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Pd-catalyzed cross-coupling/heterocyclization domino reaction: facile access to anthra[2,3-*b*]furan-5,10-dione scaffold

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ABSTRACT

A new facile route to the synthesis of 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione and its novel 2-substituted derivatives was proposed. The developed scheme was based on a Pd-catalyzed cross-coupling/heterocyclization domino reaction of 3-bromo-2-hydroxy-4,11-dimethoxyanthraquinone with terminal alkynes.

1. Introduction

Heterocyclic derivatives of 9,10-anthracenedione (anthraquinone) represent an interesting class of substances for application in many areas of chemistry,[1–5] including medical chemistry and searching for novel drug candidates.[6,7] Previously, a series of linear furanoanthraquinones (anthra[2,3-*b*]furan-5,10-diones) was revealed as potent topoisomerase I poisons capable of inhibiting the growth of tumor cells with activated mechanisms of multidrug resistance.[8] It also has been found that a substituent at the 2-position of the heterocyclic core affects the cytotoxicity of these compounds. Several effective routes to the preparation anthra[2,3-*b*]furan-5,10-diones have been developed.[9] However, the applicability of these methods for the diversification of substituents at the 2-position of the furan core and subsequent investigation of potential anticancer properties of these compounds is limited. In the present work, we have developed a new synthesis of 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-diones based on a Pd-catalyzed cross-coupling/heterocyclization domino reaction of 3-bromo-2-hydroxy-4,11-dimethoxyanthraquinone with terminal alkynes.

Heterocyclization of (*ortho*-hydroxyphenyl)acetylenes represents an effective method for the annulation of the furan core to arenes. The process, in most cases, proceeds in *one-pot* during cross-coupling of *o*-halophenols with acetylenes.[10,11] This method of cyclization leading to 2-substituted furan-fused rings was significantly improved by the development of Pd-catalyzed Sonogashira cross-coupling.[12–18]

A similar methodology has been previously adapted for the synthesis of anthra[2,3-*b*]furan-5,10-diones.[19,20] For instance, 2-phenylanthra[2,3-*b*]furan-5,10-dione was readily prepared by cross-coupling of 2-hydroxy-3-iodoanthraquinone with phenylacetylene using $Pd(PPh_3)_2Cl_2$/CuI as the catalyst. However, the heterocyclization described above to anthra[2,3-*b*]furan-5,10-diones is poorly suitable for the synthesis of biologically active compounds in this series. This scheme does not allow one to obtain derivatives bearing appropriate substituents at the *peri*-positions of anthra[2,3-*b*]furan-5,10-diones and confines a subsequent introduction of pharmacophore groups. The main limiting factor of the synthesis of 4,11-disubstituted anthra[2,3-*b*]furan-5,10-diones by the aforementioned methodology is the inaccessibility of the starting anthraquinone derivatives with the functionalized 1,4-positions (e.g., Hal, OAlk, etc.) suitable for corresponding modification.

Previously, it was shown that the methoxy group at the *peri*-positions of hetareneanthraquinones can be easily converted to the hydroxyl or amino groups.[9] Hence, our goal here is to develop the

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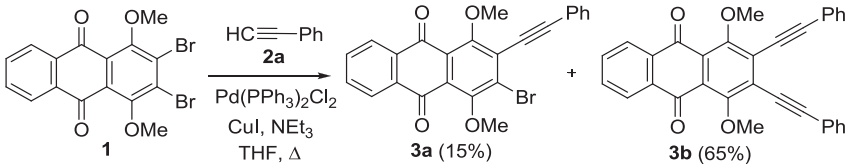
novel scheme of heterocyclization leading to derivatives of 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione.

