Synthesis of benzo[*g*]quinoline-5,10-diones

E. A. Kolodina, N. I. Lebedeva, and M. S. Shvartsberg★

Institute of Chemical Kinetics and Combustion,
Siberian Branch of the Russian Academy of Sciences,
3 ul. Institutskaya, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383) 330 7350. E-mail: shvarts@kinetics.nsc.ru

Addition of HCl to 2-amino-3-(4-methyl-3-oxopentynyl)-1,4-naphthoquinone in $CHCl_3$ at 20 °C is followed by its cyclization to 4-chloro-2-isopropylbenzo[*g*]quinoline-5,10-dione. Chlorine atom in this compound can be easily replaced by dialkylamino group upon treatment with secondary amines. 4-Dialkylamino-2-isopropylbenzo[*g*]quinoline-5,10-dione is also formed by the direct reaction of the starting ketone with secondary amines. Syntheses of 2-amino-3-(4-methyl-3-oxopentynyl)-1,4-naphthoquinone from 2-bromo- and 2-amino-3-iodo-1,4-naphthoquinones are also described.

Key words: 2-amino-3-(4-methyl-3-oxopentynyl)-1,4-naphthoquinone, synthesis, heterocyclization, substituted benzo[*g*]quinoline-5,10-diones.

A fair number of biologically active substances of natural and synthetic origin have quinoline or quinolinequinone pharmacophoric group in their molecules. Among them are, for example, antibiotics (20*S*)-camptothecin,[1,2] streptonigrin,[3] lavendamycin,[4] alkaloid cleistopholine,[5,6] arylquinolines,[7,8] 6,7-disubstituted quinoline-5,8-diones.[9,10] Practical value of these compounds permanently stimulates a quest for the efficient ways for their synthesis and investigation of pharmacological properties of related structures.[11—13]

Earlier, we synthesized substituted benzo[*h*]quinoline-7,10-diones by heterocyclization of 6-acylethynyl-5-amino-1,4-naphthoquinones.[14] The cyclization method consisted in the addition of secondary amines at the triple bond of the acetylene ketone with subsequent acid-catalyzed 4-dialkylamino-substituted pyridine ring closure.[15] In the compounds obtained, the quinone ring was not incorporated into the quinoline fragment, though it was annulated with its benzene ring.

In the present work, in the framework of the "acetylene approach", we attempted to synthesize benzo[*g*]quinoline-5,10-diones, *i.e.*, quinolinequinones, in which the quinone ring is annulated directly with the heterocycle and, consequently, is a part of the quinoline fragment of the molecule. Note that compounds, containing substituted quinolinedione moiety, usually show antitumor activity.[9,10,13]

For annulation of the quinone ring of 1,4-naphthoquinone with pyridine one, it is necessary to have in the acetylene precursor the cyclo-forming substituents in positions 2 and 3. Therefore, 2-amino-3-(4-methyl-3-oxopentynyl)-1,4-naphthoquinone (**1**) has been chosen as a model key acetylene. Unfortunately, methods for the introduction of acetylene substituents into a quinone ring, in contrast to methods for their introduction into aromatic rings, are insufficiently elaborated.[16] As far as we know, only one procedure for the Pd-catalyzed cross-coupling of 2-bromo- and 2,3-dibromonaphthoquinones with Cu^I acetylides is described.[17] This version of the reaction, as a rule, proceeds with low yields, is accompanied by considerable resinification, and can be applied for not all the terminal acetylenes. Nevertheless, we have successfully used this method for the cross-coupling of 2-bromo-1,4-naphthoquinone (**2**) with secondary acetylene alcohol, *viz.*, with 2-methylpent-4-yn-3-ol (**3**) (Scheme 1). However, hydroxyalkynylquinone **4** obtained turned out to be a very labile compound, its isolation and purification were a great challenge to us. That is why, alcohol **4** was subjected to oxidative amination at the free position of the quinone ring without isolation.[18] 2-Amino-3-(3-hydroxy-4-methylpentynyl)-1,4-naphthoquinone (**5**), being the more stable due to the +M-effect of the amino group, was obtained in 44% total yield. Its selective oxidation with the Collins reagent in CH_2Cl_2 at 0—2 °C led to the key ketone **1** in 67% yield.

