et_2O, 3:1). M.p. 48–50 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1653, 1615, 1577, 1511, 1435, 1329, 1303, 1250, 1219, 1204, 1158, 1046 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.78 (s, 1 H, OH), 7.00 (d, J = 8.3 Hz, 2 H, 2 Ar-*H*), 6.82 (d, J = 8.4 Hz, 2 H, 2 Ar-*H*), 6.40 (d, J = 2.1 Hz, 1 H, Ar-*H*), 6.27 (d, J = 1.9 Hz, 1 H, Ar-*H*), 4.20 (s, 2 H, Ar-CH_2-Ar′), 3.79 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.77 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.6, 165.7, 163.9, 157.7, 145.3, 132.7 129.2 (2 C), 113.6 (2 C), 111.8, 104.8, 99.0, 55.1, 55.0, 51.6, 41.1 ppm. HR-MS (ESI): calcd. for $C_{17}H_{19}O_5$ $[M + H]^+$ 303.1232; found 303.1236. $C_{17}H_{18}O_5$ (302.32): calcd. C 67.54, H 6.00; found C 67.39, H 6.00.

Methyl 2-Hydroxy-4-methoxy-6-(3-methoxybenzyl)benzoate (9c): White solid. R_f = 0.65 (hexanes/Et_2O, 3:1). M.p. 48–52 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1654, 1611, 1578, 1489, 1436, 1329, 1259, 1203, 1159, 1048, 957, 775 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.79 (s, 1 H, OH), 7.19 (t, J = 7.9 Hz, 1 H, Ar-*H*), 6.73 (dd, J = 2.3, 8.1 Hz, 1 H, Ar-*H*), 6.69 (d, J = 7.8 Hz, 1 H, Ar-*H*), 6.64 (m_c, 1 H, Ar-*H*), 6.41 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.30 (d, J = 2.6 Hz, 1 H, Ar-*H*), 4.24 (s, 2 H, Ar-CH_2-Ar′), 3.78 (s, 3 H, OMe), 3.77 (s, 3 H, OMe), 3.76 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.5, 165.7, 163.9, 159.5, 144.4, 142.4, 129.0, 120.7, 114.3 112.1, 110.7, 104.9, 99.1, 55.1, 54.9, 51.5, 42.0 ppm. HR-MS (ESI): calcd. for $C_{17}H_{19}O_5$ $[M + H]^+$ 303.1232; found 303.1231. $C_{17}H_{18}O_5$ (302.32): calcd. C 67.54, H 6.00; found C 67.62, H 6.01.

Methyl 2-Hydroxy-4-methoxy-6-(2-methoxybenzyl)benzoate (9d): White solid. R_f = 0.60 (hexanes/Et_2O, 3:1). M.p. 76–78 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1649, 1614, 1575, 1433, 1325, 1241, 1222, 1202, 1155, 1047, 752 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.76 (s, 1 H, OH), 7.19 (ddd, J = 3.2, 5.9, 8.4 Hz, 1 H, Ar-*H*), 6.88 (d, J = 8.0 Hz, 1 H, Ar-*H*), 6.84–6.82 (m, 2 H, 2 Ar-*H*), 6.38 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.18 (d, J = 2.7 Hz, 1 H, Ar-*H*), 4.23 (s, 2 H, Ar-CH_2-Ar′), 3.84 (s, 3 H, OMe), 3.77 (s, 3 H, OMe), 3.74 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.9, 165.6, 164.0, 157.0, 145.1, 129.3 (2 C), 127.2, 120.5, 111.5, 110.0, 105.3, 99.0, 55.3, 55.2, 51.6, 35.9 ppm. HR-MS (ESI): calcd. for $C_{17}H_{19}O_5$ $[M + H]^+$ 303.1232; found 303.1244. $C_{17}H_{18}O_5$ (302.32): calcd. C 67.54, H 6.00; found C 67.66, H 5.99.

