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Synthesis of Balsaminone A, a Naturally Occurring Pentacyclic Dinaphthofuran Quinone

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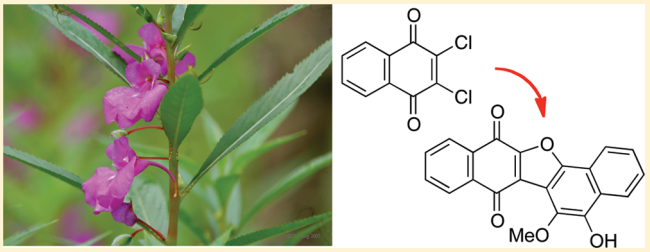
Supporting Information

ABSTRACT: A short synthesis of the natural product balsaminone A, a dinaphthofuran quinone, is described. The key steps of the synthesis are base-induced coupling of 1,4-dihydroxy-2-naphthaldehyde with 2,3-dichloronaphthoquinone to give a pentacyclic dinaphthofuran directly, followed by conversion of the aldehyde into the desired methoxy group via the corresponding phenol. The synthesis, in which the structure of a key pentacyclic intermediate is corroborated by X-ray crystallography, confirms the original structural assignment of the natural product.



Quinones, particularly naphthoquinones, are widespread in nature[1] and are essential for many life processes. Although quinones, a large group of natural pigments, do contribute to natural color, their major role is in redox processes. For example, pyrroloquinoline quinone (PQQ) is a redox cofactor, and the naphthoquinone phylloquinone (vitamin K_1) occurs in green plants and participates in photosynthetic electron transport. Other quinone natural products also possess potent biological activity: for example, adriamycin (doxorubicin) is a front-line cancer chemotherapy treatment.

In 1998, two unusual dinaphthofuran quinone derivatives named balsaminone A (**1a**) and B (**1b**) were isolated from the pericarp of fruit of *Impatiens balsamina* L. (Balsaminaceae) (garden or rose balsam, sometimes known as touch-me-not) together with the known compound 2-methoxy-1,4-naphthoquinone.[2] The compounds have significant antipruritic activity, and the aerial parts of the plant have been used for the treatment of articular rheumatism, bruises, and beri-beri in Chinese traditional medicine. Balsaminone A was isolated as red needles that decomposed gradually in air but more rapidly in chloroform solution. The structure was determined to be 5-hydroxy-6-methoxydinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (**1a**) by a combination of spectroscopic methods. Balsaminone B was determined to be the corresponding β-D-glucoside **1b** (Figure 1).

Our own interest in quinone natural products dates back to an early synthesis of coenzyme PQQ[3] and more recently to other families of benzoquinones,[4−9] and we now report the first synthesis of balsaminone A.

Over a century ago, Liebermann reported that the reaction of 2,3-dichloro-1,4-naphthoquinone (**2**) with resorcinol gave naphthofuran **3**.[10] The reaction has subsequently been used by others in routes to substituted naphthoquinones[11] and a range of tetra- and pentacyclic napthoquinone compounds with anticancer activity,[12−14] and therefore it seemed reasonable that

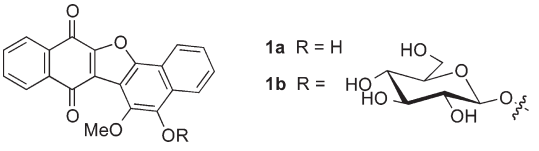


Figure 1. Balsaminones A (**1a**) and B (**1b**) isolated from the pericarp of fruit of the *I. balsamina* L. (Balsaminaceae).

balsaminone A (**1a**) could be formed from a suitable precursor **4** that itself resulted from reaction of naphthoquinone **2** with an appropriate 1,4-dihydroxynaphthalene **5**, where the R group can be converted into a methoxy group following the formation of the pentacyclic system (Scheme 1).

In considering the choice of 1,4-dihydroxynaphthalene starting material **5**, ideally a methoxy group or other oxygen-containing functionality was needed as the 2-substituent, R. A range of such compounds **5** (R = OMe, OH, OAc, OMs) was prepared, but all failed to condense with 2,3-dichloronaphthoquinone **2**. Therefore, it was decided to investigate substituents, R, that possessed different electronic properties, starting with an acetyl group on the basis that a subsequent Baeyer−Villiger reaction would deliver the required oxygen functionality.

Thus, 2-acetyl-1,4-dihydroxynaphthalene (**6**), most conveniently prepared by boron trifluoride mediated Fries rearrangement of 1,4-diacetoxynaphthalene,[15] was reacted with 2,3-dichloronaphthoquinone (**2**) in pyridine in the presence of potassium carbonate. Pleasingly, this reaction proceeded smoothly and gave the desired pentacyclic dinaphthofuran quinone **7** in good yield, the structure of which was confirmed by X-ray crystallography (Figure 2). Subsequent benzylation gave the corresponding benzyloxy compound **8** (Scheme 2).