The synthesis of ketone **1** from bromide **2** has a number of practical inconveniences. The preparation of amino alcohol **5**, including all the operations from condensation of bromide **2** with acetylene **3** to the isolation of product **5** in pure form, should be carried out continuously, without long time interruptions, since the crude alcohols **4** and **5** decompose and undergo polymerization even in a solution. In addition, chromatographic purification of alcohol **5** should be performed in small portions to

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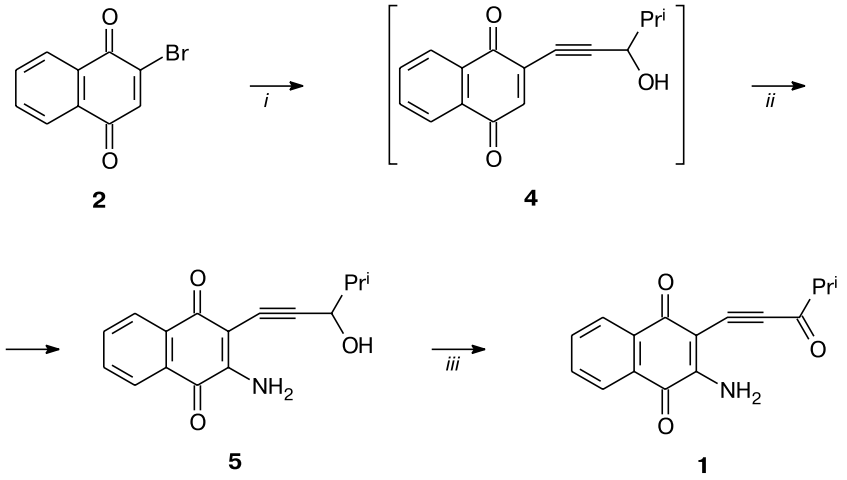
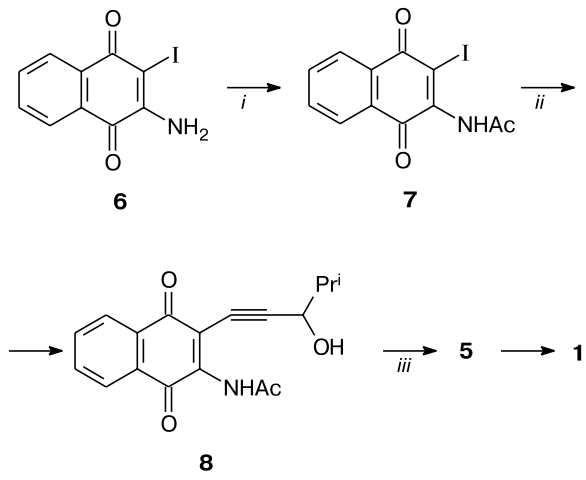
Scheme 1



Reagents: *i*. HC≡CCHOHPr^{i} (**3**), CuI, $Pd(PPh_3)_2Cl_2$, Et_3N, DMSO, $CHCl_3$; *ii*. Aq. NH_3, dioxane; *iii*. $CrO_3 \cdot 2Py$, CH_2Cl_2.

