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SYNTHESIS OF THIOPHENO-QUINIZARINE DERIVATIVES

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4,11-Dihydroxyanthra[2,3-b]thiophene-5,10-dione (thiophenoquinizarine) and its 3-methyl derivative were obtained by the cyclization of quinizarin-2-yl derivatives of mercaptoacetaldehyde or mercaptoacetone in acid medium. 4,11-Dimethoxy- and 4,11-dibutoxyanthra[2,3-b]thiophene-5,10-dione were synthesized by the alkylation of the hydroxyl group in the synthesized anthrathiophenes with dimethylformamide dimethylacetal or butyl iodide respectively. Radical bromination of 4,11-dimethoxy-3-methylanthra[2,3-b]thiophene-5,10-dione, depending on the amount of N-bromo-succinimide taken, leads to the formation of 3-bromomethyl- or 3-dibromomethyl-4,11-dimethoxy-anthra[2,3-b]thiophene-5,10-diones. The action of sodium acetate on the obtained bromo derivatives with subsequent hydrolysis of the intermediate acetates led to the synthesis of 3-hydroxymethyl- or 3-formyl-4,11-dimethoxy-anthra[2,3-b]thiophene-5,10-diones.

Keywords: 4,11-dihydroxyanthra[2,3-*b*]thiophene-5,10-dione, 4,11-dimethoxy-3-methylanthra[2,3-*b*]-thiophene-5,10-dione, 2-mercaptoquinizarine, alkylation, hydrolysis, radical bromination, cyclization.

Several derivatives of heterocyclic analogs of 5,12-naphthacenequinone possess high biological activity and are promising in the search for new antitumor preparations with improved chemotherapeutic properties [1-4]. However some of them are little studied, which is mainly explained by the absence of convenient methods for their synthesis and modification. One of such little studied classes are the derivatives of anthra[2,3-*b*]-thiophene-5,10-dione. There is information in the literature on the preparation of some compounds of this class, however in the majority of studies [5-8] the synthesis is reported of derivatives of anthra[2,3-*b*]thiophene-5,10-dione having no substituents in the *peri* positions of the quinonoid ring, important both for functionalization of the chromophore and also in the search for new biologically active compounds. The exception is a patent in which the synthesis of 4,11-diphenoxyanthra[2,3-*b*]thiophene-5,10-dione is described, patented as a photo-chromic dyestuff for rerecording compact disks [1]. However the key compound for its preparation, 4,11-dihydroxyanthra[2,3-*b*]thiophene-5,10-dione (thiophenoquinizarine), to which the authors assigned the structure 5,10-dihydroxyanthra[2,3-*b*]thiophene-4,11-dione with a complete absence of physicochemical and spectral characteristics, is formed in 22% yield from difficultly available compounds. In addition, the preparation of 4,11-dihydroxyanthra[2,3-*b*]thiophene-5,10-dione is described in [9], however its synthesis is carried out in ten stages. The further search for biologically active compounds in the anthra-

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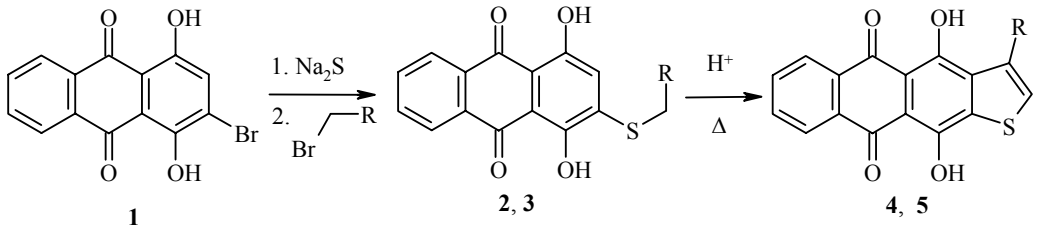
[2,3-*b*]thiophene-4,11-dione series therefore requires the development of preparative methods of synthesis of its *peri*-substituted derivatives. The aim of our work is the development of a new method of synthesis and the modification of derivatives of 4,11-dihydroxy[2,3-*b*]thiophene-5,10-dione (thiophenoquinizarine).