2. Results and discussion

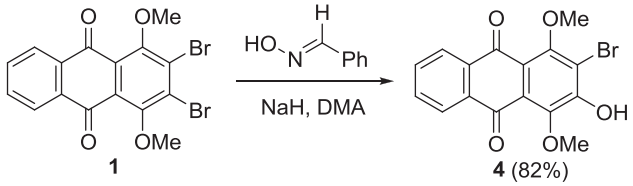
Recently, 2,3-dibromo-4,11-dimethoxyanthraquinone (**1**) was described[21] as a useful synthetic precursor for annulation of the furan core to the anthraquinone moiety. As the first step, we have investigated the possibility of selective substitution of one halogen atom in 2,3-dibromoanthraquinone **1** with the residue of alkynes by Sonogashira cross-coupling. However, it was found that the reaction of 2,3-dibromoanthraquinone **1** with phenylacetylene (**2a**) using a catalytic amount of $Pd(PPh_3)_2Cl_2/PPh_3/CuI$ in tetrahydrofuran (THF) leads to the monosubstituted anthraquinone **3a** in a low yield (15%) (Scheme 1). The major product of cross-coupling is compound **3b**. This observation can be likely explained by the fact that the formed 2-bromo-1,4-dimethoxy-3-(phenylethynyl)anthraquinone (**3a**) more readily reacted with phenylacetylene (**2a**) than the starting dibromide **1**, yielding 1,4-dimethoxy-2,3-bis(phenylethynyl)anthraquinone (**3b**) even at a stoichiometric ratio of reagents with incomplete conversion of the starting dibromide **1**. Thus, the cross-coupling of 2,3-dibromoanthraquinone **1** has not provided an effective introduction of the single alkynes residue into the anthraquinone core. Nevertheless, this method paves the way for the synthesis of the 2,3-bis(alkyne)anthraquinones (e.g., **3b**), which can be used as intermediates for the preparation of novel analogs of enediyne antibiotics that undergo Bergman-type cyclization.[22,23]



Scheme 1. Sonogashira cross-coupling of 2,3-dibromoanthraquinone **1** with phenylacetylene **2a**.

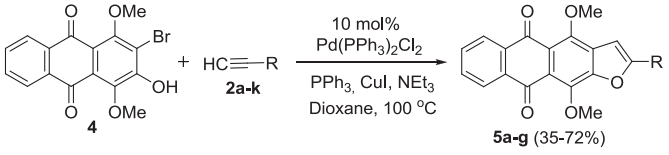
The difficulties of applying 2,3-dibromo-4,11-dimetoxyanthraquinone (**1**) for the introduction of one alkyne chain and subsequent annulation of the furan cycle encouraged us to modify the synthesis. Therefore, we have investigated the possibility of selective substitution of one bromine atom in compound **1** with a hydroxyl group. The proposed transformation can afford the opportunity of avoiding the problem discussed above and paves the way for anthraquinone-based analogs of *ortho*-halophenols as promising precursors for furan assembly by Sonogashira cross-coupling.

Previously, a mild method of the chlorine atom substitution by the treatment of benzaldehyde oxime anion as the nucleophile was proposed for the hydroxylation of anthraquinone derivatives.[9] Following this way, the reaction of 2,3-dibromo-4,11-dimethoxyanthraquinone (**1**) with benzaldoxime anions generated from benzaldehyde oxime and NaH in *N*,*N*-dimethylacetamide (DMA) readily affords a high yield of the corresponding 2-bromo-3-hydroxy-4,11-dimethoxyanthraquinone (**4**) (Scheme 2). It should be noted that the product of substitution of both bromine atoms was not formed in this reaction due to the deactivating effect of the phenoxide anion of **4** resulted under basic reaction conditions. Obviously, a similar method with a halogen substitution can be applied for the synthesis of derivatives of purpurine (1,2,4-trihydroxyanthracene-9,10-dione) protected at the 1,4-positions. The availability of such protected anthraquinones is significantly complicated by features of reactivity of purpurine and migration of protecting groups.[24]



Scheme 2. Transformation of 2,3-dibromoanthraquinone **1** to purpurine derivative **4**.