minimize its residence time on the adsorbent and, hence, its loss. All of this complicates the scaling of the experiment and makes the synthesis of ketone **1** in required amount difficult. On the assumption that the limitations of the cross-coupling method used with accompanied preparative difficulties can be overcome by the replacement of the starting bromo derivative by iodo derivative, which usually is more reactive in the catalytic substitution at the sp^2-hybridized carbon atom, we carried out an alternative synthesis of ketone **1**. 2-Amino-3-iodo-1,4-naphthoquinone (**6**) was the starting compound, which became available due to the recently developed excellent methods for the preparation and iodination of 2-amino-1,4-naphthoquinone.[19,20] It was found that iodide **6**, similarly to 2-amino-3-bromo-1,4-naphthoquinone, does not enter the Pd,Cu-catalyzed cross-coupling with acetylenes, however, their *N*-acetyl derivatives are reactive. 2-Acetylamino-3-iodo-1,4-naphthoquinone (**7**) reacted with Cu^{I} acetylide, prepared *in situ* from alcohol **3** in the presence of $Pd(PPh_3)_2Cl_2$, but, in contrast to bromide **2**, already at room temperature and with generation of heat. The yield of acetylated amino alcohol **8** (Scheme 2) was 67%.

Scheme 2



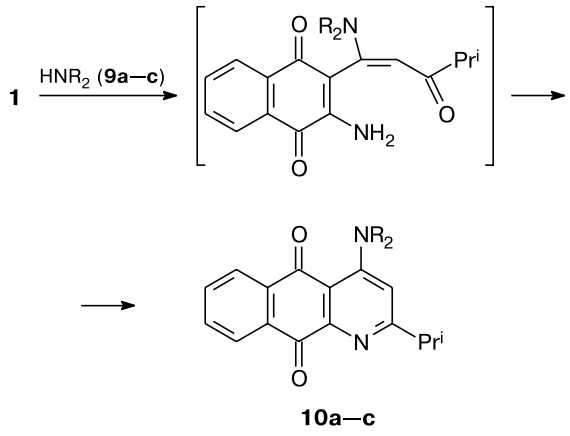
Reagents: *i*. Ac_2O, H_2SO_4, $CHCl_3$; *ii*. HC≡CCHOHPr^{i} (**3**), CuI, $Pd(PPh_3)_2Cl_2$, Et_3N, DMSO, $CHCl_3$; *iii*. NaOH, aqueous EtOH, dioxane.

A removal of the acetyl protection from the amino group was readily fulfilled by the slow addition of 1% NaOH in aq. ethanol to a cold solution of alcohol **8** in dioxane. The yield of amino alcohol **5** reaches 87%. As it was assumed, this pathway to alcohol **5** is devoid of the preparative inconveniences mentioned above and gives one an opportunity to obtain acetylene ketone **1** in the necessary amounts.

When the heterocyclization of aminoketone **1** through the amino adducts[14] takes place, the reaction with secondary amines **9a—c** does not stop after the addition step, yet it is completed by the pyridine ring closure to form 4-dialkylamino-2-isopropylbenzo[*g*]quinoline-5,10-diones **10a—c** (Scheme 3).

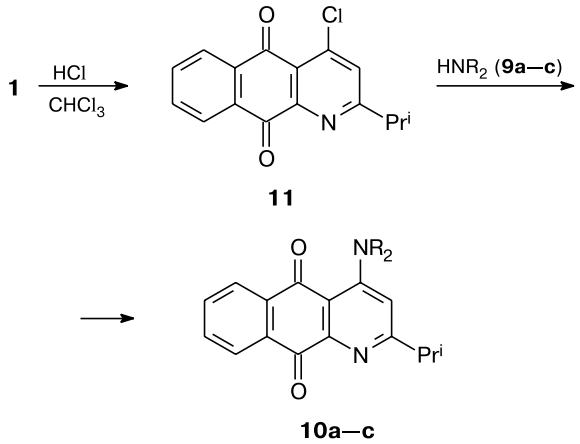
The tandem process of addition—cyclization was accompanied by the formation of a large amount of by-products, the difficulties in their separation caused problems with purification and additional loss in the target heterocycles **10**. Aminoquinolinequinones **10a,b** were isolated in 36—37% yield. Correlation of rates of the main and the side reactions of ketone **1** with diethylamine (**9c**), apparently, is unfavorable. As it can be assumed, the rate of the main reaction in this case is decreased due to the steric factor, while the side processes proceed intensively because of the susceptibility of naphthoquinones to strong

