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HETEROCYCLIC ANALOGS OF 5,12-NAPHTHACENEQUINONE 8.* SYNTHESIS OF FURANO-ANTHRAQUINONES

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During the condensation of 2,3-dichloroquinizarine with methyl pivaloylacetate in the presence of potassium carbonate in dimethyl sulfoxide the main reaction products are derivatives of angular 3-pivaloylanthra[1,2-b]furan-2,6,11(3H)-trione (about 70%) and anthra[2,1-d][1,3]dioxole-6,11-dione (15%), whereas the yield of the targeted linear methyl 2-tert-butyl-4,11-dihydroxyanthra[2,3-b]furan-5,10-dione-3-carboxylate is only 2%. Methods are developed for modification of the obtained 3-pivaloylanthra[1,2-b]furan-2,6,11(3H)-trione, making it possible to use it for the synthesis of the tert-butyl derivatives of linear anthra[2,3-b]furan-5,10-dione or angular anthra[1,2-b]furan-6,11-dione.

Keywords: anthra[2,1-*d*][1,3]dioxole-6,11-dione, anthra[2,3-*b*]furan-5,10-dione, anthra[1,2-*b*]furan-6,11-dione, anthra[1,3-*b*]furan-2,6,11(3H)-trione, 2,3-dichloroquinizarine, methyl pivaloylacetate, condensation, modification.

It is known that the anthra[2,3-*b*]furan-5,10-dione series (the furan analogs of 5,12-naphthacenequinone) contains some highly toxic derivatives that are precursors in the biosynthesis of the aflatoxins produced by *Aspergillus flavus* [2]. However, methods for the production of this class of compounds and their biological activity remain little investigated. One of the most convenient methods for the synthesis of substituted 4,11-dihydroxyanthra[2,3-*b*]furan-5,10-diones is the method based on the condensation of 2,3-dichloroquinizarine with the enolates of acetoacetic ester and its analogs [3]. While continuing to develop methods for the production of new anthra[2,3-*b*]furan-5,10-diones, we studied the possibility of using a similar approach for the synthesis of anthrafurandiones containing a *tert*-butyl group with methyl pivaloylacetate as 1,3-dicarbonyl compound.

* For Communication 7 see [1].

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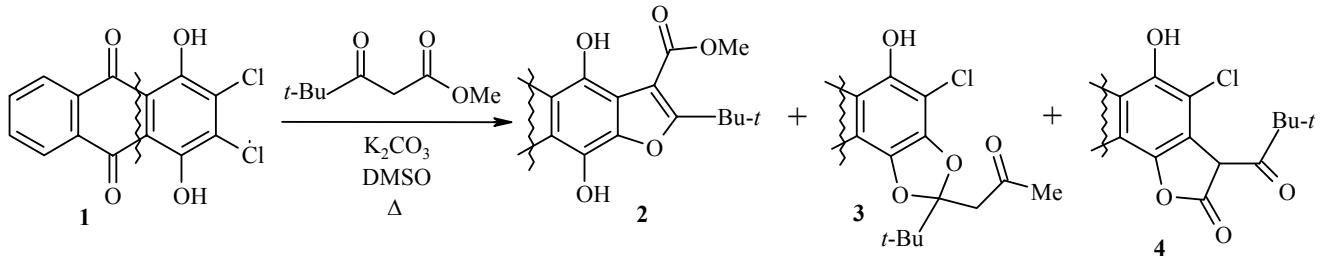
Study of the products from the condensation of methyl pivaloylacetate with 2,3-dichloroquinizarine showed that replacement of the acetyl in acetoacetic ester by a pivaloyl group has a substantially negative effect on the yield of the anthra[2,3-*b*]furan-5,10-dione derivative. Thus, during the cyclization of 2,3-dichloroquinizarine **1** by heating in the presence of potassium carbonate with acetoacetic ester in DMSO the yield of the furanoquinizarine derivative amounts to more than 60%. With methyl pivaloylacetate under analogous conditions a mixture of products, from which we isolated the targeted methyl 2-*tert*-butyl-4,11-dihydroxyanthra[2,3-*b*]furan-5,10-dione-3-carboxylate (**2**) with a yield of less than 2% by chromatography, was obtained. A compound similar to it in chromatographic mobility and isolated with a yield of ~10% was identified as a derivative of anthra[2,1-*d*][1,3]dioxole-6,11-dione **3**.



The main component (65-70%) of the reaction mixture was a derivative differing from the other reaction products in its properties. Thus, on Merck TLC plates it appears as a violet-black spot, fixed when ethyl acetate is used as eluent. At the same time it is mobile on Silufol plates in chloroform, and in this case the spot is yellow. After isolation in the individual form it was found that this compound has strong solvatochromic

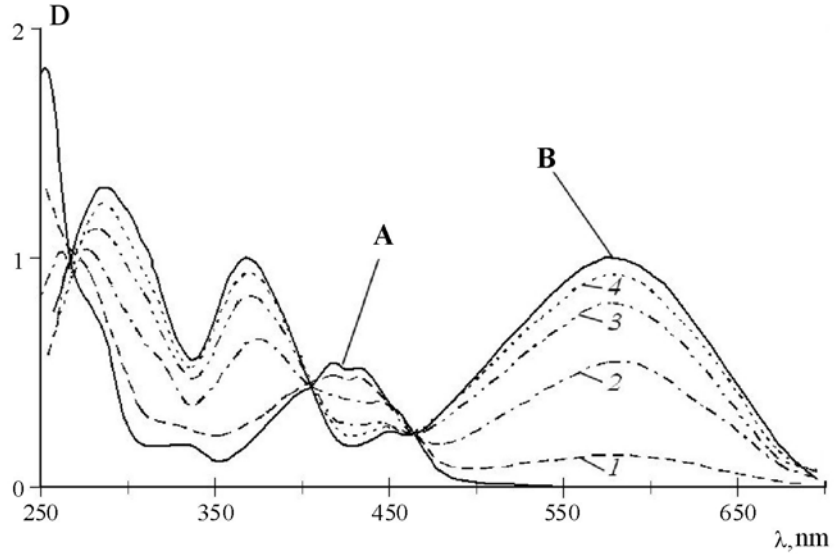
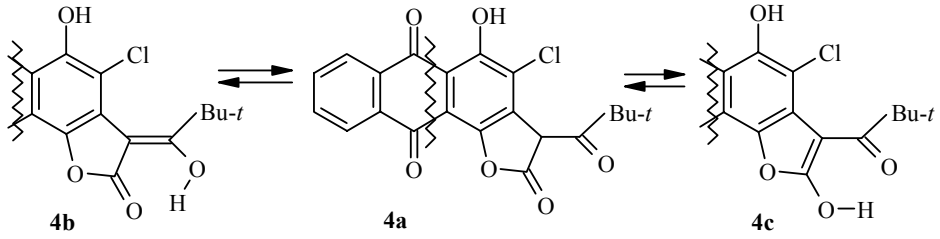