The cross-coupling of 2-bromo-3-hydroxy-4,11-dimethoxyanthraquinone (**4**) with phenylacetylene (**2a**) was studied in the next step of our investigation. In the conditions of the Sonogashira reaction (Pd(0)/CuI, Py, 80–90 °C), the desired product 4,11-dimethoxy-2-phenylanthra[2,3-*b*]furan-5,10-dione (**5a**) was obtained by a cascade of substitution reaction of a halogen with alkyne and the subsequent addition of a hydroxyl group to the triple bond of an intermediate compound. Interestingly, intermediate analog of *o*-(1-alkynyl)phenols was not observed during the cross-coupling between anthraquinone **4** with phenylacetylene (**2a**), even at a lower reaction temperature. In the optimized reaction conditions, the heterocyclization of 2-bromo-3-hydroxy-4,11-dimetoxyanthraquinone (**4**) with phenylacetylene (**2a**) using $Pd(PPh_3)_2Cl_2/PPh_3/CuI$ as the catalyst system in dioxane–NEt_3 (2:1) at 100 °C yields the desired anthra[2,3-*b*]furan-5,10-dione **5a** (65% yield). Similarly, a series of 2-substituted 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-diones **5b**–**g** have been prepared in moderate-to-good yields through the Pd(0)-catalyzed domino reaction of anthraquinone **4** with a number of terminal alkynes **2b**–**g** (Scheme 3). However, not all of the tested terminal acetylenes react to form the target products. We were unable to obtain the corresponding anthra[2,3-*b*]furan-5,10-diones from the starting compound **4** and functionalized alkynes **2h**–**k** using the same reaction conditions. The structure of acetylene derivatives **2a**–**k** and synthesized anthra[2,3-*b*]furan-5,10-diones **5a**–**g**, and their yields are listed in Table 1.



Scheme 3. Pd-catalyzed cross-coupling/heterocyclization domino reaction of 3-bromo-2-hydroxy-4,11-dimethoxyanthraqinone (**4**) with a series of acetylenes leads to anthra[2,3-*b*]furan-5,10-diones **5a**–**g**.

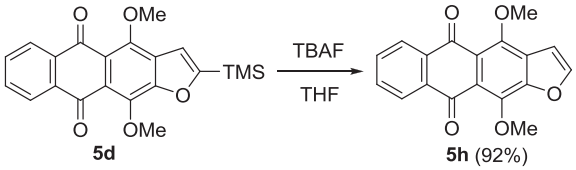
Finally, several modifications of 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-diones bearing functional groups at the 2-position were

Table 1
The structures of starting alkynes **2a**–**k** and target 2-substituted 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-diones **5a**–**g** prepared from 3-bromo-2-hydroxyanthraqinone **4** (Scheme 3)

Entry	Alkynes **2**	Structure of alkynes	**5**	R	Yield[a]
1	**2a**	HC≡CPh	**5a**	Ph	65%
2	**2b**	HC≡CCH_2OH	**5b**	CH_2OH	43%
3	**2c**	HC≡CCH_2OTHP	**5c**	CH_2OTHP	59%
4	**2d**	HC≡CTMS	**5d**	TMS	55%
5	**2e**	HC≡C*t*-Bu	**5e**	*t*-Bu	72%
6	**2f**	HC≡CCH_2NMe_2	**5f**	CH_2NMe_2	35%
7	**2g**	HC≡CCH_2NHBoc	**5g**	CH_2NHBoc	39%
8	**2h**	HC≡CCH_2NH_2	—	CH_2NH_2	0%
9	**2i**	HC≡CCO_2H	—	CO_2H	0%
10	**2j**	HC≡CCO_2Me	—	CO_2Me	0%
11	**2k**	HC≡$CCH(OEt)_2$	—	$CH(OEt)_2$	0%

[a] Yield of isolated product.

carried out. Removal of the THP-protective group of anthra[2,3-*b*]furan-5,10-dione **5c** by treatment with catalytic amounts of *p*-toluenesulfonic acid in MeOH leads to carbinol **5b** in quantitative yields. The treatment of the 4,11-dimethoxy-2-(trimethylsilyl)anthra[2,3-*b*]furan-5,10-dione (**5d**) with tetrabutylammonium fluoride (TBAF) in THF[25] produces a high yield of the desired 2,3-unsubstituted anthra[2,3-*b*]furan-5,10-dione **5h** (Scheme 4). Previously, 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione (**5h**) was obtained by two independent ways[9] in total yields of 4% and 2%, respectively. On the other hand, the yield of the compound **5h** from commercially available quinizarin by the new scheme based on the Sonogashira cross-coupling reached 36%.