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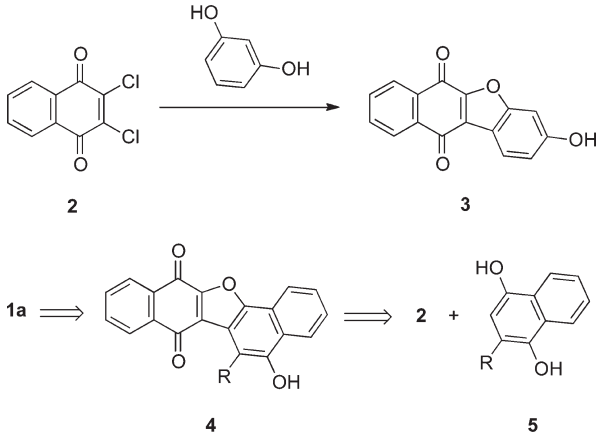
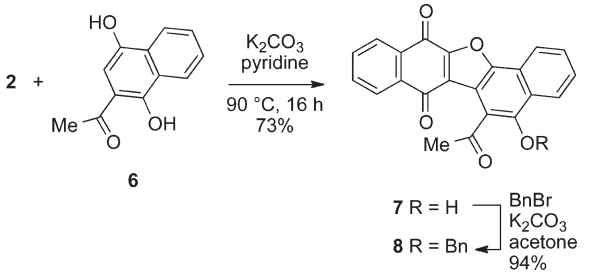
All that remained was to convert the ketone **8** into the corresponding acetate ester by Baeyer–Villiger oxidation. A number of reagents were tried—*m*-CPBA with sodium bicarbonate in dichloromethane, sodium percarbonate and hydrogen peroxide under acidic and basic conditions, urea–hydrogen peroxide adduct (UHP), hydrogen peroxide–TFA, UHP–TFA, peracetic acid in acetic acid—but all without success. The reasons for the lack of reactivity of ketone **8** under Baeyer–Villiger conditions are not clear, although the X-ray structure does suggest that the ketone is quite hindered. Therefore, the synthesis of the presumably less hindered and more reactive aldehyde was investigated.

Scheme 1. Liebermann's Synthesis of Naphthofuran Quinone 3 and Our Proposed Synthesis of Balsaminone A



Scheme 2. Synthesis of 6-Acetyl-5-hydroxydinaphtho[2,3-*b*:2′1′-*d*]furan-7,12-dione (7)



Although the condensation of dihydroxnaphthalene **11** with 2,3-dichloronaphthoquinone (**2**) was low-yielding, it did allow for completion of the synthesis by standard functional group interconversions. Thus, in a sequence of high-yielding steps, aldehyde **13** underwent Baeyer–Villiger/Dakin oxidation with *m*-CPBA to give formate ester **14**. Hydrolysis and methylation gave the benzyloxy compound **16**, deprotection of which by hydrogenolysis over Pearlman's catalyst gave balsaminone A (**1a**) (Scheme 3). Finally, balsaminone A was converted into its acetate **17** to aid comparison with the natural product. A detailed comparison of the ^{1}H and ^{13}C NMR spectroscopic data for balsaminone A and its acetate derivative showed that the data for our synthetic material very closely matched those reported for the natural product (see the Supporting Information).[2]

In conclusion, we have completed a short synthesis of the pentacyclic dinaphthofuroquinone balsaminone A. The synthesis, in which the structure of a key pentacyclic intermediate is corroborated by X-ray crystallography, confirms the original structural assignment of the natural product.

EXPERIMENTAL SECTION

General Experimental Information. Commercially available reagents were used throughout without further purification unless otherwise stated. Anhydrous tetrahydrofuran and dichloromethane were freshly distilled. Light petroleum refers to the fraction of petroleum boiling between 40 and 60 °C. All reactions were carried out under a nitrogen or argon atmosphere. Thin-layer chromatography was carried out using aluminum-backed plates coated with silica gel. The plates were

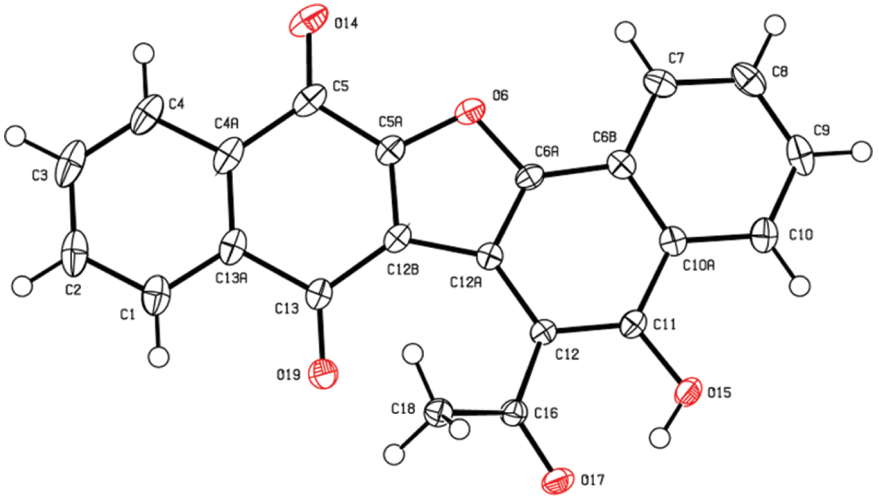


Figure 2. X-ray crystal structure of 6-acetyl-5-hydroxydinaphtho[2,3-*b*:2′1′-*d*]furan-7,12-dione (**7**).