Fig. 1. The electronic absorption spectra of solutions ($5 \cdot 10^{-5}$ M) of anthra[1,2-*b*]furan-2,6,11-trione **4** in chloroform **A**, DMSO **B**, and their mixtures in ratios 1:5 (*1*), 2:3 (*2*), 3:2 (*3*), and 5:1 (*4*).

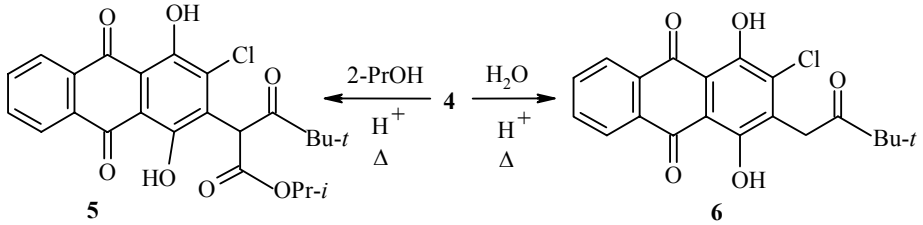
characteristics. Thus, its solutions in nonpolar hydrocarbon and weakly polar solvents (hexane, benzene, toluene, methylene chloride, chloroform, tetrachloromethane, ethyl acetate) are yellow. In the fine structure of the long-wave maximum the electronic absorption spectra in these solvents are reminiscent of the absorption spectrum of 1-hydroxyanthraquinone [4], shifted somewhat towards the long-wave region (Fig. 1). At the same

time solutions of this compound in alcohols, DMF, and DMSO have a dark-blue color and are characterized by a strong absorption maximum in the region of 570-580 nm. It was established on the basis of NMR, mass spectrometry, and elemental analysis that this is a derivative of the angular 3-pivaloylanthra[1,2-*b*]furan-2,6,11(3H)-trione **4**.

The presence of the pivaloylacetate fragment, conjugated with the anthraquinone chromophore and capable of tautomeric transformations, in the structure of compound **4** gives rise to its solvatochromic characteristics. Thus, according to the data from the ^{1}H and ^{13}C NMR spectra, in solution of $CDCl_3$ this compound exists entirely in the keto form **4a**, which has a yellow color. At the same time, in solution in DMSO-d_6 this derivative exists predominantly in two tautomeric forms (their ratio varies depending on the temperature, concentration, and other factors), and their spectra do not contain the characteristic signal of the proton at position 3 of the heterocyclic ring in the region of $\delta \approx 5.4$ ppm. Spectrophotometric investigation of the absorption spectra in mixtures of chloroform and DMSO showed the presence of three isobestic points and confirmed that compound **4** exists in several tautomeric forms, the equilibrium between which is affected by solvation factors (Fig. 1). In all probability the enolic forms of this compound **4b** and **4c**, which are more deeply colored than the keto form **4a** on account of entry of auxochromic groups into conjugation with the chromophore, predominate in polar solvents.

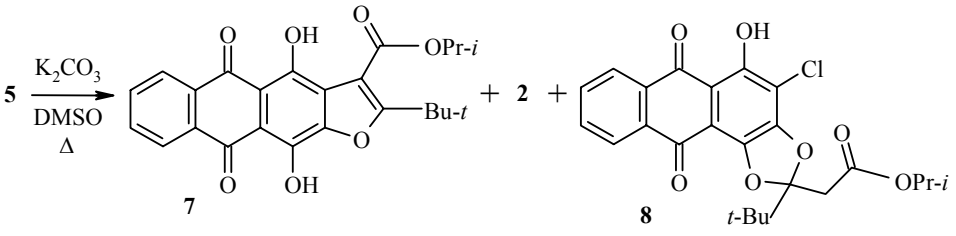


The low yield in the cyclization of the linear anthrafurandione **2** and the high yield of the angular anthra[1,2-*b*]furan-2,6,11(3H)-trione **4** compelled us to look for its transformation into derivatives of anthra-[2,3-*b*]furan-5,10-dione. It was found that this compound, like other angular heterocyclic derivatives of anthraquinone with heteroatoms at the *peri* positions of the quinone fragment, are unstable [5]. Thus, this compound is easily transesterified, for example, during boiling in isopropyl alcohol in the presence of acid, and is converted into a quinizarine derivative of the isopropylpivaloyl acetate **5**. Unlike the initial anthrafurantrione **4**, compound **5** does not have such clearly defined solvatochromic characteristics in spite of the presence of the pivaloyl fragment. Under the conditions of acid hydrolysis of the anthrafurantrione **4** by boiling in 1,4-dioxane, the obtained keto acid is decarboxylated and gives the derivative of methyl *tert*-butyl ketone **6** with a yield of 72%.