Scheme 3



R_2 = —$(CH_2)_5$— (**a**), —$(CH_2)_2$—O—$(CH_2)_2$— (**b**), Et_2 (**c**)

Scheme 4



R_2 = —$(CH_2)_5$— (**a**), —$(CH_2)_2$—O—$(CH_2)_2$— (**b**), Et_2 (**c**)

bases, like Et_2NH (**9c**). Probably, this was the cause of extremely low yield of aminoquinone **10c**.

The disadvantages of heterocyclization of compounds of type **1** on account of high nucleophilicity (basicity) of the reaction media, as well as of impossibility of refunctionalization of obtaining dialkylaminoquinolinediones **10**, prompted us to launch a quest for alternative conditions for the pyridine ring closure.

It is known[21] that addition of hydrogen halides to α-acetylene ketones proceeds regio- and stereoselectively. The reaction of equimolar amounts of reagents at low temperature (–40 °C) preferably leads to *Z*-β-halovinyl ketones, which are easily converted to *E*-isomers at 20 °C in the presence of a small excess of hydrogen halide. We assumed that addition of hydrogen halides to *vic*-3-oxoalkyn-1-yl derivatives of aminoquinones, following the same regularities, will be accompanied by the acid-catalyzed cyclization to form 4-halo-substituted pyridine ring. The labile halogen atom in the pyridine ring of compounds obtained can be further substituted for various functional groups. In fact, the reaction of aminoketone **1** with HCl (2.5—3 equiv.) in anhydrous chloroform led to 4-chloro-2-isopropylbenzo[*g*]quinoline-5,10-dione **11** (Scheme 4).

The reaction proceeds at ~20 °C for 5—6 h; the yield of chloroquinolinequinone **11** is 70%. The lability of the chlorine atom was confirmed by the transformation of quinolinedione **11** to amino derivatives **10a—c**, also obtained by the cyclization of the key aminoketone **1** through the amino adducts. The reaction was carried out in excess amines **9a—c** at ~20 °C. The reaction time with cyclic amines **9a,b** did not exceed 3 h, while with Et_2NH (**9c**) it reached 14 h. The yields of compounds **10a—c** were 75—95%. It should be pointed out a considerable upfield shift of signal of the proton of the pyridine ring in the ^{1}H NMR spectra when the chlorine atom is replaced by the amino group: δ 7.60 and ~6.9 for chloride **11** and amines **10a—c**, respectively.

We experimentally confirmed that the proposed method for the pyridine ring formation through the tandem reaction of hydrohalogenation—cyclization has quite a general character and can be applied to the synthesis of quinolines, quinolinequinone and quinoline fragments of fused polycyclic structures.

Experimental

^{1}H NMR spectra were recorded on a Bruker DPX-200 spectrometer (200 MHz) in $CDCl_3$ at 25 °C, IR spectra were recorded on a Bruker Vector 22 spectrometer in $CHCl_3$, UV spectra were recorded on a Shimadzu 2401PC spectrometer in hexane. Monitoring of the course of the reactions and purity of compounds were performed by TLC on Silufol UV 254 plates. 2-Bromo-1,4-naphthoquinone (**2**) was obtained by bromination of commercially available 1,4-naphthoquinone according to the procedure described earlier,[22] 2-amino-3-iodo-1,4-naphthoquinone (**6**) was synthesized by amination of 1,4-naphthoquinone to 2-amino-1,4-naphthoquinone[19] with subsequent iodination with I_2—morpholine complex.[20] Acetylene alcohol **3** is a commercial product.