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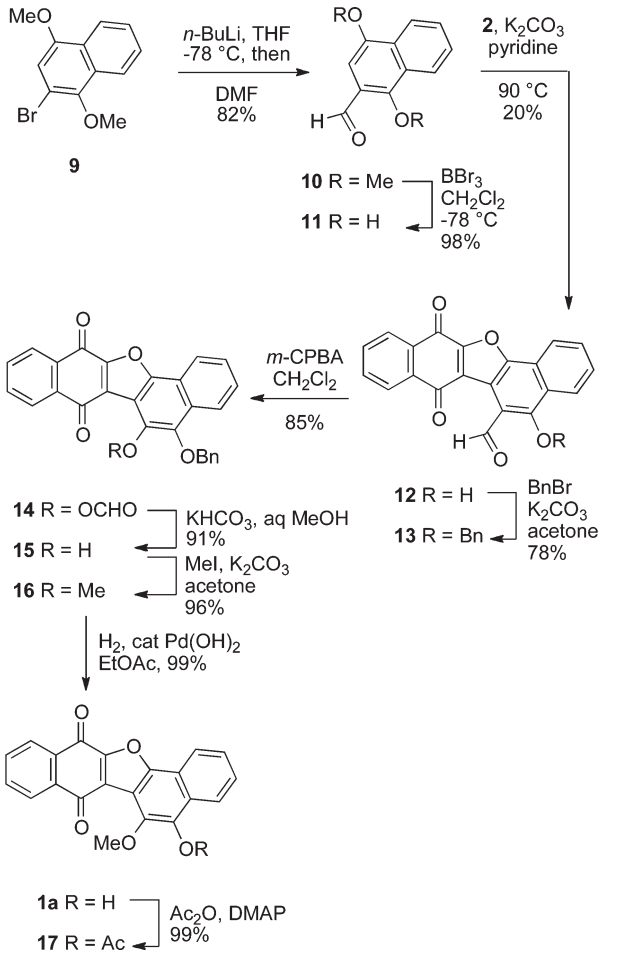
visualized under UV light at 254 nm and/or by vanillin or permanganate stains. Flash column chromatography was carried out using silica gel with the eluent specified. Infrared spectra were recorded in the range 4000−600 cm^{-1} as solutions in chloroform or as a solid in attenuated total reflectance (ATR) mode. NMR spectra were recorded NMR spectra were recorded at the frequencies stated. Chemical shifts are quoted in ppm and *J* values in Hz. Chemical shift values are referenced against residual proton in the deuterated solvents. In the ^{13}C NMR spectra, signals corresponding to CH, CH_2, or CH_3 are assigned from DEPT-90 and -135 spectra; all others are quaternary C. High- and low-resolution mass spectra were recorded on a time-of-flight spectrometer.

Scheme 3. Synthesis of 5-Benzyl-6-formyloxydinaphtho[2,3-*b*:2′1′-*d*]furan-7,12-dione (13) and Its Subsequent Conversion into Balsaminone A



2-Acetyl-1,4-dihydroxynaphthoquinone (6). A stirred mixture of boron trifluoride−THF complex (4 mL) and 1,4-diacetoxynaphthalene[17] (1.00 g, 4.09 mmol) was heated at 120 °C for 3 h. The resulting solution was cooled to room temperature, poured into ice-cooled water (100 mL), and extracted with dichloromethane (3 × 100 mL). The combined organic layers were washed with water (100 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (20% ethyl acetate in light petroleum) to give the title compound (0.41 g, 50%) as an off-white solid: mp 205−207 °C (lit.[16] mp 202−204 °C); MS found M − H^+ 201.0551, calcd for $C_{12}H_{10}O_3$ − H^+ 201.0557; ν_{max} ($CHCl_3$)/cm^{-1} 3691, 3603, 1629, 1604, 1466, 1396, 1325, 1273, 1241, 1066; δ_H (400 MHz; DMSO) 13.50 (1 H, s), 9.85 (1 H, s, br), 8.30 (1 H, m), 8.12 (1 H, m), 7.71(1 H, m), 7.60 (1 H, m), 7.10 (1 H, s) 2.66 (3 H, s); δ_C (100 MHz; DMSO) 205.2 (C), 154.7 (C), 145.1 (C), 130.0 (C), 129.8 (CH), 126.9 (CH), 125.5 (C), 124.1 (CH), 122.7 (CH), 113.0 (C), 105.5 (CH), 27.7 (Me).