For the synthesis of thiophenoquinizarine we used one of the methods of synthesis of benzo[*b*]thiophenes based on the cyclization of derivatives of α-arylthiocarbamoyl compounds in an acidic medium [10-12]. α-Arylthiocarbonyl compounds, key for the annelation of the thiophene nucleus to the quinizarine residue, were obtained from 2-mercaptoquinizarine, formed by the action of sodium sulfide on 2-bromoquinizarine (**1**) in DMF. Subsequent treatment with the diethylacetal of bromoacetaldehyde or bromoacetone leads to the formation of α-arylthio derivatives of acetaldehyde **2** or acetone **3**. The traditional method of cyclization of α-arylthiocarbonyl compounds into benzo[*b*]thiophenes on heating in polyphosphoric acid (PPA) proved to be unsuitable for the cyclization of derivatives **2** and **3**. However the cyclization of the mercaptoacetaldehyde derivative **2** into thiophenoquinizarine **4** was successfully effected on heating it in a mixture of sulfuric and acetic acids, and the best yield (85%) of the target compound was obtained on slow addition of a solution of derivative **2** to a boiling mixture of acids. For the cyclization of the mercaptoacetone derivative **3**, heating in 73% H_2SO_4 proved to be optimal, and led to the formation of 3-methylthiophenoquinizarine **5** in 84% yield.

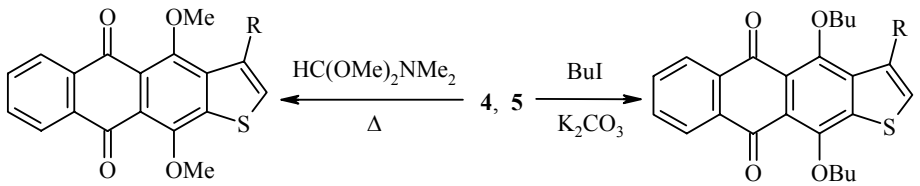


1 **2**, **3** **4**, **5**

2 R = $CH(OEt)_2$; **3** R = Ac; **4** R = H; **5** R = Me

The synthesized thiophenoquinizarine **4** and its 3-methyl derivative **5** possess extremely low solubilities in the majority of solvents, which in the main hinders their identification by NMR spectroscopy and the study of their chemical properties. Recording their ^{1}H NMR spectra was unsuccessful in DMSO-d_6 at 100°C, since at lower temperatures these compounds practically completely crystallize out from solution. In the ^{1}H NMR spectrum of thiophenoxyquinizarine the signals of the protons at positions 2 and 3 are observed as doublets at 8.21 and 7.79 ppm with J = 5.6 Hz, close to the value of the coupling constant for benzothiophene [13].

Evidently we were unsuccessful in obtaining the O-methyl derivatives of hydroxy compounds **4** and **5** under the usual conditions for alkylating hydroxyanthraquinones, by boiling in acetone with dimethyl sulfate in the presence of potassium carbonate, due to their low solubility [14]. However their O,O-dimethyl derivatives were successfully obtained by the procedure of [15] on heating thiophenoquinizarines **4** and **5** with dimethylformamide dimethylacetal in DMF.



