Functionalized naphtho[2,3-*h*]quinoline-7,12-diones

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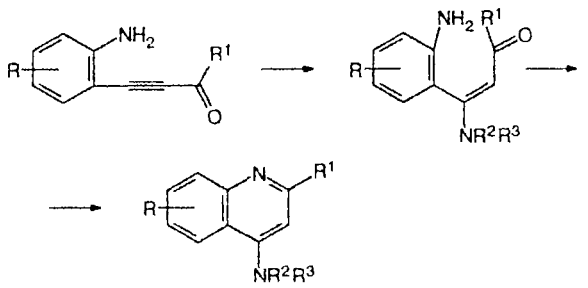
The addition of secondary and primary amines to ethyl (1-amino-9,10-anthraquinon-2-yl)propynoate affords an easily separable mixture of the corresponding ethyl 3-dialkylamino- or 3-alkylamino-3-(1-amino-9,10-anthraquinon-2-yl)acrylate and 3-dialkylamino- or 3-alkylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (in ~4 : 1 ratio). Intramolecular cyclization of the resulting substituted ethyl acrylates results in the formation of 4-dialkylamino- or 4-alkylamino-2-chlorinated pyridine rings. Subsequent nucleophilic substitution of the chlorine atom gives 2-functionalized 4-dialkylamino- or 4-alkylaminonaphtho[2,3-*h*]quinoline-7,12-diones.

Key words: ethyl (1-amino-9,10-anthraquinon-2-yl)propynoate, addition of amines, intramolecular cyclization; 4-dialkylamino-, 4-alkylamino-, 3-dialkylamino-, and 3-alkylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-triones; 2-substituted 4-dialkylamino- and 4-alkylaminonaphtho[2,3-*h*]quinoline-7,12-diones.

Previously,[1] a method for the synthesis of 4-alkylamino- and 4-dialkylaminoquinolines has been developed; the method consists of the addition of primary or secondary amines to *vic*-(acylethynyl)arylamines and subsequent cyclization of the resulting adducts under conditions of acid or base catalysis.

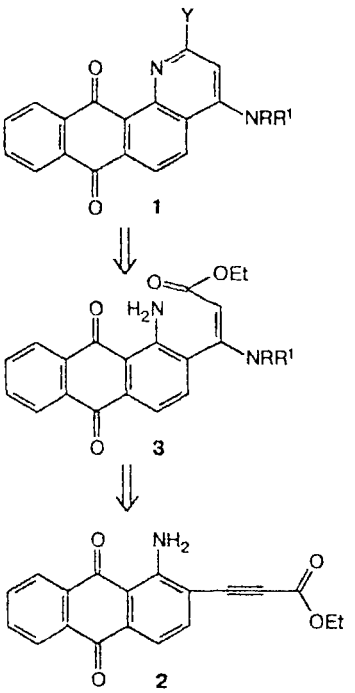


We suggested that variation of the functional group in the acetylenic substituent of the key compound and/or the adding reagent would make it possible to broaden markedly the scope of the method and to extend it to the preparation of quinolines containing diverse substituents in the heterocycle.

In this work, we attempted to synthesize previously unknown 2-functionally substituted 4-dialkylamino- and 4-alkylaminonaphtho[2,3-*h*]quinoline-7,12-diones (**1**) from ethyl (1-amino-9,10-anthraquinon-2-yl)propionate **2** (see the preliminary communication[2]). The general synthetic route is shown in Scheme 1.

Realization of this route depends crucially on the regio- and stereochemistry of the nucleophilic addition

Scheme 1



of amines to ester **2**. The triple bond in **2** is activated not only by the alkoxycarbonyl group but also by the anthraquinone nucleus,[3] and these two substituents exert nonconcerted orienting effects on the nucleophile entering the molecule. The ester group is a weaker acceptor