5d **5h** (92%)

Scheme 4. Deprotection of **5d** leads to 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione (**5h**).

3. Conclusion

In summary, we have developed a new effective method to synthesize 4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione (**5h**) and its 2-substituted derivatives based on a Pd-catalyzed cross-coupling/heterocyclization domino reaction of 3-bromo-2-hydroxy-4,11-dimethoxyanthraquinone with terminal alkynes. This methodology paves the way for diversification of this prospective scaffold at the 2-position of the furan heterocycle required for in-depth studies of the structure-activity relations in a series of anthra[2,3-*b*]furan-5,10-diones. Furthermore, the novel original route of synthesizing difficult-to-produce derivatives of 3-hydroxy-4,11-dimethoxyanthraquinone was developed. We propose the new methodology of furan core annulation to arenes based on the combination of nucleophilic substitution of one halogen atom in *o*-dihaloarenes by the treatment of benzaldehyde oxime anion and subsequent cross-coupling with alkynes.

4. Experimental

4.1. General information

NMR spectra were recorded on a Varian VXR-400 instrument operating at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). Chemical shifts were measured in DMSO-d_6, $CDCl_3$ using tetramethylsilane as internal standard. Analytical TLC was performed on Silica Gel F_{254} plates (Merck) and column chromatography on Silica Gel Merck 60. Melting points were determined on a Buchi SMP-20 apparatus and are uncorrected. High-resolution mass spectra were recorded with electron-spray ionization on a Bruker Daltonics microOTOF-QII instrument. All solutions were dried over Na_2SO_4 and evaporated at reduced pressure on a Buchi-R200 rotary evaporator at a temperature below 45 °C. All products were vacuum dried at room temperature. All solvents, chemicals, and reagents were obtained commercially and used without purifications. The IR-spectra were obtained on a Nicolet-iS10 Fourier transform IR spectrometer (Thermo scientific, USA) with DTGS detector, splitter KBr and a Smart Performer module equipped with a ZnSe-crystal (ATR). The spectra were run on the range of 3000–650 cm^{-1} with a resolution of 4 cm^{-1}. The spectra were proceeded using the OMNIC-7.0 program package.

4.2. 2-Bromo-1,4-dimethoxy-3-(phenylethynyl)anthracene-9,10-dione (3a), 1,4-dimethoxy-2,3-bis(phenylethynyl)anthracene-9,10-dione (3b)

A solution of 2,3-dibromoanthraquinone **1**[21] (250.0 mg, 0.59 mmol), phenylacetylene (**2a**) (0.13 mL, 1.20 mmol), $Pd(PPh_3)_2Cl_2$ (42.1 mg, 0.06 mmol), PPh_3 (31.5 mg, 0.12 mmol), and Et_3N (2.00 mL, 14.33 mmol) in THF (4.00 mL) in a Schlenk tube was degassed with argon and charged with CuI (1.1 mg, 6 μmol). The resulting mixture was stirred at 60 °C for 3 h. The reaction mixture was diluted with water and neutralized by the addition of aqueous HCl to pH=5 and the product was extracted with ethyl acetate (2×15 mL). The extract was washed twice with water, dried ($MgSO_4$), and the solvent evaporated in vacuo. The residue was purified by column chromatography using toluene–ethyl acetate (1:0/5:1) as eluting solvent to afford the compound **3a** in 15% yield (39.6 mg), R_f=0.7 (toluene–ethyl acetate=5:1) and compound **3b** in 65% yield (179.7 mg) R_f=0.6 (toluene–ethyl acetate=5:1).