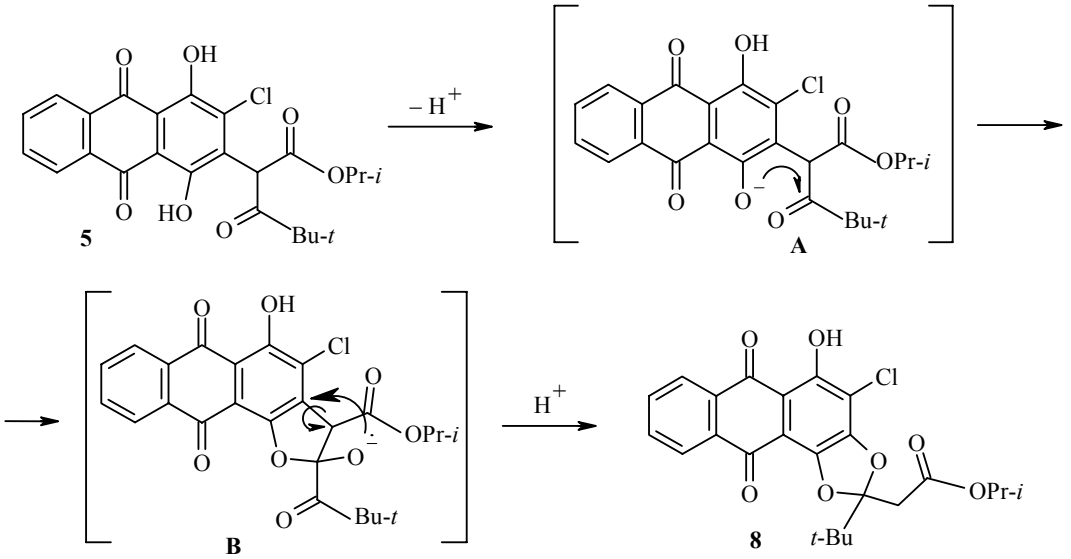


The cyclization of compound **5** by heating in the presence of potassium carbonate in DMSO gives a somewhat better result than the condensation of 2,3-dichloroquinizarine **1** with methyl pivaloylacetate. However, in this case the main reaction product (more than 60%) is the angular 3-pivaloylanthra[1,2-*b*]furan-

2,6,11(3H)-trione **4**, while the yield of the linear isomer **7** is not greater than 20%. It is interesting that change in the order of mixing of the reagents leads to the preferential formation of the derivative of anthra[2,1-*d*]-[1,3]dioxole-6,11-dione **8**, whereas the linear anthrafurandione **7** is formed in trace quantities. Although it does increase the yield of the linear anthrafurandione, the introduction of the bulky ester group into the pivaloyl-acetate residue does not substantially prevent the formation of the angular derivative **4**. Consequently, the low yield of the anthra[2,3-*b*]furan-5,10-diones **2** and **7** during cyclization of the pivaloylacetate derivatives is due to the presence of the bulky *tert*-butyl group in its side chain, and this evidently has a negative effect on the geometry and/or stability of the transition state. This agrees with data in [3], where the smallest yield of the linear anthrafurandione was recorded during the cyclization of 2,3-dichloroquinizarine **1** with ethyl benzoylacetate, which also contains a bulky substituent (phenyl group) in the side chain.

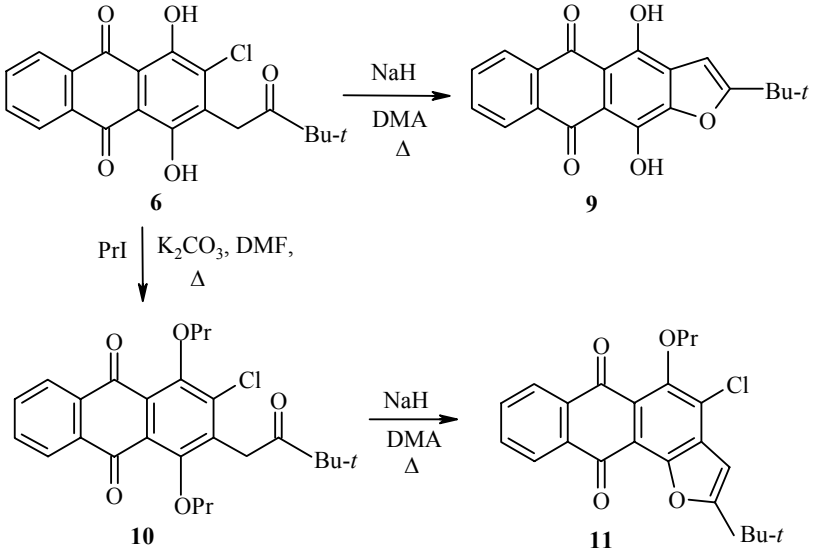


As in the case of its analog **3**, the formation of compound **8** cannot be explained by the formation of an acetal as a result of the addition of the phenol group of the quinizarine derivative to the carbonyl group of the pivaloylacetate. The reason for such isomerization in both cases clearly is rearrangement caused by ionization of the phenol group presumably taking place through the adduct **B**, in which successive substitution of the acetyl fragment by the hydroxide anion gives the derivative of anthra[2,1-*d*][1,3]dioxole-6,11-dione **8**. The obtained substituted anthra[2,1-*d*][1,3]dioxole-6,11-diones **3** and **8** may be of interest in the search for drugs since they are derivatives of morindaparvin A – a biologically active ingredient isolated from *Morinda parvifolia* – extracts of which have been used from ancient times in traditional Chinese medicine [6].



In a number of cases methods involving the cyclization of benzyl ketones containing leaving groups at the *ortho* position under the influence of bases have proved effective for annelation of the furan ring [7]. This