Methyl 2-(3,4-Dimethoxybenzyl)-6-hydroxy-4-methoxybenzoate (9e): White solid. R_f = 0.24 (hexanes/Et_2O, 3:1). M.p. 83–85 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1650, 1615, 1576, 1513, 1435, 1328, 1252, 1220, 1203, 1158, 1141, 1028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.71 (s, 1 H, OH), 6.74 (d, J = 8.2 Hz, 1 H, Ar-*H*), 6.61 (d, J = 1.9 Hz, 1 H, Ar-*H*), 6.56 (dd, J = 1.9, 8.2 Hz, 1 H, Ar-*H*), 6.35 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.21 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.16 (s, 2 H, Ar-CH_2-Ar′), (s, 2 H, Ar-CH_2-Ar′), 3.80 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 3.73 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.4, 165.5, 163.8, 148.6, 147.0, 145.0, 133.1, 120.3, 111.8, 111.6, 111.0, 104.7, 98.9, 55.62, 55.59, 55.0, 51.5, 41.3 ppm. HR-MS (ESI): calcd. for $C_{18}H_{21}O_6$ $[M + H]^+$ 333.1338; found 333.1321. $C_{18}H_{20}O_6$ (332.35): calcd. C 65.05, H 6.07; found C 65.05, H 6.12.

Methyl 2-(2,5-Dimethoxybenzyl)-6-hydroxy-4-methoxybenzoate (9f): White solid. R_f = 0.34 (hexanes/Et_2O, 3:1). M.p. 72–74 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1651, 1615, 1578, 1499, 1434, 1327, 1253, 1216, 1158, 1113, 1048, 1027 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.76 (s, 1 H, OH), 6.80 (d, J = 8.8 Hz, 1 H, Ar-*H*), 6.69 (dd, J = 3.1, 8.8 Hz, 1 H, Ar-*H*), 6.41 (d, J = 3.0 Hz, 1 H, Ar-*H*), 6.37 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.19 (d, J = 2.6 Hz, 1 H, Ar-*H*), 4.20 (s, 2 H, Ar-CH_2-Ar′), 3.79 (s, 3 H, OMe), 3.77 (s, 3 H, OMe), 3.74 (s, 3 H, OMe), 3.68 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.8, 165.7, 164.0, 153.6, 151.4, 144.8, 130.7, 116.2, 111.6, 110.8, 110.7, 105.2, 99.0, 55.9, 55.6, 55.2, 51.7, 36.1 ppm. HR-MS (ESI): calcd. for $C_{18}H_{21}O_6$ $[M + H]^+$ 333.1338; found 333.1327. $C_{18}H_{20}O_6$ (332.35): calcd. C 65.05, H 6.07; found C 64.96, H 6.11.

Methyl 2-(3,5-Dimethoxybenzyl)-6-hydroxy-4-methoxybenzoate (9g): White solid. R_f = 0.41 (hexanes/Et_2O, 3:1). M.p. 72–74 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1650, 1606, 1594, 1430, 1327, 1252, 1203, 1156, 1066, 830 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.75 (s, 1 H, OH), 6.39 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.30 (t, J = 2.2 Hz, 1 H, Ar-*H*), 6.28 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.24 (d, J = 2.1 Hz, 2 H, 2 Ar-*H*), 4.18 (s, 2 H, Ar-CH_2-Ar′), 3.78 (s, 6 H, 2 OMe), 3.74 (s, 6 H, 2 OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.5, 165.7, 163.9, 160.6 (2 C), 144.3, 143.2, 112.1, 106.6 (2 C), 104.9, 99.2, 97.5, 55.2, 55.1 (2 C), 51.6, 42.2 ppm. HR-MS (ESI): calcd. for $C_{18}H_{21}O_6$ $[M + H]^+$ 333.1338; found 333.1335. $C_{18}H_{20}O_6$ (332.35): calcd. C 65.05, H 6.07; found C 64.96, H 6.02.

General Procedure for the Synthesis of 1-Hydroxy-3-methoxyanthracen-9(10*H*)-ones 10b–h from Methyl 6-Benzyl-2-hydroxy-4-methoxybenzoates 9b–g: 9b–g (1.00 mmol) was dissolved in polyphosphoric acid (PPA, 3.5 mL) and heated with stirring to 65 °C for 14 h. After cooling to 20 °C, iced water (35 mL) was added carefully. The aqueous layer was extracted with CH_2Cl_2 (3× 50 mL), and the combined organic layers were dried (Na_2SO_4) and the volatiles rotary-evaporated. The residue was chromatographed (hexanes/CH_2Cl_2, 3:1 → 1:1 → CH_2Cl_2) to provide **10b–h**.