2-Acetylamino-3-iodo-1,4-naphthoquinone (7). A solution of 2-amino-3-iodo-1,4-naphthoquinone (**6**)[19] (0.82 g, 2.7 mmol) and Ac_2O (4.0 g, 3.7 mL, 39.2 mmol) in anhydrous $CHCl_3$ (30 mL), acidified with 3 drops of concentrated H_2SO_4, was stirred at 20 °C for 2 h 15 min. The reaction mixture was diluted with $CHCl_3$ (150 mL) and neutralized with a solution of $NaHCO_3$ (0.9 g) in water (10 mL). The organic layer was separated and washed with water (20 mL). The combined aq. layer, containing suspended product **7**, was filtered, the precipitate was dried to obtain compound **7** (0.17 g). The solvent was evaporated *in vacuo* from the chloroform extract. Residual Ac_2O was evaporated *in vacuo* together with few small portions of toluene. The dry residue was triturated in toluene (15 mL), cooled, and filtered off to obtain compound **7** (0.63 g). Total yield of amide **7**

was 0.80 g (85.5%), m.p. 213—214 °C (toluene—hexane). Found (%): C, 42.47; H, 2.44; I, 37.17. $C_{12}H_8INO_3$. Calculated (%): C, 42.25; H, 2.36; I, 37.20. ^{1}H NMR, δ: 2.26 (s, 3 H, Me); 7.69 (br.s, 1 H, NH); 7.70—7.80 (m, 2 H, H(6), H(7)); 8.05—8.20 (m, 2 H, H(5), H(8)).

2-Acetylamino-3-(3-hydroxy-4-methylpentynyl)-1,4-naphthoquinone (8). A mixture of acetylene alcohol **3** (1.3 g, 13.3 mmol), CuI (2.6 g, 13.6 mmol), and Et_3N (0.84 g, 1.15 mL, 8.3 mmol) in anhydrous DMSO (16 mL) and $CHCl_3$ (2 mL) was stirred for 5—7 min under Ar atmosphere, then iodide **7** (2.6 g, 7.6 mmol) and $Pd(PPh_3)_2Cl_2$ (30 mg) in $CHCl_3$ (6 mL) were added to the reaction mixture accompanied by the spontaneous rise of temperature to 30—33 °C. The stirring was continued for 30 min until the starting **7** in the mixture was consumed, after that, the reaction mixture was diluted with $CHCl_3$ (50 mL) and poured in water (300 mL). The precipitate formed was separated and washed with $CHCl_3$. The organic layer was separated, the aqueous layer was extracted with $CHCl_3$. The combined chloroform extract was washed with water and dried with $MgSO_4$. After the solvent was removed *in vacuo*, the residue (2.5 g) was heated in toluene (50 mL) at 50—60 °C, concentrated to 10 mL in volume, cooled to −(5—10) °C, and filtered to obtain acetylamino alcohol **8** (1.6 g, 67.5%), m.p. 148—149 °C (toluene). Found (%): C, 69.29; H, 5.54; N, 4.29. $C_{18}H_{17}NO_4$. Calculated (%): C, 69.44; H, 5.50; N, 4.50. ^{1}H NMR, δ: 1.05, 1.07 (both d, 6 H, Me_2C, J = 6.7 Hz); 1.80—2.10 (m, 1 H, CH); 2.28 (s, 3 H, Ac); 4.48 (d, 1 H, CHO, J = 5.7 Hz); 7.65—7.85 (m, 2 H, H(6), H(7)); 8.02 (br.s, 1 H, NH); 8.00—8.20 (m, 2 H, H(5), H(8)). IR, ν/cm^{-1}: 1670, 1726 (C=O); 2218 (C≡C); 3365 (NH); 3500 br (OH).