*4.2.1. 2-Bromo-1,4-dimethoxy-3-(phenylethynyl)anthracene-9,10-dione (**3a**).* Yellow solid, mp 153–155 °C; ν_{max} 3372, 2211 (C≡C), 1676 (C=O), 1593, 1542, 1511, 1455, 1370, 1333, 1302, 1263 (C–O–C), 1103, 1030 (C–O–C), 975, 739, 675 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.19–8.16 (2H, m, C*H*^{5,8}), 7.77–7.74 (2H, m, C*H*^{6,7}), 7.66–7.63 (2H, m, Ph), 7.43–7.38 (3H, m, Ph), 4.13 (3H, s, O*Me*), 4.02 (3H, s, O*Me*); δ_C (100 MHz, $CDCl_3$) 182.2 (C=O), 181.8 (C=O), 158.1, 154.2, 133.9, 133.8, 133.8 (2CH), 132.0 (CH), 130.9, 130.1, 129.6 (2CH), 128.8 (2CH), 126.7 (CH), 126.7, 126.6 (CH), 122.2, 122.2, 102.9, 84.1, 62.2 (OMe), 62.0 (OMe). HRMS (ESI) calcd for $C_{24}H_{16}BrO_4$, 447.0226 $(M+H)^+$; found, 447.0212.

*4.2.2. 1,4-Dimethoxy-2,3-bis(phenylethynyl)anthracene-9,10-dione (**3b**).* Yellow solid, mp 175–176 °C; ν_{max} 3364, 1671 (C=O), 1592, 1537, 1325, 1254 (C–O–C), 1026 (C–O–C), 984, 750, 682 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.18–8.16 (2H, m, C*H*^{5,8}), 7.74–7.72 (2H, m, C*H*^{6,7}), 7.63–7.61 (4H, m, Ph), 7.41–7.36 (6H, m, Ph), 4.14 (6H, s, 2O*Me*); δ_C (100 MHz, $CDCl_3$) 182.1 (C=O), 157.5, 134.1, 133.7 (CH), 131.9 (CH), 129.3 (2CH), 129.2, 128.5 (2CH), 126.7, 126.6 (CH), 122.5, 102.3, 83.8, 62.0 (2OMe). HRMS (ESI) calcd for $C_{32}H_{21}O_4$, 469.1434 $(M+H)^+$; found, 469.1426.

4.3. 2-Bromo-3-hydroxy-1,4-dimethoxyanthracene-9,10-dione (4)

A mixture of NaH (0.40 g, 10 mmol, 60% suspension in vaseline oil) and benzaldoxime (1.40 g, 11 mmol) in DMA (20 mL) was stirred for 30 min at 30–35 °C under argon. 2,3-Dibromoanthraquinone **1**[21] (2.34 g, 5.5 mmol) was dissolved in THF (50 mL) and the

obtained solution was cooled in an ice bath and added dropwise to the solution of benzaldoxime cooled to 0 °C. The reaction mixture was stirred for 1 h at room temperature, diluted with a mixture of water and ice, and neutralized by aqueous HCl to pH=5. The yellow precipitate was filtered, washed with water, dried, and washed with hexane. The residue was recrystallized from toluene to give an 82% yield of compound **4** (1.64 g) as yellow solid, mp 223–225 °C; ν_{max} 3369 (OH), 1665 (C=O), 1594, 1526, 1455, 1395, 1353, 1312, 1239 (C–O–C), 1128, 1060, 1027 (C–O–C), 849, 797, 744, 694 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 11.26 (1H, br s, OH), 8.05–8.02 (2H, m, C*H*^{5,8}), 7.84–7.78 (2H, m, C*H*^{6,7}), 3.82 (3H, s, O*Me*), 3.80 (3H, s, O*Me*); δ_C (100 MHz, DMSO-d_6) 182.0 (C=O), 180.2 (C=O), 155.6, 155.1, 144.9, 134.0, 133.6, 133.5 (CH), 133.3 (CH), 126.1 (CH), 126.0 (CH), 125.9, 125.8, 118.5, 114.0, 61.6 (OMe), 61.1 (OMe). HRMS (ESI) calcd for $C_{16}H_{12}BrO_5$, 362.9863 $(M+H)^+$; found, 362.9857.