1-Hydroxy-3,7-dimethoxyanthracen-9(10*H*)-one (10b): Yellow solid, 45%. R_f = 0.68 (CH_2Cl_2). M.p. 136–138 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1599, 1578, 1500, 1357, 1322, 1298, 1280, 1229, 1204, 1147 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.37 (s, 1 H, OH), 7.74 (d, J = 2.8 Hz, 1 H, Ar-*H*), 7.29 (d, J = 8.5 Hz, 1 H, Ar-*H*), 7.15 (dd, J = 2.8, 8.5 Hz, 1 H, Ar-*H*), 6.44 (m_c, 1 H, Ar-*H*), 6.40 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.20 (s, 2 H, Ar-CH_2-Ar′), 3.90 (s, 3 H, OMe), 3.85 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 187.8, 165.7, 165.3, 158.6, 144.0, 132.8, 132.1, 129.3, 121.8, 110.9, 108.4, 105.9, 99.2, 55.5, 55.4, 32.0 ppm. HR-MS (ESI): calcd. for $C_{16}H_{13}O_4$ $[M - H]^+$ 269.0814; found 269.0819.

1-Hydroxy-3,6-dimethoxyanthracen-9(10*H*)-one (10c): Yellow solid, 50% (isolated along with 11% of **10h** and separated from this compound by chromatography). R_f = 0.65 (CH_2Cl_2). M.p. 158–160 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1598, 1500, 1364, 1303, 1250, 1155, 1022, 818, 673 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.52 (s, 1 H, OH), 8.21 (d, J = 8.8 Hz, 1 H, Ar-*H*), 6.94 (dd, J = 2.5, 8.8 Hz, 1 H, Ar-*H*), 6.80 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.39 (d, J = 2.2 Hz, 1 H, Ar-*H*), 6.37 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.20 (s, 2 H, Ar-CH_2-Ar′), 3.88 (s, 3 H, OMe), 3.84 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 187.2, 165.6, 165.0, 163.4, 143.2, 142.7, 129.2, 124.6, 113.9, 111.8, 110.7, 105.8, 99.2, 55.5, 55.4, 32.9 ppm. HR-MS (ESI): calcd. for $C_{16}H_{15}O_4$ $[M + H]^+$ 271.0970; found 271.0984.

1-Hydroxy-3,5-dimethoxyanthracen-9(10*H*)-one (10d): Yellow solid, 38%. R_f = 0.54 (CH_2Cl_2). M.p. 158–162 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1579, 1315, 1285, 1154, 1085, 955, 820, 792, 709 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.40 (s, 1 H, OH), 7.90 (d, J = 8.4 Hz, 1 H, Ar-*H*), 7.40 (pt, J = 8.0 Hz, 1 H, Ar-*H*), 7.08 (dd, J = 2.8, 8.5 Hz, 1 H, Ar-*H*), 6.49 (m_c, 1 H, Ar-*H*), 6.40 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.12 (s, 2 H, Ar-CH_2-Ar′), 3.93 (s, 3 H, OMe), 3.86 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.1, 165.6, 165.4, 156.2, 143.8, 132.0, 129.3, 127.3, 118.5, 113.5, 110.9, 106.2, 99.2, 55.6, 55.5, 27.7 ppm. HR-MS (ESI): calcd. for $C_{16}H_{15}O_4$ $[M + H]^+$ 271.0970; found 271.0976.

1-Hydroxy-3,6,7-trimethoxyanthracen-9(10*H*)-one (10e): Yellow solid, 63%. R_f = 0.60 ($CHCl_3$/EtOH, 99:1). M.p. 196–200 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1628, 1594, 1579, 1419, 1380, 1299, 1272, 1224, 1201, 1152, 1109, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.48 (s, 1 H, OH), 7.72 (s, 1 H, Ar-*H*), 6.80 (s, 1 H, Ar-*H*), 6.44–6.43 (m, 1 H, Ar-*H*), 6.41 (d, J = 2.3 Hz, 1 H, Ar-*H*), 4.21 (s, 2 H, Ar-CH_2-Ar′), 3.98 (s, 3 H, OMe), 3.97 (s, 3 H, OMe), 3.86 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 187.2, 165.4, 164.9, 153.6, 148.5, 143.5, 135.1, 124.4, 110.6, 109.4, 107.8, 105.9, 99.2, 56.1, 56.0, 55.5, 32.4 ppm. HR-MS (ESI): calcd. for $C_{17}H_{17}O_5$ $[M + H]^+$ 301.1076; found 301.1073.