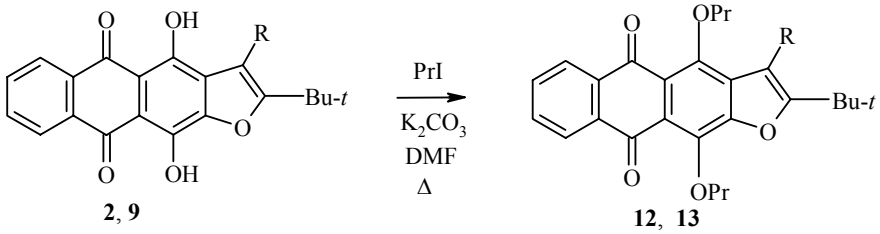
method also proved effective for the production of derivatives of anthra[2,3-*b*]furan-5,10-dione. However, the cyclization of methyl *tert*-butyl ketone **6** takes place under harsher conditions than the cyclization of the keto ester **5** – with heating in the presence of an excess of a strong base (NaH) in N,N-dimethylacetamide. Under these conditions practically the only product is *tert*-butyl-4,11-dihydroxyanthra[2,3-*b*]furan-5,10-dione **9**, but on account of strong resin formation in the mixture its yield amounts to about 30%. The tarring may be due to the presence of the hydroxy groups in the initial compound **6**. Alkylation with propyl iodide in the presence of potassium carbonate was therefore used for their protection, and as a result its O,O-dipropyl derivative **10** was obtained. Actually the ketone **10** undergoes cyclization almost without resin formation under the action of NaH, but in this case the angular 2-*tert*-butyl-4-chloro-5-propoxyanthra[1,2-*b*]furan-6,11-dione (**11)** is formed with almost quantitative yield. Thus, in the ketone **10** the alkoxy group at position 1 is more reactive for nucleophilic substitution than the chlorine at position 3.



6 **9** **10** **11**

DMA – N,N-dimethylacetamide

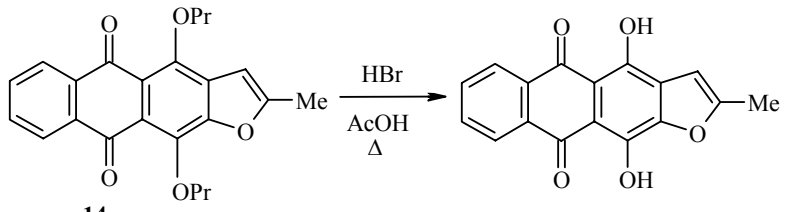
From the furanoquinizarine derivatives **2** and **9** their O,O-dipropyl derivatives **12** and **13** were obtained by alkylation with propyl iodide in the presence of potassium carbonate in DMF.



2, **9** **12**, **13**

2, 12 R = CO_2Me, **9, 13** R = H

To compare the spectral characteristics of the obtained furanoquinizarine derivatives **2**, **7**, and **9** we synthesized another of its derivatives 4,11-dihydroxy-2-methylanthra[2,3-*b*]furan-5,10-dione (**15)** by dealkylation of 4,11-dipropoxyanthrafurandione **14** (prepared by the method in [8]) by treatment with HBr in acetic acid.



14 **15**

In conclusion it is necessary to mention the changes observed in the electronic absorption spectra of the obtained compounds. The long-wave absorption maxima for the quinizarine derivatives **2**, **5-7**, **9**, and **15** lie in the region of 470-510 nm, which practically coincides with the position of the long-wave absorption in the spectrum of quinizarine [9]. However, the spectra of the furanoquinizarine derivatives **2**, **7**, **9**, and **15** are characterized by the presence in the visible region of three absorption bands, which appear in the form of two maxima and an inflection in the more shortwave region and are most clearly defined for derivatives **9** and **15** (Fig. 2). These compounds, not containing alkoxycarbonyl groups at position 3 of the chromophore and differing in the alkyl group at position 2, have practically identical electronic absorption spectra. The "two-humped" absorption characteristic of them, which is absent in the spectrum of quinizarine, is a distinctive feature of a series of its other heterocyclic derivatives [10] and is explained by the existence of three excited states, differing in the contribution from the 9,10-, 1,10-, and 1,4-anthraquinoid structures, in these compounds. Also close in the character and intensity of the bands are the absorption spectra of 4,11-dialkoxy derivatives of anthra[2,3-*b*]furan-5,10-dione **12-14**, the long-wave maxima of which lie in the region of 385-397 nm. Comparison of their absorption spectra with the absorption spectrum of anthra[1,2-*b*]furan-6,11-dione **11**, shows that the angular analog **11** is characterized by a hypsochromic shift of the absorption maximum, while its intensity is higher than for the linear derivatives. The electronic absorption spectra of anthra[2,1-*d*][1,3]dioxole-6,11-diones **3** and **8** practically coincide with the absorption spectrum of 1-hydroxyanthraquinone both in the position of the long-wave maximum and in its characteristic fine structure [4]. An interesting feature of all the linear anthra[2,3-*b*]furan-5,10-diones **2**, **7**, **9**, and **12-15** is the presence of fluorescence in the solutions with emission maxima in the region of 570-585 nm, whereas fluorescence is uncharacteristic of all the angular derivatives **3**, **4**, **8**, and **11**.

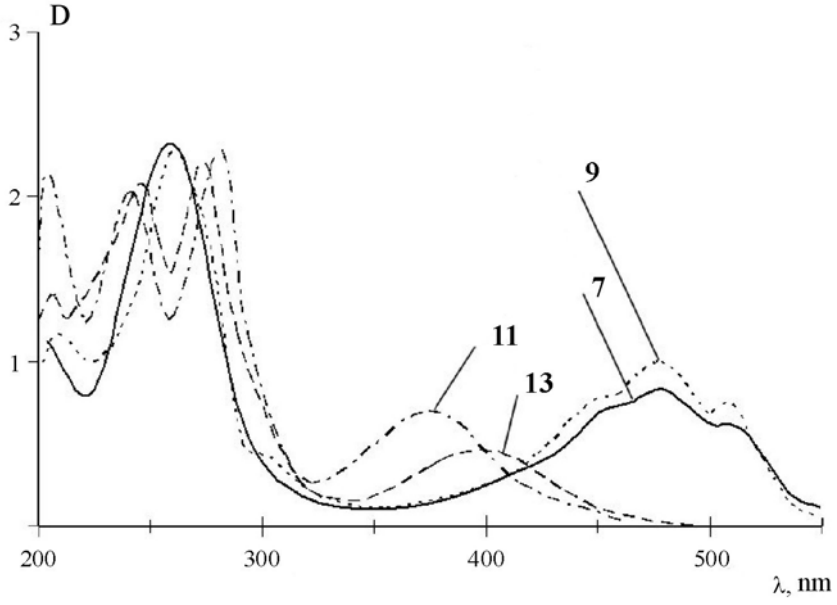


Fig. 2. The electronic absorption spectra of anthrafurandiones **7**, **9**, **11**, and **13** in ethanol.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer (400 MHz) in $CDCl_3$ (compounds **2**-**13**) and DMSO-d_6 (compound **15**) with TMS as internal standard. The mass spectra were recorded on a Finnigan-MAT SSQ 710 chromato-mass spectrometer (USA); ionization energy 70 eV, direct sample injection into ion source, sample heated to 350°C, ionization chamber 150°C. The absorption spectra were recorded on a Hitachi U2000 spectrometer. The reactions and the purity of the compounds were monitored by TLC on Silufol and silica gel 60 F_{254} plates (Merck). Preparative chromatography was carried out on Merck 60 silica gel.