6-Acetyl-5-hydroxydinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (7). A mixture of 2,3-dichloro-1,4-naphthoquinone **2** (0.10 g, 0.44 mmol), 2-acetyl-1,4-dihydronaphthalene **6** (0.13 g, 0.66 mmol), and potassium carbonate (0.60 g, 4.40 mmol) in pyridine (10 mL) was heated to 90 °C for 16 h. The reaction mixture was cooled to room temperature, ice-cooled water (50 mL) was added, and the mixture was extracted with dichloromethane (100 mL). The organic layer was washed with hydrochloric acid solution (2 M; 2 × 100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (20% ethyl acetate in light petroleum) to give the title compound (0.11 g, 73%) as a red solid: mp 248−250 °C; found M + H^+ 357.0746, calcd for $C_{22}H_{12}O_5$ + H^+ 357.0757, M + Na^+ 379.0570, $C_{22}H_{12}O_5$ + Na^+ 379.0577; ν_{max} ($CHCl_3$)/cm^{-1} 3691, 3011, 1671, 1596, 1545, 1466, 1352, 1253, 1061; λ_{max} (MeOH)/nm 292 (log ε 3.87), 452 (3.43); δ_H (400 MHz; $CDCl_3$)

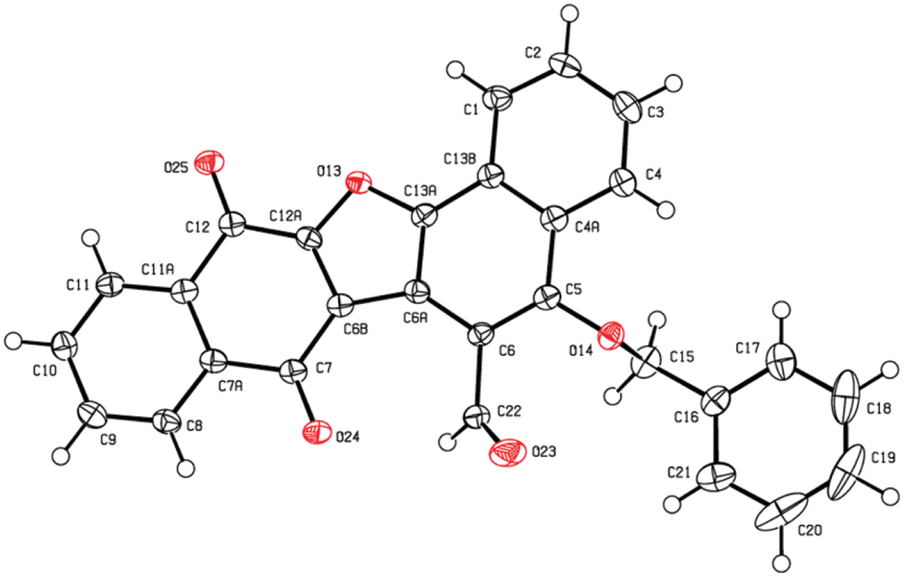


Figure 3. X-ray crystal structure of 5-benzyl-6-formyloxydinaphtho[2,3-*b*:2′1′-*d*]furan-7,12-dione (**13**).

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13.03 (1 H, s), 8.55 (1 H, d, *J* 8.4), 8.45 (1 H, d, *J* 8.0), 8.30−8.23 (2 H, m), 7.88−7.81 (3 H, m), 7.76−7.72 (1 H, m), 2.58 (3 H, s); δ_C (100 MHz; $CDCl_3$) 203.6 (C), 180.8 (C), 174.3 (C), 159.3 (C), 153.0 (C), 148.5 (C), 134.3 (CH), 133.9 (CH), 133.7 (C), 132.1 (C), 131.2 (CH), 128.5 (CH), 127.3 (CH), 126.7 (CH), 126.6 (C), 126.3 (C), 125.8 (C), 124.1 (C), 121.3 (C), 115.9 (C), 109.8 (C), 30.6 (Me). Anal. Found: C, 74.23; H, 3.41. Calcd for $C_{22}H_{12}O_5$: C, 74.16; H, 3.39.

6-Acetyl-5-(benzyloxy)dinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (8). To a solution of phenol **7** (0.65 g, 1.82 mmol) in acetone (50 mL) were added potassium carbonate (0.75 g, 5.47 mmol) and benzyl bromide (0.93 g, 5.47 mmol). The reaction mixture was heated to reflux for 4 h with constant stirring. The acetone was removed under reduced pressure, and the residue was diluted with dichloromethane (100 mL). The organic layer was washed with water (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (20% ethyl acetate in light petroleum) to give the title compound (0.76 g, 94%) as a yellow solid: mp 192−194 °C; found M + Na^+ 469.1030, calcd for $C_{29}H_{18}O_5$ + Na^+ 469.1046; ν_{max} ($CHCl_3$)/cm^{-1} 3414, 3011, 1734, 1673, 1556, 1343, 1253, 1059, 993, 953; δ_H (400 MHz; $CDCl_3$) 8.60 (1 H, m), 8.32−8.25 (3 H, m), 7.83−7.74 (4 H, m), 7.58 (2 H, m), 7.51−7.44 (3 H, m), 5.13 (2 H, s), 2.87 (3 H, s); δ_C (100 MHz; $CDCl_3$) 202.0 (C), 180.6 (C), 174.6 (C), 153.2 (C), 150.6 (C), 149.6 (C), 136.5 (C), 134.3 (CH), 134.0 (CH), 133.2 (C), 132.3 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 127.4 (C), 127.3 (CH), 126.9 (CH), 125.4 (C), 123.8 (CH), 121.9 (CH), 115.0 (C), 79.0 (CH_2), 33.0 (Me).