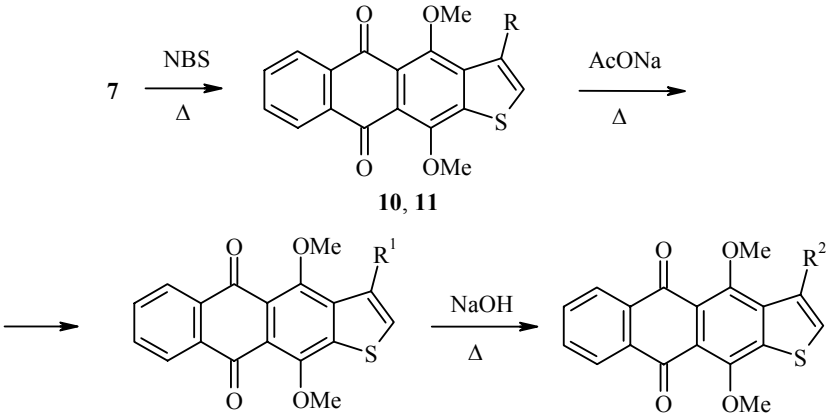
6, **7** **8**, **9**

4, **6**, **8** R = H; **5**, **7**, **9** R = Me

Since the structure of the initial derivatives of 4,11-dihydroxyanthra[2,3-*b*]thiophene-5,10-dione **4** may be described by a series of tautomeric forms (in [16] it was described as 5,10-dihydroxyanthra[2,3-*b*]thiophene-4,11-dione), but proof of its precise structure (for example by ^{13}C NMR spectra) was not successfully obtained by us, the structure of its O-methyl derivatives also remained an open problem. The precise structure of the dimethyl derivative of thiophenoquinizarine **6** was proved unequivocally by NMR spectroscopic methods. Thus a significant positive (+14%) NOE on the signal of the H-3 proton at 7.75 ppm on saturating the signal of the methoxy groups indicates their spatial proximity. In the reverse experiment on saturating the signal of the H-3 proton a positive NOE was observed (+4 and +13%) on the signals of the methoxy group protons at 4.02 ppm and on the signal of the H-2 proton at 8.12 ppm. In this way the O-methyl derivatives obtained on methylation of thiophenoquinizarine **4** and its 3-methyl derivative **5** were assigned the structures of the 4,11-dimethoxy derivatives of anthra[2,3-*b*]thiophene-5,10-dione **6** and **7**. In addition the dimethoxy derivative **6,** according to spectral characteristics, melting point, and chromatographic data, proved to be identical with 4,11-dimethoxy-anthra[2,3-*b*]thiophene-5,10-dione obtained by an alternative method [9]. The structure of the methylation products indicates that the initial thiophenoquinizarine exists in the tautomeric form 4,11-dihydroxy-anthra[2,3-*b*]thiophene-5,10-dione (**4**).

In addition we have established that alkylation of dihydroxyanthrathiophenes **4** and **5** may be carried out by alkyl iodides in DMF at 90-100°C. For example, 4,11-dibutoxyanthra[2,3-*b*]thiophene-5,10-diones **8** and **9** were obtained by the action of butyl iodide in the presence of potassium carbonate.

Derivatives of pyrroloquinizarine (4,11-dihydroxynaphtho[2,3-*f*]indole-5,10-dione) containing pharmacophoric groups in position 3 possess high biological activity [3,4], consequently we synthesized a series of derivatives of thiophenoquinizarine, which were promising for further subsequent functionalization at position 3 of the chromophore. Thus on brominating the 3-methyl derivative **7** in the presence of benzoyl peroxide on irradiation, depending on the amount of N-bromosuccinimide, 3-bromomethyl- (**10**) or 3-dibromomethyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (**11**) were obtained. The bromination of compound **7** stops at the dibromomethyl derivative **11**, and we were unsuccessful in obtaining the corresponding tribromo derivative even on boiling for many hours with an excess of NBS, which is probably explained by steric difficulties.



10 R = CH_2Br; **11** R = $CHBr_2$; **12** R^1 = CH_2OAc; **13** R^1 = $CH(OAc)_2$;
14 R^2 = CH_2OH; **15** R^2 = CHO

The 3-acetoxymethyl and 3-diacetoxymethyl derivatives **12** and **13** were obtained by substituting the bromine atoms in derivatives **10** and **11** on heating with sodium acetate. 3-Hydroxymethyl- (**14**) and 3-formyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-diones (**15**) were obtained by the hydrolysis of the acetoxy groups in derivatives **12** and **13**.