1-Hydroxy-3,5,8-trimethoxyanthracen-9(10*H*)-one (10f): Orange solid, 60%. R_f = 0.42 ($CHCl_3$/EtOH, 99:1). M.p. 138–140 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1627, 1581, 1500, 1480, 1430, 1299, 1270, 1249, 1196, 1151, 1080, 972 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.58 (s, 1 H, OH), 7.05 (d, J = 9.1 Hz, 1 H, Ar-*H*), 6.90 (d, J = 9.1 Hz, 1 H, Ar-*H*), 6.44–6.42 (m, 1 H, Ar-*H*), 6.38 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.12 (s, 2 H, Ar-CH_2-Ar′), 3.95 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 3.84 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 188.9, 165.4, 164.9, 155.1, 149.7, 142.5, 131.4, 120.8, 114.9, 111.9, 110.3, 105.2, 99.3, 56.5, 55.8, 55.4, 28.3 ppm. HR-MS (ESI): calcd. for $C_{17}H_{17}O_5$ $[M + H]^+$ 301.1076; found 301.1075.

1-Hydroxy-3,6,8-trimethoxyanthracen-9(10*H*)-one (10g): Orange solid, 58%. R_f = 0.36 (CH_2Cl_2). M.p. 150–152 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1624, 1596, 1570, 1332, 1290, 1262, 1222, 1201, 1148, 1092 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.74 (s, 1 H, OH), 6.39 (d, J = 2.3 Hz, 1 H, Ar-*H*), 6.37 (d, J = 2.3 Hz, 1 H, Ar-*H*), 6.31 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.29–6.27 (m, 1 H, Ar-*H*), 4.15 (s, 2 H, Ar-CH_2-Ar′), 3.93 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.79 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 187.8, 165.3, 164.3, 164.0, 163.1, 145.5, 141.7, 114.2, 111.6, 104.6, 104.1, 99.3, 97.7, 56.0, 55.4, 55.3, 34.0 ppm. HR-MS (ESI): calcd. for $C_{17}H_{17}O_5$ $[M + H]^+$ 301.1076; found 301.1080.

1-Hydroxy-3,8-dimethoxyanthracen-9(10*H*)-one (10h): Orange solid, 11% (isolated along with 50% **10c** and separated from this compound by chromatography). R_f = 0.35 (CH_2Cl_2). M.p. 122–124 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1623, 1594, 1572, 1498, 1430, 1383, 1294, 1261, 1205, 1164, 1146, 1082 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.55 (s, 1 H, OH), 7.47 (dd, J = 7.7, 8.4 Hz, 1 H, Ar-*H*), 6.95 (dd, J = 0.8, 7.8 Hz, 1 H, Ar-*H*), 6.92 (d, J = 8.4 Hz, 1 H, Ar-*H*), 6.36 (s, 2 H, 2× Ar-*H*), 4.25 (s, 2 H, Ar-CH_2-Ar′), 3.99 (s, 3 H, OMe), 3.82 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 188.7, 165.5, 164.8, 161.3, 143.3, 142.2, 134.0, 120.4, 120.3, 112.0, 110.0, 104.9, 99.3, 56.1, 55.4, 33.6 ppm. HR-MS (ESI): calcd. for $C_{16}H_{15}O_4$ $[M + H]^+$ 271.0970; found 271.0971.

General Procedure for the Synthesis of 1-Hydroxy-3-methoxyanthracene-9,10-diones 2b–h from 1-Hydroxy-3-methoxyanthracen-9(10*H*)-ones 10b–h: Water (2.0 mL) and cerium ammonium nitrate (CAN, 438 mg, 0.80 mmol, 4.0 equiv.) were added with stirring to **10b–h** (0.20 mmol) in THF (8.0 mL) at 20 °C. After 14 h, the solvents were evaporated. The resultant solids were chromatographed ($CHCl_3$/hexanes, 1:1 → 3:1 → $CHCl_3$/EtOH, 99:1) to render **2b–h**.