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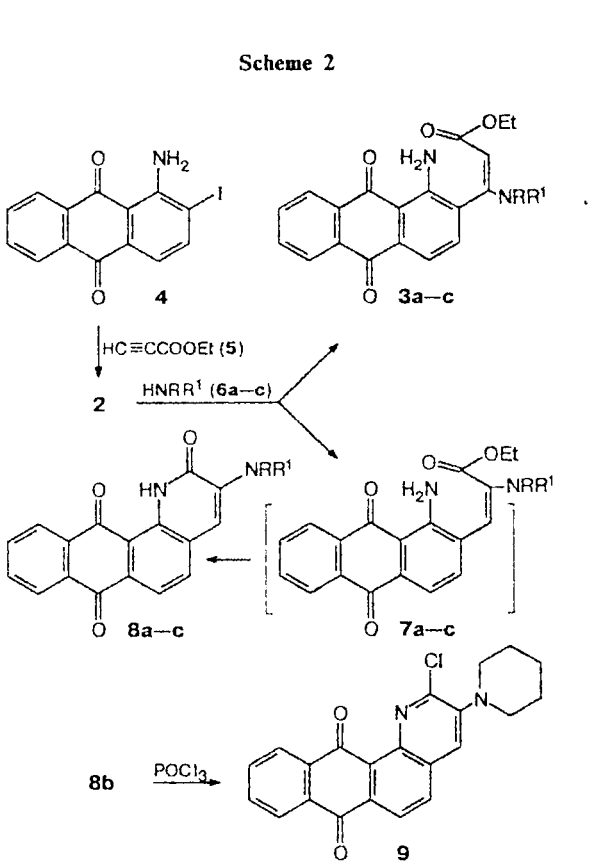
than the acyl group and it cannot be claimed *a priori* that the direction of the amine addition to **2** would be the same as that observed for (acylethynyl)anthraquinones. In addition, intramolecular cyclization can occur only in the case where the adducts formed have *E*-configuration. It was also important to find conditions for direct or indirect — *via* the corresponding lactams (2-quinolones) — transformation of **3** into 2-functionally substituted naphthoquinolinediones **1**.

Cross-coupling of 1-amino-2-iodo-9,10-anthraquinone (**4**)[4] with ethyl propynoate (**5**) seems to be the most rational method for the synthesis of key acetylene **2**. However, it was found[5] that under the typical conditions of the Sonogashira reaction,[6] *i.e.*, in Et_3N in the presence of $Pd(PPh_3)_2Cl_2$ and CuI, condensation of **5** with aryl halides is impossible; therefore, it was proposed to use orthopropynoate as a chemical equivalent of ester **5**. Since we believed that these difficulties were due to the sensitivity of acid **5** to amines, we attempted to carry out condensation of iodide **4** directly with **5** in the absence of an amine. It was found that the reaction occurs rather readily under the conditions of cross-coupling in a solution of Na_2CO_3 in aqueous dioxane described in our previous study;[7] the yield of anthraquinonylpropynoate **2** amounted to 74% (Scheme 2).