It is necessary to mention the changes observed in the electronic absorption spectra of the synthesized compounds. The initial derivatives of 2-mercaptoquinizarines **2**, **3** and the products of their cyclization, thiophenoquinizarines **4** and **5** have intense absorption in the region of 500 nm. However annelation of the thiophene nucleus to the quinizarine chromophore causes a significant change in the character of the long-wave absorption bands of derivatives **4** and **5**. The formation of the heterocycle leads to the display of three long-wave absorption bands together with an increase in absorption intensity, characteristic of other heterocyclic derivatives of quinizarine [17, 18]. Comparison of the absorption spectra of thiophenoquinizarine **4** and its 3-methyl derivative **5** shows a bathochromic shift of the absorption bands together with growth in intensity due to the donor effect of the methyl group. The presence of one long-wave absorption band in the 400 nm region is characteristic of the alkoxy derivatives of anthra[2,3-*b*]thiophene-5,10-dione **6-15**. For the 4,11-dimethoxy derivatives its position correlates with the donor–acceptor properties of the substituent in position 3, and in the series of substituents CH_3, CH_2Br, $CHBr_2$, H, and CHO a hypsochromic shift from 414 to 398 nm is observed.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Varian VXR 400 spectrometer (400 and 100 MHz) in DMSO-d_6 (compounds **2-6, 8, 14**) and $CDCl_3$ (compounds **7, 9-13, 15**), internal standard was TMS. The mass spectra were recorded on a SSQ 710 chromato-mass spectrometer (Finnigan-MAT, USA), ionizing voltage was 70 eV, with direct insertion of samples into the ion source, heating samples to 350°C, temperature of ionization chamber 150°C. Absorption spectra were recorded on a Hitachi U2000 spectrometer in EtOH. A check on the progress of reactions and the purity of compounds was carried out by TLC on Silufol UV 254 plates, and preparative chromatography of compounds was on Merck 60 silica gel.

2-[(2,2-Diethoxyethyl)thio]-1,4-dihydroxyanthracene-9,10-dione (2). A solution of sodium sulfide nonahydrate (8.27 g, 34 mmol) in water (16.5 ml) was added with stirring to a solution of 2-bromoquinizarine (**1**) (10.0 g, 31 mmol), in DMF (100 ml). The mixture was stirred for 30 min and then filtered. The diethyl acetal of bromoacetaldehyde (5.0 g, 50 mmol) was added to the dark blue mother liquor of the sodium salt of 2-mercaptoquinizarine, and the mixture was stirred for 4 h at 90°C. The mixture was cooled, acetic acid (3.0 ml) was added, and the mixture was poured into water (300 ml). The solid was filtered off, washed with water, and dried. The solid was recrystallized from toluene. Yield 8.64 g (70%) as red crystals; mp 139-140°C. UV spectrum, λ_{max} nm (log ε): 264 (4.5, 304 (3.9), (418), (471), 497 (4.0), (521). ^1H NMR spectrum, δ, ppm (*J*, Hz): 13.36 (1H, s, OH); 12.19 (1H, s, OH); 8.15 (2H, m, H-5,8); 7.92 (2H, m, H-6,7); 7.15 (1H, s, H-3); 4.77 (1H, t, J = 5.2, CH); 3.61 (4H, m, OCH_2); 3.25 (1H, d, J = 5.2, SCH_2); 1.16 (6H, m, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 388 (18) $[M]^+$, 342 (14), 297 (20), 285 (11), 103 (100). Found, %: C 62.05; H 5.50. $C_{20}H_{20}O_6S$. Calculated, %: C 61.84; H 5.19.

2-[(2-Oxopropyl)thio]anthracene-9,10-dione (3). Freshly prepared bromoacetone (9.5 ml, 100 mmol) was added dropwise at -5°C to a solution of 2-mercaptoquinizarine, obtained from 2-bromoquinizarine (**1**) (20.0 g, 62 mmol), by a procedure analogous to the preparation of compound **2**, the mixture was stirred for 20 min, and then acetic acid (5.0 ml) was added. The reaction mixture was poured into water (600 ml), the solid was filtered off, dried, dissolved in boiling acetic acid (800 ml), the hot solution was filtered, and cooled. The precipitated crystals were filtered off, washed twice with acetic acid, with 2-propanol, and dried. Yield 14.1 g (68%) of red crystals; mp 198-199°C. UV spectrum, λ_{max}, nm (log ε): 263 (4.5), 303 (3.9), (423), (467), 493 (4.0), (520). ^1H NMR spectrum, δ, ppm : 8.12 (2H, m, H-5.8); 7.88 (2H, m, H-6,7); 6.98 (1H, s, H-3); 4.28 (2H, s, CH_2); 2.31 (3H, s, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 328 (12) $[M]^+$, 285 (22), 157 (10), 126 (13), 77 (22), 43 (100). Found, %: C 62.01; H 3.56. $C_{17}H_{12}O_5S$. Calculated, %: C 62.19; H 3.68.