1-Hydroxy-3,7-dimethoxyanthracene-9,10-dione (2b): Yellow solid, 80%. R_f = 0.80 ($CHCl_3$/EtOH, 99:1). M.p. 206–208 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1588, 1571, 1337, 1284, 1214, 1101, 961, 837, 801, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 12.83 (s, 1 H, OH), 8.22 (d, J = 8.7 Hz, 1 H, Ar-*H*), 7.72 (d, J = 2.6 Hz, 1 H, Ar-*H*), 7.37 (d, J = 2.5 Hz, 1 H, Ar-*H*), 7.24 (dd, J = 2.7, 8.7 Hz, 1 H, Ar-*H*), 6.68 (d, J = 2.5 Hz, 1 H, Ar-*H*), 3.99 (s, 3 H, OMe), 3.94 (s, 3 H, OMe) ppm; the ^1H NMR signal for the OH proton matches the value reported in the literature.[19] ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C): δ = 186.8, 181.4, 166.6, 165.5, 164.7, 135.8, 135.5, 130.0, 127.3, 120.8, 111.1, 110.0, 107.7, 106.3, 56.0, 55.9 ppm. HR-MS (EI): calcd. for $C_{16}H_{12}O_5$ $[M]^+$ 284.0685; found 284.0669.

1-Hydroxy-3,6-dimethoxyanthracene-9,10-dione (2c): Yellow solid, 87%. R_f = 0.78 ($CHCl_3$/EtOH, 99:1). M.p. 198–200 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1626, 1591, 1448, 1380, 1283, 1217, 1152, 979, 830, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.00 (s, 1 H, OH), 8.23 (d, J = 8.7 Hz, 1 H, Ar-*H*), 7.70 (d, J = 2.7 Hz, 1 H, Ar-*H*), 7.36 (d, J = 2.6 Hz, 1 H, Ar-*H*), 7.26 (dd, J = 2.8, 8.6 Hz, 1 H, Ar-*H*), 6.70 (d, J = 2.8 Hz, 1 H, Ar-*H*), 3.98 (s, 3 H, OMe), 3.93 (s, 3 H, OMe) ppm; the ^1H NMR spectra match the data reported in the literature.[20] ^{13}C NMR (125 MHz, $CDCl_3$, 45 °C): δ = 186.2, 182.5, 166.0, 165.3, 164.5, 135.8, 135.3, 129.3, 127.0, 121.0, 110.7, 110.6, 107.6, 106.9, 56.0 (2 C) ppm. HR-MS (ESI): calcd. for $C_{16}H_{13}O_5$ $[M + H]^+$ 285.0763; found 285.0762.

1-Hydroxy-3,5-dimethoxyanthracene-9,10-dione (2d): Yellow solid, 71%. R_f = 0.70 ($CHCl_3$/EtOH, 99:1). M.p. 174–176 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1631, 1611, 1584, 1442, 1378, 1284, 1238, 1210, 1143, 968 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 12.77 (s, 1 H, OH), 7.97 (dd, J = 0.9, 7.5 Hz, 1 H, Ar-*H*), 7.73 (dd, J = 7.7, 8.4 Hz, 1 H, Ar-*H*), 7.34–7.32 (m, 2 H, 2 Ar-*H*), 6.66 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.05 (s, 3 H, OMe), 3.93 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 186.6, 181.7, 166.5, 164.9, 160.6, 136.6, 135.7, 135.2, 121.4, 119.3, 118.0, 110.3, 107.5, 105.6, 56.6, 56.0 ppm. HR-MS (ESI): calcd. for $C_{16}H_{13}O_5$ $[M + H]^+$ 285.0763; found 285.0771.