Methyl 2-*tert*-Butyl-4,11-dihydroxyanthra[2,3-*b*]furan-5,10-dione-3-carboxylate (2), Methyl 2-(2-*tert*-Butyl-5-hydroxyanthra[2,1-*d*][1,3]dioxole-6,11-dion-2-yl)acetate (3), and 4-Chloro-5-hydroxy-3-pivaloyl-anthra[1,2-*b*]furan-2,6,11(3H)-trione (4). A mixture of 2,3-dichloroquinizarine **1** (5.0 g, 16 mmol), of calcined potassium carbonate (14 g, 100 mmol), and methyl pivaloylacetate (5.0 ml, 31 mmol) in DMSO (100 ml) was heated at 130°C with stirring in a stream of argon for 3 h (monitored by TLC). The reaction mass was cooled and poured carefully into a mixture of water (200 ml) and of conc. HCl (30 ml) with stirring. The product was extracted with a hot 2:1 mixture of ethyl acetate and toluene (3×300 ml). The combined extracts were washed with water (3×100 ml), dried, and evaporated. The residue was recrystallized twice from toluene, and the crystals were washed with toluene and dried. We obtained 3.6 g (56%) of yellow crystals of the anthrafurantrione **4**; mp 247-248°C. The mother solutions after crystallization of the anthrafurantrione **4** were diluted with ethyl acetate and washed with 0.5% $NaHCO_3$ solution (5×50 ml) and with water to remove the residues of the anthrafurantrione **4**. By acidifying the aqueous phase and repeated extraction it is possible to isolate a further 10-15% of the anthrafurantrione **4**. The organic extract was dried, evaporated, and the residue recrystallized three times from a mixture of toluene and hexane. We obtained 0.55 g (8%) of yellow crystals of the anthradioxoledione **3**; mp 172-174°C. The mother solutions were combined and evaporated. The residue was separated by chromatography (silica gel, 10:0 → 10:1 benzene–ethyl acetate), and the products were purified by recrystallization from benzene. We isolated 95 mg (1.5%) of red needle crystals of the anthrafurandione **2** (R_f 0.6, Merck silica gel 60, 7:1 toluene–ethyl acetate, mp 209-211 °C) and 0.21 g (3%) of yellow crystals of the anthradioxoledione **3** (R_f 0.57, Merck silica gel 60, 7:1 toluene–ethyl acetate).

Methyl 2-*tert*-Butyl-4,11-dihydroxyanthra[2,3-*b*]furan-5,10-dione-3-carboxylate (2). ^1H NMR spectrum, δ, ppm: 14.11 (1H, s, HO); 13.99 (1H, s, HO); 8.36 (2H, m, H-5,8); 7.81 (2H, m, H-6,7); 4.00 (3H, s, OCH_3); 1.48 (9H, s, *t*-C_4H_9). Mass spectrum, m/z (I_{rel}, %): 394 [M^+] (100), 382 (43), 347 (72). Found, %: C 67.27; H 4.49. $C_{22}H_{18}O_7$. Calculated, %: C 67.00; H 4.60.

Methyl 2-(2-*tert*-Butyl-4-chloro-5-hydroxyanthra[2,1-*d*][1,3]dioxole-6,11-dion-2-yl)acetate (3). ^1H NMR spectrum, δ, ppm (*J*, Hz): 13.79 (1H, s, HO); 8.22 (2H, m, H-7,10); 7.76 (2H, m, H-8,9); 4.05 (1H, d, *J* = 16.7, CH_2); 3.73 (1H, d, *J* = 16.7, CH_2); 3.71 (3H, s, OCH_3); 1.48 (9H, s, *t*-C_4H_9). ^{13}C NMR spectrum, δ, ppm: 158.31 (C=O); 180.14 (C=O); 175.93 (O–C=O); 168.63; 156.83; 142.32; 137.32; 133.93; 131.75; 130.91; 121.86; 115.04; 39.47; 135.14 (CH); 134.01 (CH); 127.48 (CH); 126.68 (CH); 34.00 (CH_2); 52.50 (CH_3); 27.20 ($3CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 432 [M^+] (18), 430 (6), 346 (100), 314 (81), 286 (35). Found, %: C 61.10; H 4.69. $C_{22}H_{19}ClO_7$. Calculated, %: C 61.33; H 4.45.

4-Chloro-5-hydroxy-3-pivaloylanthra[1,2-*b*]furan-2,6,11(3H)-trione (4). ^1H NMR spectrum, δ, ppm: 13.68 (1H, s, HO); 8.31 (2H, m, H-7,10); 7.84 (2H, m, H-8,9); 5.43 (1H, s, H-3); 1.43 (9H, s, *t*-C_4H_9). ^{13}C NMR spectrum, δ, ppm: 203.19 (C=O); 188.19 (C=O); 179.38 (C=O); 167.37 (O–C=O); 156.42*; 146.39; 135.07; 133.45; 132.13; 125.41; 115.01; 113.80; 46.88; 135.50 (CH); 134.42 (CH); 127.52 (CH); 127.14 (CH); 51.43 (CH); 26.87 ($3CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 316 [M-COBu-*t*]$^+$ (32), 314 (100), 286 (7), 85 [COBu-*t*]$^+$ (100). Found, %: C 63.11; H 3.64. $C_{21}H_{15}ClO_6$. Calculated, %: C 63.25; H 3.79.