4,11-Dihydroxyanthra[2,3-*b*]thiophene-5,10-dione (4). Acetal **2** (3.0 g, 7.73 mmol) was dissolved in boiling acetic acid (450 ml) and the hot solution was added with stirring to a boiling mixture of glacial acetic

acid (300 ml) and conc. H_2SO_4 (60 ml) during 6 h. After adding all the acetal solution the mixture was boiled for 1 h and left for 2-3 days. The precipitated dark red crystals of thiophenoquinizarine **4** were filtered off, washed twice with 2-propanol, and air-dried. Yield 1.93 g (84%). For analytical purposes a sample was recrystallized from nitrobenzene, and dried in vacuum. Mp >280°C (sublimed). UV spectrum, λ_{max}, nm (log ε): (257), 262 (4.6), (288), (437), 463 (3.9), 486 (4.1), 520 (4.0). ^{1}H NMR spectrum (100°C), δ, ppm (*J*, Hz): 8.32 (2H, m, H-6,9); 8.21 (1H, d, *J* = 5.6, H-2); 7.95 (2H, m, H-7,8); 7.79 (1H, d, *J* = 5.6, H-3). Mass spectrum, *m/z* (I_{rel},%): 296 (100) $[M]^+$, 211 (10), 184 (62), 139 (95), 111 (69). Found, %: C 64.80; H 2.60. $C_{16}H_8O_4S$. Calculated, %: C 64.86; H 2.72.

4,11-Dihydroxy-3-methylanthra[2,3-*b*]thiophene-5,10-dione (5). A mixture of 73% H_2SO_4 (1000 ml) and ketone **3** (10.0 g, 30 mmol) was heated with stirring at 125°C for 2 h. The reaction mixture was left overnight at ~20°C, the precipitated solid was filtered off, washed with water, and air-dried. 3-Methyl derivative **5** (8.08 g, 84%) was obtained as a red powder. For analytical purposes a sample was recrystallized from nitrobenzene, and dried in vacuum. Mp >280°C (sublimed). UV spectrum, λ_{max}, nm (log ε): (257), 263 (4.6), (289), (439), 465 (4.0), 494 (4.2), 530 (4.2). ^{1}H NMR spectrum (100°C), δ, ppm: 8.34 (2H, m, H-6,9); 7.96 (2H, m, H-7,8); 7.80 (1H, s, H-2); 2.66 (3H, s, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 310 (100) $[M]^+$, 253 (6), 197 (11), 155 (22), 125 (11), 105 (25). Found, %: C 65.89; H 3.36. $C_{17}H_{10}O_4S$. Calculated, %: C 65.80; H 3.25.

4,11-Dimethoxyanthra[2.3-*b*]thiophene-5,10-dione (6). The dimethylacetal of DMF (10 ml, 80 mmol) was added to thiophenoquinizarine **4** (1.0 g, 3.4 mmol), and the obtained mixture was gently boiled in a stream of argon for 5 h. The reaction miuxture was evaporated in vacuum, and the dry residue recrystallized twice from nitrobenzene. Yield 64%; mp 193-195°C. UV spectrum, λ_{max}, nm (log ε): 251 (4.5), 275 (4.4), (317), 400 (3.8). ^{1}H NMR spectrum (60^{o}C), δ, ppm (*J*, Hz): 8.12 (3H, m, H-2,6,9); 7.85 (2H, m, H-7,8); 7.75 (1H, d, *J* = 5.3, H-3); 4.02 (3H, s, OCH_3); 4.01 (3H, s, OCH_3). Mass spectrum, *m/z* (I_{rel}, %): 324 (100) $[M]^+$, 295 (44), 265 (24), 253 (12). Found, %: C 66.46; H 3.76. $C_{18}H_{12}O_4S$. Calculated, %: C 66.65; H 3.73.