1-Hydroxy-3,6,7-trimethoxyanthracene-9,10-dione (2e): Yellow solid, 88%. R_f = 0.78 ($CHCl_3$/EtOH, 99:1). M.p. 226–228 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1629, 1577, 14142, 1386, 1357, 1307, 1247, 1220, 1104 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 12.81 (s, 1 H, OH), 7.62 (s, 1 H, Ar-*H*), 7.61 (s, 1 H, Ar-*H*), 7.28 (d, J = 2.4 Hz, 1 H, Ar-*H*), 6.62 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.04 (s, 3 H, OMe), 4.03 (s, 3 H, OMe), 3.91 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.2, 181.6, 165.9, 165.0, 153.8, 153.7, 135.0, 128.4, 128.2, 110.5, 108.6 (2 C), 107.8, 106.1, 56.5 (2 C), 56.0 ppm. HR-MS (ESI): calcd. for $C_{17}H_{15}O_6$ $[M + H]^+$ 315.0869; found 315.0873.

1-Hydroxy-3,5,8-trimethoxyanthracene-9,10-dione (2f): Yellow solid, 79%. R_f = 0.45 ($CHCl_3$/EtOH, 99:1). M.p. 210–215 °C (CH_2Cl_2, decomp). IR: $\tilde{\nu}$ = 1623, 1442, 1331, 1290, 1226, 1201, 1150, 979, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.01 (s, 1 H, OH), 7.37 (d, J = 9.9 Hz, 1 H, Ar-*H*), 7.35 (d, J = 9.8 Hz, 1 H, Ar-*H*), 7.25 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.66 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.02 (s, 3 H, OMe), 4.00 (s, 3 H, OMe), 3.90 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.4, 182.6, 165.7, 164.6, 154.8, 154.6, 136.0, 122.8, 122.1, 120.7 (2 C), 111.2, 106.3, 105.9, 57.1, 57.0, 55.8 ppm. HR-MS (EI): calcd. for $C_{17}H_{14}O_6$ $[M]^+$ 314.0790; found 314.0809.

1-Hydroxy-3,6,8-trimethoxyanthracene-9,10-dione (2g): Yellow solid, 74%. R_f = 0.75 ($CHCl_3$/EtOH, 99:1). M.p. 236–238 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1591, 1553, 1320, 1220, 1199, 1149, 1035, 946,

878, 756 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 13.38 (s, 1 H, OH), 7.47 (d, J = 2.3 Hz, 1 H, Ar-*H*), 7.30 (d, J = 2.7 Hz, 1 H, Ar-*H*), 6.80 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.70 (d, J = 2.5 Hz, 1 H, Ar-*H*), 4.03 (s, 3 H, OMe), 3.99 (s, 3 H, OMe), 3.91 (s, 3 H, OMe) ppm; the ^1H NMR spectra match the data reported in the literature.[21] ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 186.6, 182.8, 165.2, 165.1, 165.0, 162.9, 137.5, 134.1, 115.2, 111.4, 107.5, 106.6, 104.9, 104.1, 56.6, 56.0, 55.9 ppm. HR-MS (ESI): calcd. for $C_{17}H_{15}O_6$ $[M + H]^+$ 315.0869; found 315.0865.

1-Hydroxy-3,8-dimethoxyanthracene-9,10-dione (2h): Yellow solid, 85%. R_f = 0.78 ($CHCl_3$/EtOH, 99:1). M.p. 158–160 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1637, 1585, 1445, 1392, 1331, 1250, 1167, 978, 750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 13.23 (s, 1 H, OH), 7.95 (dd, J = 1.0, 7.6 Hz, 1 H, Ar-*H*), 7.72 (dd, J = 7.7, 8.4 Hz, 1 H, Ar-*H*), 7.36 (d, J = 8.1 Hz, 1 H, Ar-*H*), 7.31 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.71 (d, J = 2.6 Hz, 1 H, Ar-*H*), 4.07 (s, 3 H, OMe), 3.92 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 187.5, 182.7, 165.5, 165.3, 160.8, 135.7, 135.3, 134.2, 120.3, 120.2, 118.3, 111.7, 107.3, 106.5, 56.7, 55.9 ppm. HR-MS (ESI): calcd. for $C_{16}H_{13}O_5$ $[M + H]^+$ 285.0763; found 285.0775.