2-Amino-3-(3-hydroxy-4-methylpentynyl)-1,4-naphthoquinone (5). ***A.*** A solution of NaOH (prepared from NaOH (0.25 g, 6.2 mmol) in aq. ethanol (25 mL, 1 : 1, v/v)) was gradually (for 4 h) added to acetylamino alcohol **8** (1.30 g, 4.2 mmol) in dioxane (55 mL) at 13—15 °C until pH reached ~8.5—9.0 and the starting **8** was consumed. The reaction mixture was poured in water (400 mL), acidified with AcOH (1 mL), and amino alcohol **5** was extracted with $CHCl_3$. The solution of **5** was washed with water, dried with $MgSO_4$, and the solvent was evaporated *in vacuo* to obtain compound **5** (0.98 g, 87.5%), m.p. 143—144 °C (toluene). Found (%): C, 71.29; H, 5.77; N, 5.13. $C_{16}H_{15}NO_3$. Calculated (%): C, 71.36; H, 5.61; N, 5.20. ^{1}H NMR, δ: 1.08, 1.11 (both d, 6 H, Me_2C, J = 6.7 Hz); 1.90—2.15 (m, 1 H, CH); 2.94 (br.s, 1 H, OH); 4.53 (d, 1 H, CHO, J = 5.6 Hz); 5.81 (br.s, 2 H, NH_2); 7.55—7.80 (m, 2 H, H(6), H(7)); 7.95—8.15 (m, 2 H, H(5), H(8)). IR, ν/cm^{-1}: 1645, 1677 (C=O); 2212 (C≡C); 3384, 3500 (NH_2); 3604 (OH).

B. Bromoquinone **2** (2.4 g, 10.1 mmol) was involved into condensation with acetylene **3** (1.7 g, 17.3 mmol) in DMSO (40 mL) and $CHCl_3$ (30 mL) in the presence of CuI (3.8 g, 19.9 mmol), Et_3N (1.1 g, 1.5 mL, 10.8 mmol), and $Pd(PPh_3)_2Cl_2$ (40 mg) similarly to iodide **7**, yet at 48—50 °C for 20 min. The reaction mixture was diluted with $CHCl_3$ (200 mL), filtered, the filtrate was repeatedly washed with water and dried with $MgSO_4$. After the solvent was evaporated *in vacuo*, 2-(3-hydroxy-4-methylpentynyl)-1,4-naphthoquinone (**4**) obtained without purification was dissolved in dioxane (40 mL). 25% Aqueous NH_3 (20 mL) was added dropwise to the solution and it was stirred at 20 °C for 50 min, poured in water (0.5 L) and $CHCl_3$ (150 mL). The organic layer was separated, aqueous layer was extracted with $CHCl_3$. The combined extract was washed with water, dried with $MgSO_4$, and the solvent was evaporated. The residue (2.6 g) in portions (~0.3 g) in toluene—ethyl acetate (5 : 1) mixture was filtered through a layer of SiO_2 (5/40 μm; d = 35 mm, h = 20 mm). After the solvent was evaporated, amino alcohol **5** was obtained (1.2 g, 44.1% calculated from **2**).

2-Amino-3-(4-methyl-3-oxopentynyl)-1,4-naphthoquinone (1). The Collins reagent was added in portions to a solution of alcohol **5** (1.5 g, 5.6 mmol) in anhydrous CH_2Cl_2 (150 mL) at 1—2 °C for 15 min. The stirring was continued for another 30 min at this temperature. The reaction mixture was diluted with $CHCl_3$ (200 mL) and poured in a vigorously stirred solution of Na_2SO_3 (25 g) and Na_2CO_3 (15 g) in water (0.5 L). After the aqueous layer was separated, the organic layer was filtered, washed with water, dried with $MgSO_4$, and the solvent was evaporated. The residue was treated with toluene (50 mL), the salt separated was filtered off, and toluene was evaporated *in vacuo*. Ketone **1** was crystallized by trituration with hexane; the yield was 1.0 g (67.1%), m.p. 145—146 °C (toluene—hexane). Found (%): C, 71.70; H, 4.75; N, 5.19. $C_{16}H_{13}NO_3$. Calculated (%): C, 71.90; H, 4.90; N, 5.24. ^{1}H NMR, δ: 1.31 (d, 6 H, Me_2C, J = 6.9 Hz); 2.81 (sept, 1 H, CH, J = 6.9 Hz); 6.27, 6.46 (both br.s, 2 H, NH_2); 7.60—7.85 (m, 2 H, H(6), H(7)); 8.00—8.20 (m, 2 H, H(5), H(8)). IR, ν/cm^{-1}: 1649, 1662, 1682 (C=O); 2181 (C≡C); 3375, 3492 (NH_2).