4.4. 4,11-Dimethoxy-2-phenylanthra[2,3-*b*]furan-5,10-dione (5a)

A solution of 2-bromo-3-hydroxyanthraquinone **4** (250 mg, 0.69 mmol), phenylacetylene (**2a**) (0.23 mL, 2.1 mmol), $Pd(PPh_3)_2Cl_2$ (49.1 mg, 0.07 mmol), PPh_3 (36.8 mg, 0.14 mmol), and Et_3N (2.00 mL, 14.33 mmol) in 1,4-dioxane (4.00 mL) in a Schlenk tube was degassed with argon and charged with CuI (1.3 mg, 7 μmol). The resulting mixture was stirred at 100 °C for 1.5 h. The reaction mixture was diluted with water and neutralized by the aqueous HCl to pH=5 and the product was extracted with ethyl acetate (2×15 mL). The extract was washed twice with water, dried ($MgSO_4$), and the solvent evaporated in vacuo. The residue was purified by column chromatography using toluene–ethyl acetate (1:0/5:1) as eluting solvent to afford the compound **5a** in 65% yield (172.4 mg) as yellow solid, mp 250–251 °C; ν_{max} 3372, 1662 (C=O), 1356, 1296, 1263 (C–O–C), 1106, 1043, 1027 (C–O–C), 1005, 849, 744, 683 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.23–8.20 (2H, m, C*H*^{6,9}), 7.93–7.91 (2H, m, Ph), 7.74–7.72 (2H, m, C*H*^{7,8}), 7.53–7.43 (3H, m, Ph), 7.30 (1H, s, C*H*^{3}), 4.37 (3H, s, OMe), 4.16 (3H, s, OMe); δ_C (100 MHz, $CDCl_3$) 183.1 (2C=O), 159.2, 150.9, 150.4, 143.5, 134.8, 134.4, 133.3 (2CH), 130.8, 130.0 (CH), 129.1 (2CH), 128.8, 126.5 (2CH), 125.5 (2CH), 122.0, 121.6, 100.3 (CH), 62.1 (OMe), 62.0 (OMe). HRMS (ESI) calcd for $C_{24}H_{17}O_5$, 385.1071 $(M+H)^+$; found, 385.1084.

4.5. 2-(Hydroxymethyl)-4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione (5b)

This compound was prepared from 2-bromo-3-hydroxyanthraquinone **4** and propargyl alcohol (**2b**) as described for anthrafurandione **5a**. Yellow solid, mp 187–189 °C; ν_{max} 3448 (O–H), 1657 (C=O), 1437, 1360, 1338, 1287, 1255 (C–O–C), 1119, 1039, 1027 (C–O–C), 979, 867, 795, 740, 722, 694 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.20–8.17 (2H, m, C*H*^{6,9}), 7.72–7.70 (2H, m, C*H*^{7,8}), 6.96 (1H, s, C*H*^{3}), 4.85 (2H, s, C*H*$_2$OH), 4.22 (3H, s, O*Me*), 4.07 (3H, s, O*Me*); δ_C (100 MHz, $CDCl_3$) 183.2 (C=O), 183.1 (C=O), 160.4, 151.2, 151.0, 143.3, 134.6, 134.4, 133.4 (2CH), 129.3, 126.5 (2CH), 122.2, 121.3, 103.4 (CH), 62.0 (2OMe), 57.9 (CH_2). HRMS (ESI) calcd for $C_{19}H_{15}O_6$, 339.0863 $(M+H)^+$; found, 339.0857.