Scheme 2



a: R = R^1 = Et; **b**: R–R^1 = $-(CH_2)_5-$; **c**: R = H, R^1 = Bu

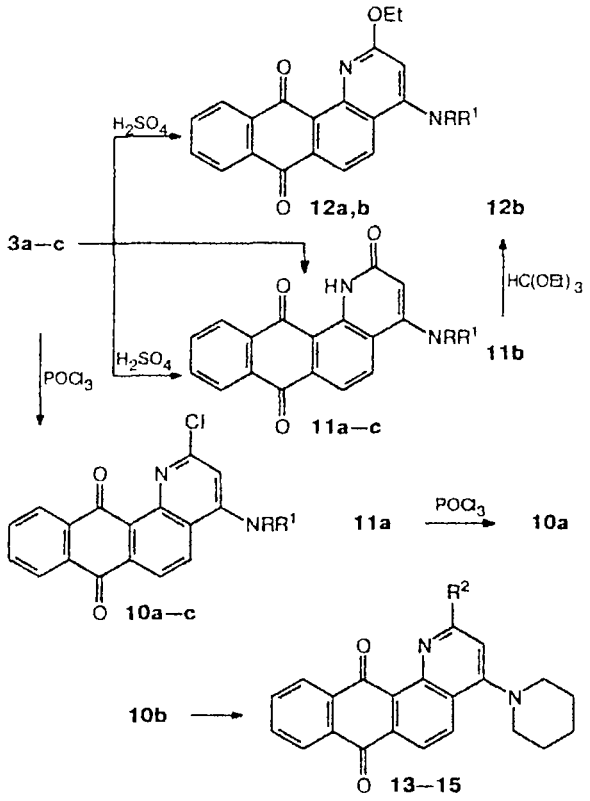
Amines **6a–c** taken in an excess were involved in the addition to **2** in dioxane at 80 °C. The reaction was completed over 4—16 h and two compounds, easily separable by chromatography on Al_2O_3, were produced in each case. According to analytical and spectral data, compounds **3a–c** resulting from the addition of amines to the triple bond in ester **2** are the major products (yields 60—66%). The IR spectra of these products contain no absorption band due to the triple bond but do contain stretching bands at 3340 and 3485—3490 cm^{-1} corresponding to the primary amino group and bands at 1645—1650, 1660—1680, and 1675—1700 cm^{-1} due to the carbonyl groups of the quinone ring and the ester group; the latter band is shifted bathochromically by 15—40 cm^{-1} in relation to its position for ester **2**. In addition to the signals for the protons of the same groups and the aromatic nucleus, the ^1H NMR spectra of **3a–c** exhibit a singlet at 4.65—5.10 ppm corresponding to the vinylic proton and multiplets for the protons of the substituents at the nitrogen atom of the *tert*- or *sec*-amino group. The geminal arrangement (at the double bond) of the substituted amino group and the nucleus is indicated by broadened signals for the protons of the methylene groups attached to nitrogen in the spectrum of **3a**.[1,8] Adducts **3a–c** are colored red-orange, unlike β-aminovinyl anthraquinone derivatives, whose color is deeper;[3] this points to the absence of "push—pull" conjugation of the alkylated amino group with the quinone nucleus and, hence, confirms once again the structure ascribed to these compounds.

The compounds formed together with **3a–c** were found to be 3-dialkylamino- or 3-alkylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-triones **8a–c** (yields 12—18%). The IR spectra of **8a–c** contain an absorption band at 3250—3265 cm^{-1} for the lactam NH bond. The ^1H NMR spectra of **8a,b** (the spectrum of **8c** was not recorded due to the poor solubility of this compound) contain a singlet at 6.60—6.90 ppm for the CH-group proton in the heterocycle and multiplets for the protons of the benzene rings and the NH group; no signals for the ethoxycarbonyl group can be detected. Compounds **8a,c** are colored black violet; **8b** is a brown red crystalline compound; and solutions of **8a–c** are violet. Apparently, pyridones **8a–c** result from lactamization of adducts **7a–c**, which are formed as primary products of the reaction of ester **2** with amines **6a–c**, together with their regioisomers **3a–c**. The ease of the intramolecular cyclization of **7a–c** is evidence that these compounds have *E*-configuration and result from the *syn*-addition of amines **6a–c** to the triple bond of alkyne **2**.

The major products of the reaction of the key acetylene **2** with amines **6**, adducts **3**, are formed in satisfactory yields and can be separated relatively easily from the accompanying lactams **8**. Therefore, **3** can in principle be used in preparative-scale syntheses of 2-functionalized 4-dialkylamino- or 4-alkylaminonaphtho[2,3-*h*]quinoline-7,12-diones (**1**).

We considered three possible routes for cyclization of **3a—c**. It was found that on heating with $POCl_3$ in dioxane at 80 °C for 1.5—5.5 h, these compounds are converted into 4-amino-2-chloronaphthoquinolinediones **10a—c** in 40—67% yields (Scheme 3).

Scheme 3



a: R = R¹ = Et

b: R—R¹ = —$(CH_2)_5$—

c: R = H, R¹ = Bu

13: R^2 = 

14: R^2 = SBu

15: R^2 = $CH(COOEt)_2$

The structure of **10a—c** is beyond doubt and is fully confirmed by analytical and spectral data. In the ^1H NMR spectrum, the unsubstituted hydrogen atom of the pyridine ring manifests itself at ~6.90 ppm in the case of dialkylamino derivatives **10a,b** or at 6.45 ppm in the case of monoalkylamino derivative **10c**.