2-Bromo-1,4-dimethoxynaphthalene (9). To a mixture of 2-bromo-1,4-naphthoquinone (4.00 g, 16.88 mmol) in tetrahydrofuran (50 mL) under an argon atmosphere was added an aqueous solution of sodium dithionite (11.6 g, 67.51 mmol) in deoxygenated water (50 mL) with vigorous stirring at room temperature. After 30 min, an aqueous solution of potassium hydroxide (9.47 g, 168.7 mmol) in water (20 mL) was added and the resulting reaction mixture was stirred for 1 h. Dimethyl sulfate (21.3 g, 168.7 mmol) was added, and the reaction mixture was stirred for another 16 h. To this reaction mixture were added ammonia (50 mL, 1.5 M) and water (250 mL), and the mixture was extracted with ethyl acetate (3 × 100 mL). The organic layers were combined, washed with hydrochloric acid (2 M; 200 mL) followed by water (2 × 200 mL) and brine (100 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (eluted with 10% ethyl acetate in light petroleum) to give the title compound (3.60 g, 80%) as a colorless solid: mp 54−56 °C; (lit.[18] mp 56−58 °C); found M + Na^+ 288.9848, calcd for $C_{12}H_{11}{}^{79}BrO_2$ + Na^+ 288.9835; ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2938, 2839, 1619, 1583, 1508, 1414, 1364, 1261, 1107; δ_H (400 MHz; $CDCl_3$) 8.24 (1 H, m), 8.10 (1 H, m), 7.54−7.60 (2 H, m), 6.92 (1 H, s), 4.00 (3 H, s), 3.99 (3 H, s); δ_C (100 MHz; $CDCl_3$) 152.3 (C), 146.8 (C), 129.0 (C), 127.4 (C), 125.8 (CH), 125.8 (C), 122.6 (CH), 121.9 (CH), 111.9 (C), 108.0 (CH), 61.5 (Me), 56.9 (Me); *m*/*z* (ESI) 290 (M^+, 19%), 288 (19), 273 (31), 257 (13), 183 (100).

1,4-Dimethoxy-2-naphthaldehyde (10). In a oven-dried round-bottom flask, a solution of 2-bromo-1,4-dimethoxynaphthalene (**9**; 3.50 g, 13.10 mmol) in THF (50 mL) was cooled to −78 °C under argon. *n*-BuLi (2.5 M in hexanes; 6.28 mL, 15.72 mmol) was added over 30 min. The reaction mixture turned orange-red. The reaction mixture was warmed to −50 °C over 1 h and cooled to −78 °C, and dimethylformamide (5.00 mL, 65.51 mmol) was added over 30 min. The reaction mixture was stirred at −78 °C for 2 h and then warmed to −40 °C. Water (20 mL) was added, and the mixture was warmed to room temperature. The aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water (50 mL) followed by brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (10% ethyl acetate in light petroleum), which gave the title compound (2.30 g, 82%) as an off-white solid: mp 112 °C (lit.[19] mp 108−109 °C); found M + Na^+ 239.0682, calcd for $C_{13}H_{12}O_3$ + Na^+ 239.0679; ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2939, 2846, 1676, 1623, 1596, 1460, 1371, 1165, 1128; δ_H (400 MHz; $CDCl_3$) 10.64 (1 H, s) 8.30 (1 H, m), 8.22 (1 H, m), 7.65 (2 H, m), 7.14 (1 H, s), 4.12 (3 H, s), 4.04 (3 H, s); δ_C (100 MHz; $CDCl_3$) 189.6 (CH), 157.1 (C), 152.3 (C), 130.4 (C), 128.9 (CH), 128.6 (C), 127.4 (CH), 124.7 (C), 123.0 (CH), 122.9 (CH), 96.4 (CH), 66.8 (Me), 56.8 (Me); *m*/*z* (ESI) 239 (M^+, 100%), 183 (32). Anal. Found: C, 72.09; H, 5.60. Calcd for $C_{13}H_{12}O_3$: C, 72.21, H, 5.59.