4,11-Dimethoxy-3-methylanthra[2,3-*b*]thiophene-5,10-dione (7) was obtained analogously to derivative **6** from 3-methylthiophenoquinizarine **5**. The dry residue was purified by column chromatography on SiO_2 (eluent toluene–ethyl acetate, 5:0 → 5:1), and recrystallized from toluene. Yield 61%, mp 178-179°C. UV spectrum, λ_{max}, nm (log ε): (238), 254 (4.5), 277 (4.0), (309), 414 (3.8). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.23 (2H, m, H-6,9); 7.76 (2H, m, H-7,8); 7.27 (1H, s, H-2); 4.12 (3H, s, OCH_3); 4.04 (3H, s, OCH_3); 2.70 (3H, d, *J* = 1.1, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 338 (100) $[M]^+$, 323 (22), 309 (35), 295 (21), 279 (25). Found, %: C 67.48; H 4.22. $C_{19}H_{14}O_4S$. Calculated, %: C 67.44; H 4.17.

4,11-Dibutoxyanthra[2,3-*b*]thiophene-5,10-dione (8). A mixture of thiophenoquinizarine **4** (0.25 g, 0.84 mmol), calcined potassium carbonate (0.7 g, 5.1 mmol), butyl iodide (0.6 ml, 5.1 mmol), acetone (5 ml), and DMF (5.0 ml) was boiled with stirring for 20 h, checking for the end of the reaction by TLC. If necessary further K_2CO_3 (0.7 g, 5.1 mmol) and butyl iodide (0.6 ml, 5.1 mmol) were added, and the mixture boiled for a further10 h. The reaction mixture was poured into water (50 ml), and the product extracted with toluene (2×10 ml). The combined extracts were washed with water (3×10 ml), dried, and evaporated. The residue was purified by column chromatography on SiO_2 (eluent toluene), and recrystallized from heptane. Yield of anthrathiophene **8** 0.27 g (78%) as yellow needle-like crystals; mp 107-109°C. UV spectrum, λ_{max}, nm (log ε): 255 (4.5), 274 (4.2), (303), 407 (3.8). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.25 (3H, m, H-2,6,9); 7.84 (2H, m, H-7,8); 7.75 (3H, d, *J* = 5.4, H-2); 4.10 (4H, m, OCH_2); 1.84 (4H, m, CH_2); 1.53 (4H, m, CH_2); 0.96 (6H, m, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 408 (4) $[M]^+$, 296 (83), 139 (15), 57 (76), 41 (100). Found, %: C 70.40; H 6.11. $C_{24}H_{24}O_4S$. Calculated, %: C 70.56; H 5.92.

4,11-Dibutoxy-3-methylanthra[2,3-*b*]thiophene-5,10-dione (9). A mixture of unpurified 3-methyl-thiophenoquinizarine **5** (0.43 g, 1.4 mmol), calcined potassium carbonate (1.2 g, 8.4 mmol), butyl iodide (0.95 ml, 8.4 mmol), and DMF (17.0 ml) was heated for 3-4 h at 85 C with stirring. The end of the reaction was determined by TLC. The reaction mixture was poured into water (100 ml), extracted with toluene, the combined organic phase was washed with water, dried, and evaporated. The residue was purified by column

chromatography on SiO_2 (eluent toluene), and recrystallized from a mixture of heptane (3.0 ml) and toluene (0.2 ml). The crystals were washed with the same mixture (1.0 ml), and dried. Yield of anthrathiophene **9** 0.21 g (36%) as yellow needle-like crystals; mp 103-104°C. UV spectrum, λ_{max}, nm (log ε): 255 (4.5), 274 (4.2), (305), 418 (3.8). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.25 (2H, m, H-6,9); 7.74 (2H, m, H-7,8); 7.24 (1H, d, *J* = 1.0, H-2); 4.26 (2H, t, *J* = 6.9, OCH_2); 4.03 (2H, t, *J* = 6.2, OCH_2); 2.70 (3H, d, *J* = 1.0, CH_3); 1.97 (4H, m, CH_2); 1.60 (4H, m, CH_2); 1.04 (6H, m, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 422 (7) $[M]^+$, 379 (5), 351 (4), 323 (7), 310 (100), 253 (16), 57 (28), 41 (81). Found, %: C 71.31; H 6.31. $C_{25}H_{26}O_4S$. Calculated, %: C 71.06; H 6.20.