Base-catalyzed cyclization of **3a—c** under mild conditions (KOH, dibenzo-18-crown-6, benzene, 20 °C) affords 4-aminolactams **11a—c** in 52—97% yields. It is noteworthy that **11a—c**, unlike 3-aminolactams **8a—c**, are colored orange or reddish-orange, and the signal of the heterocycle proton in their ^1H NMR spectra is shifted 0.75 ppm upfield in relation to the signal of the corresponding proton in the aromatic ring in **10a,b**.

Lactams **11** can be converted into chloronaphthoquinolinediones **10** by heating with $POCl_3$ in dioxane, as was shown for **11a** (80 °C, 1.5 h; yield 67%). It should be noted that the formation of 2-chloro-substituted pyridine ring is substantially hampered when the dialkylamino group in the lactam is shifted to position 3. Thus trione **8b** can be converted into 2-chloropyridine **9** only upon prolonged refluxing with excess $POCl_3$ in dioxane (~100 °C, >30 h), and the yield is only 34%.

Adducts **3a,b** were also cyclized in the presence of catalytic amounts of H_2SO_4 in benzene at 20 °C. The reaction lasted for 35—90 min and resulted in the formation of a mixture of the corresponding 2-pyridone **11a,b** and 2-ethoxypyridine **12a,b** in a molar ratio of ~2 : 1 in an overall yield of 90%. Using pyridone **11b** as an example, it was demonstrated that the reaction of **11** with orthoformic ester in the presence of H_2SO_4 affords ethoxypyridines **12** (benzene, 80 °C, 27 h; the yield of **12b** was 54%).

The ability of adducts **3** to cyclize under conditions in which their *cis-trans* isomerization is hardly possible, apparently indicates that these compounds, like their isomers, amino esters **7**, are the products of *syn*-addition of amines to (1-amino-9,10-anthraquinon-2-yl)propynoate (**2**) and have *E*-configuration.

At the same time, the possibility of cyclization of adducts **3a—c** to diones **10a—c**, having an active chlorine atom in position 2, opens up a way for the synthesis of various 2-functionally substituted derivatives in this series of compounds. To confirm this, we synthesized compounds **13—15** by nucleophilic substitution of the halogen atom in **10b** by piperidino-, alkylthio-, and di(ethoxycarbonyl)methyl groups.

Experimental

^1H NMR spectra were recorded on Jeol FX-90 and Bruker AM-250 spectrometers in $CDCl_3$ at 25 °C, IR spectra were measured on a UR-20 spectrophotometer in $CHCl_3$, and UV spectra were run on Specord UV-VIS spectrophotometer in $CHCl_3$. Thin layer chromatography on Silufol UV-254 plates (with $CHCl_3$, benzene, or benzene—ether mixtures as eluents) was used to monitor the course of the reactions and to check the purity of the products.

Ethyl (1-amino-9,10-anthraquinon-2-yl)propynoate (2). Compound **5** (0.37 g, 3.7 mmol) in 2 mL of dioxane and a solution of Na_2CO_3 (0.30 g, 2.9 mmol) in 10 mL of water heated to 80 °C were added in an atmosphere of N_2 to a solution of **4** (1.00 g, 2.9 mmol), $Pd(PPh_3)_2Cl_2$ (40 mg), and CuI (40 mg) in 17 mL of dioxane, heated to 80 °C. The mixture was stirred for 5 min at 80 °C and poured into 0.5 L of water. Product **2** was extracted with $CHCl_3$ and chromatographed on silica gel in benzene, yield 0.68 g (74.4%), m.p. 179—180 °C (from a benzene—pentane mixture). Found (%): C, 71.31; H, 4.03; N, 4.62. $C_{19}H_{13}NO_4$. Calculated (%): C, 71.47; H, 4.10; N, 4.39. ^1H NMR, δ: 1.38 (t, 3 H, CH_3, J = 7.7 Hz); 4.32 (q, 2 H, CH_2, J = 7.7 Hz); 7.52 (d, 1 H, H(3), J = 9.2 Hz); 7.73 (d, 1 H, H(4), J = 9.2 Hz); 7.70—7.95 (m, 2 H, H(6,7)); 8.15—8.40 (m, 2 H, H(5,8)). IR, ν/cm^{-1}: 1650, 1680 (C=O), 1715 (COOEt), 2220 (C≡C), 3340, 3495 (NH_2). UV, λ_{max}/nm (ε): 265 (44000), 279 sh (18800).