4-Chloro-2-isopropylbenzo[*g*]quinoline-5,10-dione (11). A solution of HCl (5—6 mL, ~4.0—4.5 mmol of HCl), prepared by saturation of $CHCl_3$—anhydrous ether (2.5 : 1) mixture with gaseous HCl, was added dropwise for 1—2 min to **1** (0.40 g, 1.5 mmol) in anhydrous $CHCl_3$ (12 mL) under stirring and Ar atmosphere. The reaction mixture was stirred at 20 °C for 6—7 h and carefully neutralized with K_2CO_3 (0.60 g) in water (15 mL). The organic layer was separated, the aqueous layer was extracted with $CHCl_3$, the combined chloroform solution was dried with $MgSO_4$, and the solvent was evaporated *in vacuo*. Compound **11** (0.30 g, 70.1%) was isolated by flash-chromatography of the residue in toluene—ethyl acetate mixture (5 : 1) on SiO_2, m.p. 122—123 °C (ether—hexane). Found (%): C, 67.40; H, 3.99; Cl, 12.40. $C_{16}H_{12}ClNO_2$. Calculated (%): C, 67.26; H, 4.23; Cl, 12.41. ^{1}H NMR, δ: 1.38 (d, 6 H, Me_2C, J = 6.9 Hz); 3.34 (sept, 1 H, CH, J = 6.9 Hz); 7.60 (s, 1 H, H(3)); 7.70—7.90 (m, 2 H, H(7), H(8)); 8.20—8.40 (m, 2 H, H(6), H(9)). UV, λ_{max}/nm (ε): 315 (3310).

2-Isopropyl-4-piperidinobenzo[*g*]quinoline-5,10-dione (10a). ***A.*** Compound **11** (0.18 g, 0.6 mmol) in piperidine (**9a**) (2.5 mL, 2.15 g, 25.3 mmol) and dioxane (6 mL) was stirred at 20 °C for 1 h until the starting **11** was consumed, the mixture was diluted with toluene (50—70 mL) and poured in water (200 mL). The toluene layer was separated, the aqueous layer was extracted with toluene. The combined toluene extract was washed with water and dried with $MgSO_4$. After the solvent was evaporated, the residue was crystallized by trituration in hexane to obtain piperidinoazaanthraquinone **10a** (0.20 g, 95.0%), m.p. 123—124 °C. Found (%): C, 75.29; H, 6.43; N, 8.67. $C_{21}H_{22}N_2O_2$. Calculated (%): C, 75.42; H, 6.63; N, 8.38. ^{1}H NMR, δ: 1.34 (d, 6 H, Me_2C, J = 6.9 Hz); 1.60—1.90 (m, 6 H, $(CH_2)_3$-β,γ); 3.21 (sept, 1 H, J = 6.9 Hz); 3.25—3.40 (m, 4 H, CH_2—N—CH_2); 6.93 (s, 1 H, H(3)); 7.65—7.85 (m, 2 H, H(7), H(8)); 8.15—8.30 (m, 2 H, H(6), H(9)). UV, λ_{max}/nm (ε): 318 (9340); 378 (1460); 394 (1400); 463 (1890).

B. Ketone **1** (0.18 g, 0.7 mmol) in piperidine (**9a**) (3 mL, 2.58 g, 30.4 mmol) was stirred at 20 °C for 30 min, after that, the

solvent was evaporated *in vacuo*. The residue in toluene—ethyl acetate (5 : 1) mixture was filtered through a short layer of SiO_2. After evaporation of the solvent, compound **10a** was obtained (0.08 g, 36.0%).