1,4-Dihydroxy-2-naphthaldehyde (11). 1,4-Dimethoxy-2-naphthaldehyde (**10**; 1.00 g, 4.62 mmol) was dissolved in dry dichloromethane (70 mL) under an argon atmosphere. The solution was cooled to −78 °C and boron tribromide (3.51 mL, 36.99 mmol) in dry dichloromethane (10 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 2 h, warmed to room temperature, and stirred at room temperature another 16 h. The reaction mixture was diluted with water (100 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue obtained was subjected to flash column chromatography in 20% ethyl acetate in light petroleum to give the title compound (0.85 g, 98%) as a greenish yellow solid: mp 202 °C (lit.[16] mp 187−189 °C); found M + Na^+, 211.0368, calcd for $C_{11}H_8O_3$ + Na^+ 211.0366; ν_{max} ($CHCl_3$)/cm^{-1} 3690, 3601, 3011, 1724, 1651, 1606, 1577, 1377, 1320, 1271, 1176, 1122, 1067; δ_H (400 MHz; DMSO-d_6) 11.25 (1 H, s) 10.21 (1 H, s), 9.96 (1 H, s), 8.33 (1 H, d, *J* 8.0), 8.16 (1 H, d, *J* 8.0), 7.70 (1 H, m), 7.62 (1 H m), 7.02 (1 H, s); δ_C (100 MHz; DMSO-d_6) 194.9 (CH), 153.5 (C), 146.4 (C), 129.9 (C), 129.7 (CH), 126.9 (CH), 126.0 (C), 124.2 (CH), 122.8 (CH), 116.1 (C), 104.8 (CH); *m*/*z* (ESI) 188 (M^+, 61%), 185 (32), 183 (21), 179 (100), 157 (34). Anal. Found: C, 69.98; H, 4.26. Calcd for $C_{11}H_8O_3$: C, 70.21, H, 4.29.

5-Hydroxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′,1′-*d*]furan-6-carbaldehyde (12). A mixture of 1,4-dihydroxy-2-naphthaldehyde (**11**; 0.50 g, 2.657 mmol), 2,3-dichloro-1,4-naphthoquinone (**2**; 0.48 g, 2.126 mmol), and potassium carbonate (3.60 g, 26.57 mmol) in anhydrous pyridine (20 mL) was heated at 95 °C under an argon atmosphere for 16 h. The reaction mixture was cooled, diluted with ice−water (20 mL), and acidified with hydrochloric acid solution (2 M). The aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were washed with water (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography in dichloromethane to give the title compound (0.17 g, 20%) as a bright orange solid: mp 302 °C; found M^+ 342.0523, calcd for $C_{21}H_{10}O_5{}^+$ 342.0535; ν_{max} ($CHCl_3$)/cm^{-1} 3691, 2361, 1724, 1671, 1621, 1599, 1545, 1376, 1350, 1251, 1064, 949; λ_{max} ($CHCl_3$)/nm 273 (log ε 4.48), 285 (4.33), 462 (3.80); δ_H (500 MHz; $CDCl_3$) 14.80 (1 H, s), 11.53 (1 H, s) 8.64 (1 H, d, *J* 8.5), 8.52 (1 H, d, *J* 8.0), 8.34 (2 H, m), 7.92 (1 H, t, *J* 8.0), 7.86 (2 H, m), 7.78 (1 H, t, *J* 8.0); δ_C (125 MHz; $CDCl_3$) 199.5 (CH), 180.9 (C), 174.4 (C), 164.1 (C), 153.8 (C), 148.0 (C), 134.4 (CH), 134.2 (CH), 133.4 (C), 132.2 (CH), 132.0 (C), 128.5 (CH), 127.8 (CH), 126.8 (CH), 126.1 (C), 126.0 (C), 125.9 (CH), 124.8 (C), 121.4 (CH), 116.9 (C), 108.0 (C); *m*/*z* (EI) 342 (M^+, 99%), 315 (23), 314 (100), 286 (15), 258 (46), 230 (26), 202 (21).

5-Benzyloxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′,1′-*d*]furan-6-carbaldehyde (13). A mixture of 5-hydroxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′,1′-*d*]furan-6-carbaldehyde (**12**; 0.22 g, 0.643 mmol), benzyl bromide (0.45 g, 3.856 mmol), and potassium carbonate (0.53 g, 3.85 mmol) in DMF (10 mL) was stirred at room temperature for 48 h. The reaction mixture was diluted with ice-cold water (50 mL) and stirred vigorously for 1 h. The solution was filtered, and the solid was dried and purified by flash column chromatography in dichloromethane to give the title compound (0.21 g, 78%) as a yellow solid: mp 252 °C; found M + Na^+ 455.0892, calcd for $C_{28}H_{16}O_5$ + Na^+ 455.0890; ν_{max} ($CHCl_3$)/cm^{-1} 1674, 1595, 1550, 1371, 1340, 1282,

1244, 1060, 942; λ_{max} ($CHCl_3$)/nm 260 nm (log ε 4.01), 267 (4.14), 284 (4.22), 435 (3.86); δ_H (400 MHz; $CDCl_3$) 11.14 (1 H, s) 8.56 (1 H, d, *J* 8.0), 8.33 (3 H, m), 7.84 (3 H, m), 7.72 (1 H, m), 7.62 (2 H, m), 7.45 (3 H, m), 5.32 (2 H, s); δ_C (100 MHz; $CDCl_3$) 191.5 (CH), 180.5 (C), 174.6 (C), 155.2 (C), 153.9 (C), 150.4 (C), 136.6 (C), 134.5 (CH), 134.0 (CH), 133.5 (C), 131.9 (C), 130.3 (CH), 129.4 (C), 128.9 (CH), 128.7 (CH), 128.7 (C), 128.6 (CH), 127.7 (CH), 126.7 (CH), 126.2 (C), 125.6 (CH), 123.5 (C), 121.6 (CH), 120.8 (C), 117.1 (C), 79.8 (CH_2); *m*/*z* (ESI) 455 (M^+, 39%), 430 (32), 365 (31), 362 (25), 227 (24). Anal. Found: C, 77.74; H, 3.74. Calcd for $C_{28}H_{16}O_5$: C, 77.77, H, 3.73.