The addition of diethylamine (6a) to ester 2. A solution of ester **2** (0.60 g, 1.9 mmol) and amine **6a** (1.38 g, 12.6 mmol) in 30 mL of dioxane was stirred for 16 h at 80 °C, concentrated *in vacuo* to 6 mL, and diluted with 90 mL of pentane. The precipitate that formed (0.65 g) was filtered off. Chromatography on Al_2O_3 in $CHCl_3$ gave compounds **3a** and **8a**.

Ethyl 3-(1-amino-9,10-anthraquinon-2-yl)-3-diethylaminoacrylate (3a), yield 0.44 g (59.7%), m.p. 164—165 °C (from a benzene—pentane mixture). Found (%): C, 70.20; H, 6.04; N, 6.97. $C_{23}H_{24}N_2O_4$. Calculated (%): C, 70.39; H, 6.16; N, 7.14. ^{1}H NMR, δ: 0.85—1.25 (m, 9 H, CH_3); 2.95—3.40 (m, 4 H, NCH_2); 3.89 (q, 2 H, OCH_2, J = 7.7 Hz); 4.90 (s, 1 H, =CH); 7.02 (br.s, 2 H, NH_2); 7.27 (d, 1 H, H(3), J = 8.3 Hz); 7.69 (d, 1 H, H(4), J = 8.3 Hz); 7.60—7.85 (m, 2 H, H(6,7)); 8.10—8.40 (m, 2 H, H(5,8)). IR, ν/cm^{-1}: 1645, 1680 (C=O), 1700 (COOEt), 3340, 3485 (NH_2). UV, λ_{max}/nm (ε): 248 sh (42056), 283 (34579), 475 (7944).

3-Diethylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (8a), yield 0.08 g (12.4%), m.p. 215—217 °C (from a benzene—pentane mixture). Found (%): C, 72.66; H, 5.14; N, 8.13. $C_{21}H_{18}N_2O_4$. Calculated (%): C, 72.82; H, 5.24; N, 8.09. ^{1}H NMR, δ: 1.27 (t, 6 H, CH_3, J = 7.7 Hz); 6.62 (s, 1 H, H(4)); 7.62 (d, 1 H, H(5), J = 9.3 Hz); 7.98 (d, 1 H, H(6), J = 9.3 Hz); 7.65—7.90 (m, 2 H, H(9,10)); 8.15—8.40 (m, 2 H, H(8,11)); 12.67 (br.s, 1 H, NH). IR, ν/cm^{-1}: 1650, 1665 (C=O), 3265 (NH). UV, λ_{max}/nm (ε): 268 (30455), 346 (23636), 438 sh (3000), 537 (10818).

Ethyl 3-(1-amino-9,10-anthraquinon-2-yl)-3-morpholinoacrylate (3b) and 3-morpholinonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (8b) The reaction of **2** (0.25 g, 0.9 mmol) and **6b** (0.31 g, 8.6 mmol) in 12 mL of dioxane under the conditions described for the addition of **6a** (reaction time 6 h) gave compounds **3b** and **8b**.