4.6. 4,11-Dimethoxy-2-((tetrahydro-2*H*-pyran-2-yloxy)methyl)anthra[2,3-*b*]furan-5,10-dione (5c)

This compound was prepared from 2-bromo-3-hydroxyanthraquinone **4** and 2-(prop-2-ynyloxy)tetrahydro-2*H*-pyran (**2c**) as described for anthrafurandione **5a**. Yellow solid, mp 93–95 °C; ν_{max} 3363, 1666 (C=O), 1358, 1338, 1291, 1259 (C–O–C), 1114, 1028 (C–O–C), 798, 736, 679 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.19–8.17 (2H, m, C*H*^{6,9}), 7.71–7.69 (2H, m, C*H*^{7,8}), 6.99 (1H, s, C*H*^{3}), 4.81 (1H, t, *J* 13.6 Hz, OC*H*OCH$_2$), 4.87 (1H, d, *J* 13.6 Hz, C*H*HOTHP), 4.69 (1H, d, *J* 13.6 Hz, CH*H*OTHP), 4.24 (3H, s, O*Me*), 4.10 (3H, s, O*Me*), 3.94–3.88 (1H, m, OCHOC*H*H), 3.60–3.55 (1H, m, OCHOCH*H*), 1.87–1.54 (6H, m, 3C*H*$_2$); δ_C (100 MHz, $CDCl_3$) 183.2 (C=O), 183.0 (C=O), 158.3, 151.1 (2C), 143.4, 134.6, 134.5, 133.3 (2CH), 129.4, 126.5 (2CH), 122.1, 121.2, 104.6 (CH), 98.1 (CH), 62.1 (OMe), 62.0 (CH_2O), 61.9 (OCH_2), 61.0 (OMe), 30.2 (CH_2), 25.3 (CH_2), 19.0 (CH_2). HRMS (ESI) calcd for $C_{24}H_{23}O_7$, 423.1438 $(M+H)^+$; found, 423.1447.

4.7. 4,11-Dimethoxy-2-(trimethylsilyl)anthra[2,3-*b*]furan-5,10-dione (5d)

This compound was prepared from 2-bromo-3-hydroxyanthraquinone **4** and ethynyltrimethylsilane (**2d**) as described for anthrafurandione **5a**. Yellow solid, mp 57–59 °C; ν_{max} 1665 (C=O), 1588, 1362, 1326, 1290, 1249 (C–O–C), 1109, 1091, 1035 (C–O–C), 977, 911, 843 (Si–Me), 798, 759, 692 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.19–8.17 (2H, m, C*H*^{6,9}), 7.70–7.68 (2H, m, C*H*^{7,8}), 7.21 (1H, s, C*H*^{3}), 4.28 (3H, s, O*Me*), 4.11 (3H, s, O*Me*), 0.39 (9H, s, Si*Me*$_3$); δ_C (100 MHz, $CDCl_3$) 183.4 (C=O), 183.1 (C=O), 168.3, 154.1, 151.2, 143.6, 134.8, 134.7, 133.2 (2CH), 129.3, 126.4 (2CH), 121.8, 120.8, 114.9 (CH), 62.0 (OMe), 61.6 (OMe), −2.0 ($SiMe_3$). HRMS (ESI) calcd for $C_{21}H_{21}O_5Si$, 381.1153 $(M+H)^+$; found, 381.1145.

4.8. 2-*tert*-Butyl-4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione (5e)

This compound was prepared from 2-bromo-3-hydroxyanthraquinone **4** and 3,3-dimethylbutyne (**2e**) as described for anthrafurandione **5a**. Yellow solid, mp 179–181 °C; ν_{max} 3396, 1664 (C=O), 1363, 1328, 1297, 1259 (C–O–C), 1185, 1111, 1035 (C–O–C), 930, 798, 734, 672 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.19–8.17 (2H, m, C*H*^{6,9}), 7.70–7.68 (2H, m, C*H*^{7,8}), 6.65 (1H, s, C*H*^{3}), 4.26 (3H, s, O*Me*), 4.08 (3H, s, O*Me*), 1.42 (9H, s, C*Me*$_3$); δ_C (100 MHz, $CDCl_3$) 183.3 (C=O), 183.2 (C=O), 171.1, 150.6, 150.3, 143.3, 134.7, 134.4, 133.2 (2CH), 130.3, 126.4 (2CH), 121.1, 121.0, 98.7 (CH), 61.8 (OMe), 61.6 (OMe), 33.4, 28.6 (3Me). HRMS (ESI) calcd for $C_{22}H_{21}O_5$, 365.1384 $(M+H)^+$; found, 365.1386.