Synthesis of Macrosporin (1) from Resorcylate 9a

Methyl 2-Hydroxy-6-(4-hydroxy-3-methylbenzyl)-4-methoxybenzoate (9i): Pd/C (10%, 35 mg) was added to **9a** (352 mg, 0.90 mmol) in EtOAc (18 mL) under argon, and the gas was changed to hydrogen. The mixture was stirred at 20 °C for 18 h, when the gas was changed to nitrogen. Silica (2.0 g) was added, and the solvent was evaporated. Chromatography of the resultant residue on silica (hexanes/Et_2O, 1:1) gave **9i** (257 mg, 0.85 mmol, 95%) as a white solid. R_f = 0.20 (hexanes/Et_2O, 3:1). M.p. 84–86 °C (CH_2Cl_2). IR: $\tilde{\nu}$ = 1649, 1614, 1577, 1434, 1329, 1257, 1202, 1158, 1115, 1047 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 11.83 (s, 1 H, OH), 6.83 (d, J = 1.7 Hz, 1 H, Ar-*H*), 6.77 (dd, J = 1.9, 8.2 Hz, 1 H, Ar-*H*), 6.67 (d, J = 8.1 Hz, 1 H, Ar-*H*), 6.40 (d, J = 2.6 Hz, 1 H, Ar-*H*), 6.27 (d, J = 2.7 Hz, 1 H, Ar-*H*), 5.42 (s, 1 H, OH), 4.15 (s, 2 H, Ar-C*H*$_2$-Ar′), 3.81 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 2.21 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.7, 165.5, 163.9, 152.0, 145.6, 132.5, 131.0, 126.8, 123.6, 114.7, 111.9, 104.9, 98.9, 55.2, 51.7, 41.1, 15.7 ppm. HR-MS (EI): calcd. for $C_{17}H_{18}O_5$ $[M]^+$ 302.1154; found 302.1155. $C_{17}H_{18}O_5$ (302.32): calcd. C 67.54, H 6.00; found C 67.41, H 5.93.

1,7-Dihydroxy-3-methoxy-6-methylanthracen-9(10*H*)-one (10i): Trimethylsilyl triflate (0.60 mL, 3.3 mmol, 10 equiv.) was added with stirring to **9i** (100 mg, 0.33 mmol) in CH_2Cl_2 (8.0 mL) at 20 °C. After 18 h, CH_2Cl_2 (90 mL) and water (50 mL) were added and the phases separated. The aqueous layer was further extracted with CH_2Cl_2 (4 × 100 mL), and the combined organic layers were dried (Na_2SO_4) and the volatiles rotary-evaporated. The residue was chromatographed on silica (hexanes/THF, 19:1 → 9:1 → 3:1) to give **10i** (68 mg, 0.25 mmol, 76%) as a pale-yellow solid. R_f = 0.30 (hexanes/THF, 9:1). M.p. 230–234 °C (THF, decomp.). IR: $\tilde{\nu}$ = 3415, 1624, 1596, 1572, 1463, 1420, 1371, 1355, 1290, 1098, 1056, 954, 8560 cm^{-1}. ^1H NMR (400 MHz, [D_8]THF, 25 °C): δ = 13.44 (s, 1 H, OH), 8.65 (s, 1 H, Ar-*H*), 7.54 (s, 1 H, Ar-*H*), 7.16 (s, 1 H, OH), 6.46–6.49 (m, 1 H, Ar-*H*), 6.36 (d, J = 2.4 Hz, 1 H, Ar-*H*), 4.17 (s, 2 H, Ar-C*H*$_2$-Ar′), 3.83 (s, 3 H, OMe), 2.27 (s, 3 H, Ar-C*H*$_3$) ppm. ^{13}C NMR (125 MHz, [D_8]THF, 25 °C): δ = 188.5, 166.6, 166.1, 155.6, 145.1, 132.7, 132.4, 130.8 (2 C), 111.4, 110.9, 106.1, 99.6, 55.6, 32.2, 16.4 ppm. HR-MS (CI): calcd. for $C_{16}H_{15}O_4$ $[M + H]^+$ 271.0970; found 271.0963.