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* Here and subsequently all the signals without assignments belong to the quaternary carbon atoms.

Isopropyl 2-(3-Chloro-1,4-dihydroxyanthracene-9,10-dion-2-yl)-4,4-dimethyl-3-oxopentanoate (5). A mixture of anthrafurantrione **4** (1.2 g, 3 mmol), of isopropyl alcohol (100 ml), and sulfuric acid (0.5 ml) was boiled with stirring for 5 h, while 60-50 ml of distillate was removed. The reaction mass was diluted with ethyl acetate, washed with water and 1% $NaHCO_3$ solution (2×50 ml), and dried. The solution was evaporated, and the residue was purified by column chromatography on SiO_2 (eluent, toluene–ethyl acetate, 5:0 → 5:1) and recrystallized from toluene. The yield was 1.05 g (76%) of red crystals of the keto ester **5**; mp 179-181°C. ^{1}H NMR spectrum, δ, ppm: 13.68 (1H, s, HO); 13.48 (1H, s, HO); 8.30 (2H, m, H-5,8); 7.84 (2H, m, H-6,7); 5.81 (1H, s, CH); 5.28 (1H, m, OCH); 1.31 (15H, m, *t*-C_4H_9, OCH($C\underline{H}_3$)$_2$). ^{13}C NMR spectrum, δ, ppm: 207.36 (C=O); 186.60 (C=O); 186.50 (C=O); 167.24 (O–C=O); 156.44; 153.56; 134.53; 134.03; 133.06; 132.69; 112.26; 110.25; 45.52; 134.94 (CH); 134.79 (CH); 127.11 (CH); 127.05 (CH); 70.15 (CH); 53.57 (CH); 27.03 ($3CH_3$); 21.52 ($2CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 460 [M^+] (2), 458 (6), 341 (8), 314 (100), 288 (22). Found, %: C 62.67; H 5.21. $C_{24}H_{23}ClO_7$. Calculated, %: C 62.82; H 5.05.

2-Chloro-1,4-dihydroxy-3-(3,3-dimethyl-2-oxobutyl)anthracene-9,10-dione (6). A mixture of anthrafurantrione **4** (3.0 g, 7.5 mmol), dioxane (60 ml), and conc. HCl (5.0 ml) was boiled with stirring for 10 h. The reaction mixture was diluted with ethyl acetate, washed with water, 1% $NaHCO_3$ solution (2×50 ml), and water, and dried. The solution was evaporated, and the residue was purified by column chromatography on SiO_2 (eluent, toluene–ethyl acetate, 5:0 → 5:1) and recrystallized from toluene. The yield was 2.1 g (72%) of red crystals of the ketone **6**; mp 233-234°C. ^{1}H NMR spectrum, δ, ppm: 13.56 (1H, s, HO); 13.34 (1H, s, HO); 8.32 (2H, m, H-5,8); 7.85 (2H, m, H-6,7); 4.23 (2H, s, CH_2); 1.32 (9H, s, *t*-C_4H_9). ^{13}C NMR spectrum, δ, ppm: 209.88 (C=O); 186.66 (C=O); 180.55 (C=O); 156.19; 153.72; 135.88; 134.03; 133.20; 132.91; 111.77; 110.63; 44.90; 134.77 (CH); 134.66 (CH); 127.13 (CH); 127.07 (CH); 36.31 (CH_2); 26.66 ($3CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 374 [M^+] (11), 372 (34), 288 (100), 259 (12). Found, %: C 64.63; H 4.43. $C_{20}H_{17}ClO_5$. Calculated, %: C 64.44; H 4.60.

Isopropyl 2-*tert*-Butyl-4,11-dihydroxyanthra[2,3-*b*]furan-5,10-dione-3-carboxylate (7). A mixture of the keto ester **5** (0.5 g, 1.1 mmol), calcined potassium carbonate (1 g, 10 mmol) in DMSO (20 ml) was heated with stirring for 20 min in a stream of argon at 130°C (monitored by TLC). The reaction mass was cooled and poured carefully with stirring into a mixture of 50 ml of water and 10 ml of conc. HCl. The products were extracted with a hot 2:1 mixture (3×50 ml) of ethyl acetate and toluene. The combined extracts were washed with 0.5% $NaHCO_3$ solution (5×30 ml) and water to remove the anthrafurantrione **4**, dried, and evaporated. The residue was purified by chromatography (silica gel, benzene–ethyl acetate, 10:0 → 10:1) and recrystallized from benzene. The yield was 75 mg (16%) of red needle crystals of the anthrafurandione **7**; mp 231-233°C. ^{1}H NMR spectrum, δ, ppm: 13.97 (1H, s, HO); 13.87 (1H, s, HO); 8.22 (2H, m, H-6,9); 7.70 (2H, m, H-7,8); 5.35 (1H, m, OCH); 1.48 (9H, s, *t*-C_4H_9); 1.41 (6H, d, J = 6.3, OCH($C\underline{H}_3$)$_2$). ^{13}C NMR spectrum, δ, ppm: 184.68 (C=O); 184.20 (C=O); 167.21 (O–C=O); 163.92; 156.39; 148.60; 146.16; 133.27; 133.19; 125.52; 111.31; 109.07; 107.92; 34.99; 133.86 (CH); 133.74 (CH); 126.64 (CH); 126.52 (CH); 70.01 (CH); 28.56 ($3CH_3$); 21.60 ($2CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 422 [M^+] (32), 380 (13), 362 (71), 329 (54), 288 (100). Found, %: C 68.54; H 5.11. $C_{24}H_{22}O_7$. Calculated, %: C 68.24; H 5.25.