4.9. 2-((Dimethylamino)methyl)-4,11-dimethoxyanthra[2,3-*b*]furan-5,10-dione (5f)

This compound was prepared from 2-bromo-3-hydroxyanthraquinone **4** and *N*,*N*-dimethylpropargyl amine (**2f**) as described for anthrafurandione **5a**. Yellow solid, mp 106–108 °C; ν_{max} 1666 (C=O), 1590, 1468, 1358, 1292, 1260 (C–O–C), 1039 (C–O–C), 978, 801, 740, 687 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.18–8.16 (2H, m, C*H*^{6,9}), 7.70–7.68 (2H, m, C*H*^{7,8}), 6.92 (1H, s, C*H*^{3}), 4.23 (3H, s, O*Me*), 4.09 (3H, s, O*Me*), 3.71 (2H, s, C*H*$_2$), 2.38 (6H, s, 2Me); δ_C (100 MHz, $CDCl_3$) 183.2 (C=O), 183.1 (C=O), 159.0, 150.9, 150.8, 143.4, 134.6, 134.4, 133.3 (2CH), 129.5, 126.5 (2CH), 121.9, 121.2, 104.6 (CH), 61.8 (2OMe), 55.9 (CH_2), 45.2 (2Me). HRMS (ESI) calcd for $C_{21}H_{20}NO_5$, 366.1336 $(M+H)^+$; found, 366.1331.

4.10. *tert*-Butyl (4,11-dimethoxy-5,10-dioxo-5,10-dihydroanthra[2,3-*b*]furan-2-yl)methylcarbamate (5g)

This compound was prepared from 2-bromo-3-hydroxyanthraquinone **4** and *tert*-butyl prop-2-ynylcarbamate (**2g**) as described for anthrafurandione **5a**. Yellow solid, mp 96–97 °C (decomp.); ν_{max} 3353 (N–H), 2976, 1693 (C=O), 1665 (C=O), 1515 (N–H), 1366, 1328, 1246 (C–O–C), 1161, 1047 (C–O–C), 862 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.17–8.15 (2H, m, C*H*^{6,9}), 7.70–7.68 (2H, m, C*H*^{7,8}), 7.19 (1H, br s, N*H*), 6.87 (1H, s, C*H*^{3}), 4.50 (2H, d, *J* 5.9 Hz, C*H*$_2$), 4.20 (3H, s, O*Me*), 4.05 (3H, s, O*Me*), 1.45 (9H, s, 3Me); δ_C (100 MHz, $CDCl_3$) 183.2 (C=O), 183.0 (C=O), 159.0, 155.8, 151.0,

150.8, 143.2, 134.6, 134.5, 133.3 (2CH), 129.5, 126.4 (2CH), 121.3, 121.2, 102.9 (CH), 80.3, 61.9 (2OMe), 38.1 (CH_2), 28.3 (3Me). HRMS (ESI) calcd for $C_{24}H_{24}NO_7$, 438.1547 $(M+H)^+$; found, 438.1553.

4.11. 4,11-Dimethoxyantra[2,3-*b*]furan-5,10-dione (5h)

A solution of 4,11-dimethoxy-2-(trimethylsilyl)anthra[2,3-*b*]furan-5,10-dione (**5d**) (100 mg, 0.26 mmol) and tetrabutylammonium fluoride trihydrate (94.7 mg, 0.30 mmol) in THF (5.0 mL) was stirred at room temperature for 15 min. The reaction mixture was diluted with water and extracted with ethyl acetate (2×10 mL). The extract was washed twice with water, dried ($MgSO_4$), and the solvent evaporated in vacuo. The residue was recrystallized from toluene to afford the compound **5h** in 90% yield (72.1 mg). Yellow solid, mp 148–150 °C (mp 148–150 °C,[9] from toluene); ν_{max} 3361, 1661 (C=O), 1345, 1362, 1305, 1289, 1252 (C–O–C), 1204, 1078, 1041 (C–O–C), 1009, 974 cm^{-1}.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.08.033. These data include MOL files and InChIKeys of the most important compounds described in this article.

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