5-Benzyloxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′,1′-*d*]furan-6-yl formate (14). To a solution of 5-benzyloxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′,1′-*d*]furan-6-carbaldehyde (**13**; 0.08 g, 0.185 mmol) in dichloromethane (10 mL) was added *m*-CPBA (0.15 g, 0.925 mmol). The mixture was stirred at room temperature under argon for 16 h. Saturated aqueous sodium thiosulfate (10 mL) was added, and the reaction mixture was extracted with dichloromethane (50 mL). The organic layer was washed with water (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography in dichloromethane to give the title compound (0.07 g, 85%) as a yellow-orange solid: mp 255 °C; found M + Na 471.0839, calcd for $C_{28}H_{16}O_6 + Na^+$ 471.0860; ν_{max} ($CHCl_3$)/cm^{-1} 1745, 1675, 1597, 1552, 1521, 1473, 1346, 1258, 1160, 1131, 1061, 946; λ_{max} ($CHCl_3$)/nm 285 nm (log ε 4.02), 295 (4.19), 343 (3.81), 439 (3.77); δ_H (400 MHz; $CDCl_3$) 8.63 (1 H, s), 8.54 (1 H, m), 8.27 (3 H, m), 7.82 (2 H, m), 7.72 (2 H, m), 7.57 (2 H, m), 7.57 (2 H, m), 7.45 (3 H, m), 5.26 (2 H, s); δ_C (100 MHz; $CDCl_3$) 180.0 (C), 174.5 (C), 159.6 (CH), 153.4 (C), 150.3 (C), 145.2 (C), 136.8 (C), 134.3 (CH), 134.0 (CH), 133.4 (C), 132.6 (C), 132.1 (C), 129.5 (C), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.0 (CH), 127.9 (CH), 127.4 (CH), 126.8 (CH), 125.0 (C), 123.7 (CH), 121.6 (CH), 120.2 (C), 115.6 (C), 76.7 (CH_2).

5-Benzyloxy-6-hydroxydinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (15). To a solution of 5-benzyloxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′,1′-*d*]furan-6-yl formate (**14**; 0.01 g, 0.022 mmol) in methanol (2 mL) was added a solution of potassium hydrogen carbonate (0.007 g, 0.066 mmol) in water (1 mL) at room temperature with constant stirring. The reaction mixture was stirred at room temperature for 6 h. The volatiles were removed under reduced pressure, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to flash column chromatography in dichloromethane, which gave the title compound (0.0085 g, 91%) as a dark brown solid: mp 260−262 °C; found M + Na^+ 443.0890, calcd for $C_{27}H_{16}O_5 + Na^+$ 443.0899; ν_{max} ($CHCl_3$)/cm^{-1} 3691, 3245, 3011, 1674, 1654, 1600, 1558, 1527, 1376, 1341, 1288, 1260, 1058, 1002, 952; δ_H (500 MHz; $CDCl_3$) 9.75 (1 H, s) 8.40 (1 H, d, *J* 8.0), 8.35 (2 H, m), 8.23 (1 H, d, *J* 8.0), 7.88 (2 H, m), 7.63 (3 H, m), 7.54 (1 H, m), 7.44 (2 H, m), 7.36 (1 H, m), 5.34 (2 H, s); δ_C (125 MHz; $CDCl_3$) 184.3 (C), 173.7 (C), 152.2 (C), 150.4 (C), 139.3 (C), 137.6 (C), 136.7 (C), 135.6 (CH), 134.2 (CH), 132.9 (C), 132.1 (C), 131.4 (C), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.1 (CH), 127.6 (CH), 127.6 (CH), 126.6 (C), 125.0 (CH), 122.8 (CH), 121.1 (CH), 116.2 (C), 113.7 (C), 75.0 (CH_2).