Isopropyl 2-(2-*tert*-Butyl-4-chloro-5-hydroxyanthra[2,1-*d*][1,3]dioxole-6,11-dion-2-yl)acetate (8). A solution of the keto ester **5** (0.5 g, 1.1 mmol) in DMSO (20 ml) was heated in a stream of argon at 130°C, and calcined potassium carbonate (1.4 g, 10 mmol) was added in one portion with vigorous stirring. The mixture was stirred for 10 min, cooled, and poured with stirring into a mixture of water (50 ml) and conc. HCl (10 ml). The product was extracted with a hot 2:1 mixture of ethyl acetate and toluene (3×50 ml). The combined extracts were washed with a 0.5% solution of $NaHCO_3$ (5×30 ml) and with water to remove the anthrafurantrione **4**, dried, and evaporated. The residue was purified by chromatography (silica gel, benzene–ethyl acetate, 10:0 → 10:1) and recrystallized from benzene. The yield was 0.32 g (64%) of yellow crystals of anthradioxoledione **8**; mp 165-166°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 13.78 (1H, s, HO); 8.22 (2H, m, H-7,10); 7.77 (2H, m, H-8,9); 5.05 (1H, m, OCH); 4.01 (1H, d, J = 16.6, CH_2); 3.67 (1H, d, J = 16.6, CH_2); 1.49 (9H, s,

t-C_4H_9); 1.21 (6H, d, *J* = 6.2, OCH($C\underline{H}_3$)$_2$). ^{13}C NMR spectrum, δ, ppm: 188.32 (C=O); 180.16 (C=O); 175.87 (O–C=O); 167.61; 156.77; 142.34; 137.65; 133.98; 131.79; 130.96; 121.82; 114.98; 39.41; 135.09 (CH); 133.96 (CH); 127.45 (CH); 126.66 (CH); 69.22 (CH); 34.49 (CH_2); 27.21 ($3CH_3$); 21.64 ($2CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 460 [M^+] (7), 458 (23), 374 (96), 332 (64), 314 (84), 288 (100). Found, %: C 62.60; H 5.35. $C_{24}H_{23}ClO_7$. Calculated, %: C 62.82; H 5.05.

2-*tert*-Butyl-4,11-dihydroxyanthra[2,1-*b*]furan-5,10-dione (9). To a solution of the ketone **6** (0.9 g, 2.4 mmol) in anhydrous (50 ml) N,N-dimethylacetamide with stirring in a stream of argon we added a suspension (60%) of NaH (0.48 g, 12.0 mmol) in mineral oil. The mixture was kept at 115°C for 20 min, cooled to room temperature, added to water with stirring, and neutralized with 5% HCl. The product was extracted with a hot mixture of toluene and ethyl acetate (3×30 ml), and the extract was washed with water (5×50 ml), dried with $MgSO_4$, and evaporated under vacuum. The residue was purified by column chromatography on SiO_2 (eluent toluene–ethyl acetate, 5:0 → 5:1) and recrystallized from toluene. The yield was 255 g (31%) of red needle crystals of the anthrafurandione **9**; mp >270°C (subl.). ^{1}H NMR spectrum, δ, ppm: 14.17 (1H, s, HO); 14.16 (1H, s, HO); 8.38 (2H, m, H-6,9); 7.83 (2H, m, H-7,8); 6.74 (1H, s, H-3); 1.45 (9H, s, *t*-C_4H_9). Mass spectrum, *m/z* (I_{rel}, %): 336 [M^+] (65), 321 (100). Found, %: C 71.24; H 4.61. $C_{20}H_{16}O_5$. Calculated, %: C 71.42; H 4.79.

2-Chloro-3-(3,3-dimethyl-3-oxobutyl)-1,4-dipropoxyanthracene-9,10-dione (10). A mixture of the ketone **6** (0.5 g, 1.3 mmol), of calcined potassium carbonate (1.4 g, 10 mmol), and propyl iodide (1.2 ml, 11 mmol) in DMF (50 ml) was heated for 4 h with stirring at 90-100°C (monitored by TLC). The reaction mass was poured into water (50 ml) and extracted with toluene (3×50 ml). The combined extracts were washed with water (3×50 ml), dried, and evaporated. The residue was purified by column chromatography on SiO_2 (eluent toluene–ethyl acetate, 10:1) and recrystallized from a mixture of hexane and benzene. The yield was 0.4 g (65%) of the ketone **10** in the form of light-yellow crystals; mp 96-97°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.17 (2H, m, H-6,9); 7.75 (2H, m, H-7,8); 4.26 (2H, s, CH_2CO); 4.04 (2H, t, *J* = 6.6, OCH_2); 3.83 (2H, t, *J* = 6.8, OCH_2); 2.01 (2H, m, CH_2); 1.87 (2H, m, CH_2); 1.32 (9H, s, *t*-C_4H_9); 1.13 (3H, t, *J* = 7.4, CH_3); 1.04 (3H, t, *J* = 7.4, CH_3). ^{13}C NMR spectrum, δ, ppm: 210.80 (C=O); 182.31 (C=O); 182.18 (C=O); 154.99; 151.82; 138.43; 138.27; 133.86; 133.74; 127.10; 124.95; 44.72; 133.58 (CH); 133.56 (CH); 126.52 (CH); 126.49 (CH); 76.94 (CH_2); 76.09 (CH_2); 37.42 (CH_2); 23.28 (CH_2); 23.25 (CH_2); 28.81 ($3CH_3$); 10.40 (CH_3); 10.29 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 458 [M^+] (3), 456 (10), 398 (8), 367 (24), 339 (36), 329 (41), 288 (100). Found, %: C 68.47; H 6.48. $C_{26}H_{29}ClO_5$. Calculated, %: C 68.34; H 6.40.

2-*tert*-Butyl-4-chloro-5-propoxyanthra[1,2-*b*]furan-6,11-dione (11). The compound was obtained similarly to the anthrafurandione **9** from the ketone **10** at reaction temperature 100°C. The yield was 75%; mp 163-164°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.26 (2H, m, H-7,10); 7.77 (2H, m, H-8,9); 6.59 (1H, s, H-3); 4.05 (2H, t, *J* = 6.8, OCH_2); 2.05 (2H, m, CH_2); 1.40 (9H, s, *t*-C_4H_9); 1.16 (3H, t, *J* = 7.5, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 398 [M^+] (4), 396 (13), 367 (61), 339 (100), 323 (14). Found, %: C 69.42; H 5.15. $C_{23}H_{21}ClO_4$. Calculated, %: C 69.61; H 5.33.