1,7-Dihydroxy-3-methoxy-6-methylanthracene-9,10-dione (Macrosporin, 1): $CuBr_2$ (17 mg, 0.08 mmol, 1.0 equiv.) was added with stirring to **10i** (21 mg, 0.08 mmol) in THF (1.5 mL) at 20 °C. The solution was purged with O_2 for 15 min and then stirred under O_2. After 20 h, the solvents were evaporated, and the resultant solid was chromatographed (hexanes/THF, 3:1) to yield **1** (18 mg, 0.06 mmol, 81%) as a yellow solid. R_f = 0.54 (hexanes/THF, 3:1). M.p. 300–302 °C (THF, decomp.; sublimation at 256–260 °C). IR: $\tilde{\nu}$ = 3278, 2924, 1658, 1636, 1570, 1449, 1395, 1362, 1323, 1262, 1214, 1163, 1101, 787, 625 cm^{-1}. ^1H NMR (400 MHz, [D_8]THF, 25 °C): δ = 12.88 (s, 1 H, OH), 9.98 (s, 1 H, OH), 7.99 (s, 1 H, Ar-*H*), 7.53 (s, 1 H, Ar-*H*), 7.27 (d, J = 2.5 Hz, 1 H, Ar-*H*), 6.71 (d, J = 2.5 Hz, 1 H, Ar-*H*), 3.92 (s, 3 H, OMe), 2.32 (s, 3 H, Ar-C*H*$_3$) ppm. ^{13}C NMR (100 MHz, [D_8]THF, 25 °C): δ = 187.7, 181.0, 167.2, 166.2, 162.1, 136.4, 134.4, 132.8, 131.0, 126.7, 111.5, 111.4, 107.8, 105.9, 56.2, 16.3 ppm. HR-MS (CI): calcd. for $C_{16}H_{13}O_5$ $[M + H]^+$ 285.0763; found 285.0760. The spectra match the reported data of the isolated natural product.[4a,6,9a,9b]

Attempted Cyclization of Resorcylate 9d by Using Trimethylsilyl Triflate

3-Methoxy-5-(2-methoxybenzyl)phenol (11): Trimethylsilyl triflate (0.60 mL, 3.3 mmol, 10 equiv.) was added with stirring to **9d** (100 mg, 0.33 mmol) in CH_2Cl_2 (8.0 mL) at 20 °C. After 18 h, CH_2Cl_2 (90 mL) and water (50 mL) were added and the phases separated. The aqueous layer was further extracted with CH_2Cl_2 (4 × 100 mL), and the combined organic layers were dried (Na_2SO_4) and the volatiles rotary-evaporated. The resultant oil was chromatographed on silica (hexanes/Et_2O, 9:1 → 3:1) to give unreacted **9d** (10 mg, 0.03 mmol, 10%) and benzylbenzene **11** (72 mg, 0.29 mmol, 89%) as a colorless oil. R_f = 0.20 (hexanes/Et_2O, 3:1). IR: $\tilde{\nu}$ = 1594, 1492, 1456, 1436, 1242, 1143, 1051, 1028, 752, 732, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.22 (ddd, J = 1.7, 7.8, 7.8 Hz, 1 H, Ar-*H*), 7.09 (dd, J = 1.6, 7.3 Hz, 1 H, Ar-*H*), 6.91–6.85 (m, 2 H, 2 Ar-*H*), 6.39 (m_c, 1 H, Ar-*H*), 6.27 (m_c, 1 H, Ar-*H*), 6.24 (t, J = 2.2 Hz, 1 H, Ar-*H*), 5.11 (s, 1 H, OH), 3.89 (s, 2 H, Ar-C*H*$_2$-Ar′), 3.82 (s, 3 H, OMe), 3.73 (s, 3 H, OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 160.7, 157.2, 156.5, 143.8, 130.3, 129.1, 127.5, 120.5, 110.4, 108.4, 107.3, 98.9, 55.3, 55.2, 35.7 ppm. HR-MS (ESI): calcd. for $C_{15}H_{17}O_3$ $[M + H]^+$ 245.1172; found 245.1166.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra for macrosporin (**1**), anthraquinones **2b**–**h**, resorcylates **3a**–**g**, **8a**–**g**, **9a**–**g** and **9i**, anthrones **10b**–**i**, and benzylbenzene **11**.

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