The reaction time for ketone **1** (0.5 mmol) and **9a** (0.6 mmol) in dioxane (4 mL) was increased to 3 h.

2-Isopropyl-4-morpholinobenzo[*g*]quinoline-5,10-dione (10b). ***A.*** Chloride **11** (0.15 g, 0.5 mmol) in morpholine (**9b**) (1.5 mL, 1.5 g, 17.2 mmol) and dioxane (3.5 mL) were stirred at 20 °C for 3 h, the mixture was poured in water (300 mL) and extracted with $CHCl_3$. The extract was repeatedly washed with water and dried with $MgSO_4$. After evaporation of the solvent *in vacuo*, morpholinoazaanthraquinone **10b** was obtained (0.14 g, 79.5%), m.p. 113—114 °C (ether). Found (%): C, 71.29; H, 6.21; N, 8.25. $C_{20}H_{20}N_2O_3$. Calculated (%): C, 71.41; H, 5.99; N, 8.33. ^{1}H NMR, δ: 1.35 (d, 6 H, Me_2C, J = 6.9 Hz); 3.10—3.50 (m, 5 H, CH, CH_2—N—CH_2); 3.90—4.10 (m, 4 H, CH_2—O—CH_2); 6.93 (s, 1 H, H(3)); 7.65—7.85 (m, 2 H, H(7), H(8)); 8.10—8.35 (m, 2 H, H(6), H(9)). UV, λ_{max}/nm (ε): 314 (8480); 376 (1570); 390 (1470); 453 (1600).

B. A solution of morpholine (**9b**) (0.06 g, 0.7 mmol) in dioxane (5 mL) was slowly added (for 5 h) to ketone **1** (0.13 g, 0.5 mmol) in dioxane (3 mL) with stirring; the stirring was continued at 20 °C for another 12 h. After evaporation of the solvent *in vacuo*, the residue in toluene—ethyl acetate (5 : 1) mixture was filtered through a short layer of SiO_2. After evaporation of the solvent, compound **10b** was obtained (0.06 g, 36.7%).

The reaction time for ketone **1** with excess **9b** was 1—1.5 h.

4-Diethylamino-2-isopropylbenzo[*g*]quinoline-5,10-dione (10c) was obtained similarly to compound **10a** (method ***A***) from chloride **11** (0.19 g, 0.7 mmol) in Et_2NH (**9c**) (2 mL, 1.41 g, 19.3 mmol) and dioxane (5.5 mL). The reaction time was 14 h. The yield of diethylaminoazaanthraquinone **10c** was 0.16 g (74.8%), viscous liquid, crystallizing on long standing, m.p. 71.5—72.5 °C (purified by preparative TLC on SiO_2, eluent, toluene—AcOEt, 5 : 1). Found (%): C, 74.57; H, 7.08; N, 8.56. $C_{20}H_{22}N_2O_2$. Calculated (%): C, 74.51; H, 6.88; N, 8.69. ^{1}H NMR, δ: 1.21 (t, 6 H, $(MeC)_2N$, J = 7.1 Hz); 1.33 (d, 6 H, Me_2C, J = 6.9 Hz); 3.20 (sept, 1 H, CH, J = 6.9 Hz); 3.43 (q, 4 H, NCH_2, J = 7.1 Hz); 6.88 (s, 1 H, H(3)); 7.65—7.80 (m, 2 H, H(7), H(8)); 8.10—8.30 (m, 2 H, H(6), H(9)). UV, λ_{max}/nm (ε): 245 (30900); 310 (9340); 396 (1800); 440 (2070).

The reaction of ketone **1** with **9c** under conditions for the synthesis of compound **10a** (method ***B***) was accompanied by the formation of considerable amount of by-products, which were difficult to separate from **10c**.

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