Methyl 3-*tert*-Butyl-4,11-dipropoxyanthra[2,3-*b*]furan-5,10-dione-3-carboxylate (12). The compound was obtained similarly to the derivative **10** from anthrafurandione **2**. The yield was 72%; mp 77-79°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.21 (2H, m, H-6,9); 7.72 (2H, m, H-7,8); 4.38 (2H, t, *J* = 6.6, OCH_2); 3.98 (2H, t, *J* = 7.1, OCH_2); 3.96 (3H, s, OCH_3); 1.95 (4H, m, $2CH_2$); 1.46 (9H, s, *t*-C_4H_9); 1.16 (3H, m, *J* = 7.4, CH_3); 1.04 (3H, m, *J* = 7.5, CH_3). ^{13}C NMR spectrum, δ, ppm: 182.97 (C=O); 182.63 (C=O); 166.11; 165.74; 149.98; 148.90; 142.63; 134.55; 134.26; 128.83; 122.62; 121.77; 109.27; 34.77; 133.26 (CH); 133.20 (CH); 126.55 (CH); 126.43 (CH); 77.52 (CH_2); 76.45 (CH_2); 23.51 (CH_2); 23.15 (CH_2); 52.65 (CH_3); 28.46 ($3CH_3$); 10.48 (CH_3); 9.96 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 478 [M^+] (36), 407 (34), 394 (43), 362 (100), 347 (41). Found, %: C 69.95; H 6.36. $C_{28}H_{30}O_7$. Calculated, %: C 70.28; H 6.32.

2-*tert*-Butyl-4,11-dipropoxyanthra[2,3-*b*]furan-5,10-dione (13). The compound was obtained similarly to the derivative **12** from the anthrafurandione **9**. The yield was 76%; mp 69-71°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.21 (2H, m, H-6,9); 7.71 (2H, m, H-7,8); 6.60 (1H, s, H-3); 4.41 (2H, t, *J* = 6.6, OCH_2); 4.18 (2H, t, *J* = 6.8, OCH_2); 1.97 (4H, m, $2CH_2$); 1.45 (9H, s, *t*-C_4H_9); 1.17 (6H, m, $2CH_3$). ^{13}C NMR spectrum, δ, ppm: 183.13 (C=O); 183.10 (C=O); 170.74; 150.70; 150.02; 142.62; 134.73; 134.47; 130.54; 121.54; 121.25; 33.32; 133.04 (CH); 133.00 (CH); 126.41 (CH); 126.36 (CH); 98.76 (CH); 76.48 (CH_2); 76.24 (CH_2); 23.59 (CH_2); 23.53 (CH_2); 28.63 ($3CH_3$); 10.49 ($2CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 420 [M^+] (18), 391 (28), 349 (31), 336 (53), 321 (100). Found, %: C 74.36; H 6.67. $C_{26}H_{28}O_5$. Calculated, %: C 74.26; H 6.71.

4,11-Dihydroxy-2-methylanthra[2,3-*b*]furan-5,10-dione (15). A 60-mg portion (0.16 mmol) of 2-methyl-4,11-dipropoxyanthra[2,3-*b*]furan-5,10-dione (**14**), obtained by the method in [8], was boiled for 4 h in a mixture of glacial acetic acid and of conc. HBr (1 ml). The mixture was cooled and diluted with 5 ml of water. The precipitate was filtered off, washed with water, and dried. The yield was 34 mg (73%) of red powder of the anthrafurandione **15**; mp >270° (subl.). ^{1}H NMR spectrum, δ, ppm: 13.90 (1H, s, HO); 13.79 (1H, s, HO); 8.21 (2H, m, H-6,9); 7.92 (2H, m, H-7,8); 6.88 (1H, s, H-3); 2.53 (3H, s, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 294 [M^+] (100). Found, %: C 69.09; H 3.23. $C_{17}H_{10}O_5$. Calculated, %: C 69.39; H 3.43.

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REFERENCES

1. A. E. Shchekotikhin, Yu. N. Luzikov, Yu. B. Sinkevich, V. N. Buyanov, and M. N. Preobrazhenskaya, *Khim. Geterotsikl. Soedin.*, 1532 (2008). [*Chem. Heterocycl. Comp.*, **44**, 1245 (2008)].
2. C. A. Townsend, Y. Isomura, S. G. Davis, and J. A. Hodge, *Tetrahedron*, **45**, 2263 (1989).
3. M. V. Gorelik and E. V. Mishina, *Zh. Org. Khim.*, **19**, 2185 (1983).
4. V. Ya. Fain, *Electronic Absorption Spectra and Structure of Anthraquinones* [in Russian], Sputnik$^+$ (2003), Vol. 1, *9,10-Anthraquinone and its Monosubstituted Derivatives* [in Russian], p. 107.
5. H. Raudnitz and W. Bohm, *J. Prakt. Chem.*, **123**, 284 (1929).
6. P. Chang, K. H. Lee, T. Shingu, T. Hirayama, I. H. Hall, and H. C. Huang, *J. Nat. Prod.*, **45**, 206 (1982).
7. N. Thompson and W. Grimshaw, *J. Chem. Soc.*, *Chem. Commun.*, 240 (1987).
8. A. E. Shchekotikhin, E. K. Shevtsova, and V. F. Traven, *Zh. Org. Khim.*, **43**, 1687 (2007).
9. V. Ya. Fain, *Electronic Absorption Spectra and Structure of Anthraquinones* [in Russian], Sputnik$^+$ (2003), Vol. 2, *Disubstituted 9,10-Anthraquinones* [in Russian], p. 34.
10. Yu. B. Sinkevich, A. E. Shchekotikhin, Yu. N. Luzikov, V. N. Buyanov, and L. V. Kovalenko, *Khim. Geterotsikl. Soedin.*, 1478 (2007). [*Chem. Heterocycl. Comp.*, **43**, 1252 (2007)].