5-Benzyloxy-6-methoxydinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (16). To a solution of 5-benzyloxy-6-hydroxydinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (**15**; 0.004 g, 0.010 mmol) in acetone (1 mL) were added potassium carbonate (0.004 g, 0.028 mmol) and iodomethane (0.004 g, 0.028 mmol) at room temperature with stirring. The reaction mixture was heated at 50 °C for 6 h. The volatiles were removed under reduced pressure, and the residue was diluted with water (10 mL) and extracted with dichloromethane (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue obtained was purified by flash column chromatography in dichloromethane to give the title compound (0.004 g, 96%) as a yellow-orange solid: mp 211−213 °C; found M + Na^+ 457.1066, calcd for $C_{28}H_{18}O_5 + Na^+$ 457.1046; ν_{max} ($CHCl_3$)/cm^{-1} 3690, 3011, 2932, 1674, 1597, 1550, 1516, 1471, 1346, 1256, 1065, 1014; λ_{max} ($CHCl_3$)/nm 354 (log ε 3.53), 369 (3.53), 375 (3.32), 439 (3.61); δ_H (500 MHz; $CDCl_3$) 8.53 (1 H, m), 8.33 (2 H, m), 8.28 (1 H, m), 7.84 (2 H, m) 7.67 (2 H, m), 7.64 (2 H, m), 7.47 (2 H, m), 7.41 (1 H, m), 5.32 (2 H, s), 4.22 (3 H, s); δ_C (125 MHz; $CDCl_3$) 179.9 (C), 174.8 (C), 153.4 (C), 150.8 (C), 145.3 (C), 143.6 (C), 137.4 (C), 134.3 (C), 133.8 (CH), 133.7 (CH), 132.0 (C), 130.2 (C), 128.6 (CH), 128.5 (CH), 128.3 (CH), 127.5 (CH), 126.8 (CH), 126.6 (CH), 125.8 (C), 123.1 (CH), 121.4 (CH), 118.9 (C), 116.2 (C), 76.1 (CH_2), 62.6 (Me).

Balsaminone A: 5-Hydroxy-6-methoxydinaphtho[2,3-*b*:2′,1′-*d*]furan-7,12-dione (1a). 5-Benzyloxy-6-methoxydinaphtho-[2,3-*b*:2′,1′-*d*]furan-7,12-dione (**16**; 0.01 g, 0.0115 mmol) was dissolved in ethyl acetate (10 mL), and Pearlman's catalyst (0.002 g) was added. The reaction mixture was flushed with nitrogen followed by hydrogen. The reaction mixture was stirred for 3 h under a hydrogen atmosphere and filtered through a Celite pad with exhaustive washing with 5% methanol in chloroform (100 mL). The filtrate was concentrated under reduced pressure, and the residue was subjected to silica gel flash column chromatography in chloroform to give the title compound (0.008 g, 99%) as a red solid: mp 270−272 °C (lit.[2] mp >300 °C); found M + Na^+ 367.0562, calcd for $C_{21}H_{12}O_5 + Na^+$ 367.0577; ν_{max} (KBr)/cm^{-1} 3501, 1673, 1591, 1547, 1513, 1470, 1420, 1215, 1065, 1015, 803; λ_{max} (MeOH)/nm 224 (log ε 4.74), 267 (5.24), 287 (4.12), 476 (3.40); δ_H (500 MHz; $CDCl_3$); 8.50 (1 H, m), 8.36 (1 H, m), 8.32 (2 H, m), 7.83 (2 H, m) 7.70 (2 H, m), 6.39 (1 H, s), 4.10 (3 H, s); δ_C (125 MHz; $CDCl_3$) 180.2 (C), 174.7 (C), 153.1 (C), 148.7 (C), 142.8 (C), 134.6 (C), 134.2 (CH), 133.8 (CH), 133.6 (C), 132.2 (C), 127.9 (CH), 127.4 (CH), 127.1 (CH), 126.7 (CH), 125.5 (C), 124.9 (C), 123.0 (CH), 121.2 (CH), 118.8 (C), 114.5 (C), 63.5 (Me).

6-Methoxy-7,12-dioxo-7,12-dihydrodinaphtho[2,3-*b*:2′1′-*d*]furan-5yl Acetate (17). Balsaminone A (**1a**; 0.005 g, 0.0145 mmol) and 4-dimethylaminopyridine (0.004 g, 0.029 mmol) were added to acetic anhydride (1 mL) at room temperature, and the reaction mixture was stirred at room temperature for 4 h. The reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with hydrochloric acid solution (1 M; 10 mL), followed by saturated sodium hydrogen carbonate (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography in chloroform to give the title compound (0.005 g, 99%) as an orange-red solid: mp 272−274 °C; found M + Na^+ 409.0687, calcd for $C_{23}H_{14}O_6 + Na^+$ 409.0683; ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2962, 1769, 1676, 1551, 1520, 1258, 1192, 1059, 1014, 820; λ_{max} ($CHCl_3$)/nm 260 (log ε 4.69), 279 (4.57), 289 (4.08), 429 (3.60); δ_H (500 MHz; $CDCl_3$) 8.55 (1 H, m), 8.32 (2 H, m), 7.92 (1 H, m), 7.84 (2 H, m) 7.71 (2 H, m), 4.11 (3 H, s), 2.58 (3 H, s); δ_C (125 MHz; $CDCl_3$) 179.5 (C), 174.8 (C), 169.1 (C), 153.4 (C), 152.2 (C), 143.7 (C), 137.2 (C), 134.4 (CH), 133.8 (CH), 133.7 (C), 132.0 (C), 128.9 (CH), 128.6 (C), 127.5 (CH), 127.0 (CH), 126.7 (CH), 125.6 (C), 122.0 (CH), 121.7 (CH), 118.8 (C), 115.4 (C), 63.0 (Me), 20.7 (Me).

■ ASSOCIATED CONTENT

Supporting Information. Figures giving ^1H and ^{13}C NMR spectra and CIF files giving data for the X-ray crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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