Compound **3b**, yield 0.21 g (66.3%), m.p. 195—197 °C (from a benzene—pentane mixture). Found (%): C, 71.25; H, 5.92; N, 6.72. $C_{24}H_{24}N_2O_4$. Calculated (%): C, 71.27; H, 5.98; N, 6.93. ^{1}H NMR, δ: 1.08 (t, 3 H, CH_3, J = 7.0 Hz); 1.40—1.85 (m, 6 H, C—$(CH_2)_3$—C); 3.05—3.40 (m, 4 H, CH_2NCH_2); 3.95 (q, 2 H, OCH_2, J = 7.0 Hz); 5.08 (s, 1 H, =CH); 7.20—7.30 (m, 3 H, NH_2, H(4)); 7.60—7.85 (m, 3 H, H(3,6,7)); 8.15—8.35 (m, 2 H, H(5,8)). IR, ν/cm^{-1}: 1650, 1680 (C=O), 1700 (COOEt), 3340, 3490 (NH_2). UV, λ_{max}/nm (ε): 248 sh (39474), 282 (28070), 480 (7281).

Compound **8b**, yield 0.05 g (17.9%), m.p. 256.5—257.5 °C (from a $CHCl_3$—benzene mixture). Found (%): C, 73.68; H, 4.99; N, 7.76. $C_{22}H_{18}N_2O_3$. Calculated (%): C, 73.73; H, 5.06; N, 7.82. ^{1}H (δ: 1.55—1.95 (m, 6 H, —$C(CH_2)_3$C—); 3.25—3.50 (m, 4 H, CH_2NCH_2); 6.90 (s, 1 H, H(4)); 7.70—7.90 (m, 3 H, H(5,9,10)); 8.10 (d, 1 H, H(6), J = 7.7 Hz); 8.20—8.45 (m, 2 H, H(8,11)); 12.75 (br.s, 1 H, NH). IR, ν/cm^{-1}: 1650, 1670 (C=O), 3260 (NH). UV, λ_{max}/nm (ε): 274 (29245), 336 (19811), 498 (10189).

Ethyl 3-(1-amino-9,10-anthraquinon-2-yl)-3-butylaminoacrylate (3c) and 3-butylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (8c). A solution of ester **2** (0.70 g, 2.2 mmol) and amine **6c** (1.60 g, 21.6 mmol) in 35 mL of dioxane was stirred for 4 h at 80 °C. Then the solvent and excess **6c** were removed *in vacuo*; during this process toluene was added at some intervals, in order to remove **6c** more fully. The residue was thoroughly triturated with 180 mL of pentane, and the precipitate was separated. Chromatography of the solution on silica gel (with benzene as the eluent) gave 0.56 g (65.1%) of **3c** as a liquid. Found (%): C, 70.11; H, 6.45; N, 7.09. $C_{23}H_{24}N_2O_4$. Calculated (%): C, 70.39; H, 6.16; N, 7.14. ^{1}H NMR, δ: 0.85 (m, 3 H, CH_3(—C—)$_3$N); 1.30 (t, 3 H, CH_3, J = 7.2 Hz); 1.05—1.75 (m, 4 H, CH_2CH_2—C—N); 2.80—3.15 (m, 2 H, CH_2N); 4.15 (q, 2 H, OCH_2, J = 7.2 Hz); 4.65 (s, 1 H, =CH); 7.42 (d, 1 H, H(3), J = 7.6 Hz); 7.70 (d, 1 H, H(4), J = 7.6 Hz); 7.25—7.90 (m, 2 H, H(6,7)); 8.10—8.65 (m, 3 H, H(5,8), NH). IR, ν/cm^{-1}: 1645, 1660, 1675 (C=O, COOEt), 3340, 3485 (NH_2, NHBu). UV, λ_{max}/nm (ε): 281 (21242), 293 sh (17974), 476 (6209).

The precipitate was chromatographed on silica gel in $CHCl_3$ to give 0.11 g (14.5%) of **8c**, m.p. 211—212 °C (from a $CHCl_3$—benzene mixture). Found (%): C, 72.64; H, 5.29; N, 7.91. $C_{21}H_{18}N_2O_3$. Calculated (%): C, 72.82; H, 5.24; N, 8.09. IR, ν/cm^{-1}: 1630, 1650, 1670 (C=O), 3250, 3415 (NH).