3-Bromomethyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (10). A mixture of 3-methylanthrathiophenedione **7** (2.0 g, 5.9 mmol), N-bromosuccinimide (1.1 g, 6.2 mmol), and benzoyl peroxide (0.24 g, 1 mmol) in CCl_4 (300 ml) was boiled for 2 h with stirring and irradiation (200 W lamp). The reaction mixture was cooled, filtered, and the solid washed with hot CCl_4. The filtrate was evaporated in vacuum and the residue purified by column chromatography on SiO_2 (eluent toluene–ethyl acetate, 5:0 → 5:1) and recrystallized twice from toluene. Bromo-methyl derivative **10** (1.8 g, 73%) was obtained as light yellow crystals; mp 177-178°C. UV spectrum, λ_{max}, nm (log ε): (238), 254 (4.5), 274 (4.3), (305), 410 (3.8). ^{1}H NMR spectrum, δ, ppm: 8.24 (2H, m, H-6,9); 7.76 (2H, m, H-7,8); 7.74 (1H, s, H-2); 5.04 (1H, s, CH_2); 4.16 (3H, s, OCH_3); 4.11 (3H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 182.94 (C=O); 182.61 (C=O); 155.52*; 152.46; 143.57; 136.31; 135.81; 134.53; 133.98; 121.95; 121.17; 133.67 (CH); 133.59 (CH); 132.54 (CH); 126.73 (CH); 126.55 (CH); 27.43 (CH_2); 63.93 (CH_3); 62.07 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 418 (11) $[M]^+$, 337 (76), 308 (81), 279 (86), 76 (82), 45 (100). Found, %: C 54.32; H 3.22. $C_{19}H_{13}BrO_4S$. Calculated, %: C 54.69; H 3.14.

3-Dibromomethyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (11) was obtained analogously to bromomethyl derivative **10** from 3-methylanthrathiophene-dione **7** and N-bromosuccinimide (2.2 equiv.). Yield 85%; mp 186-188°C (benzene). UV spectrum. λ_{max}, nm (log ε): 254 (4.4), 274 (4.2), (305), 405 (3.7). ^{1}H NMR spectrum, δ, ppm: 8.35 (1H, s, $CHBr_2$); 8.24 (2H, m, H-6,9); 7.79 (2H, m, H-7,8); 7.70 (1H, s, H-2); 4.18 (3H, s, OCH_3); 4.13 (3H, s, OCH_3). Mass spectrum, *m/z* (I_{rel}, %): 415 (76) $[M\text{-}Br]^+$, 374 (44), 307 (81); 45 (100). Found, %: C 46.07; H 2.32. $C_{19}H_{12}Br_2O_4S$. Calculated, %: C 45.99; H 2.44.

3-Acetoxymethyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (12). 3-Bromomethylanthrathiophenedione **10** (1.0 g, 2.4 mmol) was dissolved in the minimum amount of boiling toluene, then acetic acid (60 ml) and anhydrous sodium acetate (2.0 g, 24.5 mmol) were added, and the mixture boiled for 30 min. The reaction mass was cooled, and poured into water. The solid was filtered off, washed with water, dried, and recrystallized from toluene–heptane, 1:1. Acetoxymethyl derivative **12** (0.84 g, 88%) was obtained as light yellow crystals; mp 162-164°C. ^{1}H NMR spectrum, δ, ppm (*J*. Hz): 8.24 (2H, m, H-6,9); 7.74 (2H, m, H-7,8); 7.65 (1H, t, *J* = 1.0, H-2); 5.56 (1H, d, *J* = 1.0, CH_2); 4.11 (3H, s, OCH_3); 4.06 (3H, s, OCH_3); 2.16 (3H, s, $COCH_3$). ^{13}C NMR spectrum. δ, ppm: 182.72 (C=O); 182.53 (C=O); 170.43 (O-C=O); 154.91; 152.55; 143.45; 137.30; 134.39; 134.09; 133.93; 121.84; 120.90; 133.52 (CH); 133.46 (CH); 130.01 (CH); 126.62 (CH); 126.42 (CH); 61.56 (CH_2); 63.13 (CH_3); 61.89 (CH_3); 20.86 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 396 (62) $[M]^+$, 279 (56), 265 (22), 43 (100). Found, %: C 63.66; H 3.77. $C_{21}H_{16}O_6S$. Calculated, %: C 63.63; H 4.07.

3-Diacetoxymethyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (13) was obtained analogously to acetate **12** from the dibromomethyl derivative **11**. The solid was chromatographed on a column of SiO_2 (eluent toluene–ethyl acetate, 5:1 → 5:3), and was recrystallized from toluene. Yield 81%; mp 199-201. ^{1}H NMR spectrum, δ, ppm: 8.30 [1H, s, $CO(OAc)_2$]; 8.23 (2H, m, H-6,9); 7.91 (1H, s, H-2); 7.75 (2H, m, H 7,8); 4.13 (3H, s, OCH_3); 4.08 (3H, s, OCH_3); 2.19 (6H, s, $COCH_3$). ^{13}C NMR spectrum, δ, ppm: 182.66 (C=O); 182.59 (C=O); 168.52 (O-C=O); 154.64; 152.51; 143.46; 136.48; 134.14; 133.80; 133.63; 121.92; 120.88; 133.39 (CH); 133.28 (CH); 130.43 (CH); 126.41 (CH); 126.21 (CH); 85.12 (CH); 63.24 (CH_3); 62.08 (CH_3); 20.77 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 454 (4) $[M]^+$, 162 (5), 43 (100). Found, %: C 60.66; H 3.78. $C_{23}H_{18}O_8S$. Calculated, %: C 60.79; H 3.99.

*Here and subsequently all unassigned signals belong to quaternary carbon atoms.

3-Hydroxymethyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (14). Methanol (20 ml) and a solution of NaOH (0.4 g, 10.0 mmol) in water (5 ml) were added with stirring to a solution of 3-acetoxymethylanthrathiophene **13** (0.5 g, 1.2 mmol) in THF (30 ml). The mixture was stirred for 1 h then conc. HCl (1.0 ml) was added dropwise, and the mixture poured into water. The solid was filtered off, washed with water, dried, and recrystallized from toluene. Yield 0.33 g (78%) of hydroxymethyl derivative **14** as light yellow crystals; mp 221-222°C. ^{1}H NMR spectrum (60°C), δ, ppm: 8.07 (2H, m, H-6,9); 7.83 (1H, s, H-2); 7.81 (2H, m, H-7,8); 5.50 (1H, br. s, OH); 4.92 (2H, s, CH_2); 4.03 (3H, s, OCH_3); 4.02 (3H, s, OCH_3). ^{13}C NMR spectrum (60°C), δ, ppm: 181.93 (C=O); 181.88 (C=O); 154.36; 151.91; 142.89; 141.35; 137.06; 134.05; 133.57; 21.49; 120.19; 133.82 (CH); 133.73 (CH); 127.54 (CH); 126.21 (CH); 126.01 (CH); 59.64 (CH_2); 62.80 (CH_3); 61.47 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 354 (100) $[M]^+$, 339 (44), 322 (21), 310 (28), 295 (19), 279 (80), 265 (18), 237 (21). Found, %: C 64.65; H 3.76. $C_{19}H_{14}O_5S$. Calculated, %: C 64.40; H 3.98.

3-Formyl-4,11-dimethoxyanthra[2,3-*b*]thiophene-5,10-dione (15) was obtained analogously to carbinol **14** from diacetoxymethyl derivative **13**. Yield 71%; mp 233-235°C (toluene). UV spectrum, λ_{max}, nm (log ε): (239), 252 (4.5), 265 (4.4), (313), 398 (3.8). ^{1}H NMR spectrum, δ, ppm: 10.64 (1H, s, CHO); 8.62 (1H, s, H-2); 8.25 (2H, m, H-6,9); 7.81 (2H, m, H-7,8); 4.16 (3H, s, OCH_3); 4.10 (3H, s, OCH_3). Mass spectrum, *m/z* (I_{rel}, %): 352 (12) $[M]^+$, 338 (6), 305 (13), 281 (16); 265 (32), 221 (56), 210 (100), 195 (95). Found, %: C 64.60; H 3.46. $C_{19}H_{12}O_5S$. Calculated, %: C 64.76; H 3.43.

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