4-Diethylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (11a). A suspension of ester **3a** (0.14 g, 0.4 mmol), KOH powder (0.10 g, 1.8 mmol), and dibenzo-18-crown-6 (10 mg) in 15 mL of anhydrous benzene was stirred for 35 min at 20 °C, poured into 300 mL of water, and extracted with benzene (3×100 mL). The extract was dried with $MgSO_4$ and concentrated *in vacuo* to 3 mL. Pentane (15 mL) was added. The precipitate was filtered off and washed with 15 mL of MeCN to give 0.09 g (72.6%) of **11a**, m.p. 200—201 °C (from a $CHCl_3$—MeCN mixture). Found (%): C, 72.69; H, 5.12; N, 8.22. $C_{21}H_{18}N_2O_3$. Calculated (%): C, 72.82; H, 5.24; N, 8.09. ^{1}H NMR, δ: 1.16 (m, 6 H, CH_3); 3.26 (q, 4 H, CH_2, J = 7.7 Hz); 6.15 (s, 1 H, H(3)); 7.65—7.95 (m, 2 H, H(9,10)); 7.95—8.40 (m, 4 H, H(5,6,8,11)); 12.60 (br.s, 1 H, NH). IR, ν/cm^{-1}: 1650, 1665 (C=O), 3275 (NH). UV, λ_{max}/nm (ε): 258 (39091), 333 (3364), 441 (9909).

4-Piperidinonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (11b). Ester **3b** (0.14 g, 0.3 mmol) was cyclized in the presence of KOH (0.08 g, 1.4 mmol) and dibenzo-18-crown-6 (8 mg) in 12 mL of benzene as described for **3a** (see above); the reaction time was 3.5 h. The crude product was dissolved in $CHCl_3$, and the solvent was evaporated *in vacuo*, $CHCl_3$ being gradually replaced by MeCN. The resulting precipitate was filtered off and washed with MeCN to give 0.12 g (96.8%) of **11b**, m.p. 274—275 °C (from a benzene—pentane mixture). Found (%): C, 73.76; H, 5.16; N, 7.79. $C_{22}H_{18}N_2O_3$. Calculated (%): C, 73.73; H, 5.06; N, 7.82. ^{1}H NMR, δ: 1.60—2.00 (m, 6 H, —$C(CH_2)_3$C—); 2.95—3.25 (m, 4 H, CH_2NCH_2); 6.15 (s, 1 H, H(3)); 7.70—7.90 (m, 2 H, H(9,10)); 8.00—8.40 (m, 4 H, H(5,6,8,11)); 12.56 (br.s, 1 H, NH). IR, ν/cm^{-1}: 1650, 1665 (C=O), 3275 (NH). UV, λ_{max}/nm (ε): 260 (41038), 265 (41509), 336 (3443), 441 (10000).

4-Butylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (11c) was prepared as described for **11a** (see above); the reaction time was 12 h. The product was extracted with $CHCl_3$. The reaction of **3c** (0.24 g, 0.6 mmol) gave 0.11 g (51.9%) of **11c**, m.p. 322—324 °C (from $CHCl_3$). Found (%): C, 72.66; H, 5.22; N, 8.24. $C_{21}H_{18}N_2O_3$. Calculated (%): C, 72.82; H, 5.24; N, 8.09.

4-Diethylamino-2-chloronaphtho[2,3-*h*]quinoline-7,12-dione (10a). *A.* A solution of ester **3a** (0.16 g, 0.4 mmol) and $POCl_3$ (0.19 g, 1.2 mmol) in 16 mL of anhydrous dioxane was stirred for 1.5 h at 80 °C and carefully quenched with an aqueous solution of $NaHCO_3$. The product was extracted with benzene (3×150 mL). Chromatography on silica gel (with $CHCl_3$ as the eluent) gave 0.10 g (67.1%) of **10a**, m.p. 143.5—144.5 °C (from a benzene—pentane mixture). Found (%): C, 69.31; H, 4.74; Cl, 9.71. $C_{21}H_{17}ClN_2O_2$. Calculated (%): C, 69.14; H, 4.70; Cl, 9.72. ^{1}H NMR, δ: 1.13 (m, 6 H, CH_3); 3.32 (q, 4 H, CH_2, J = 7.7 Hz); 6.90 (s, 1 H, H(3)); 7.55—7.80 (m, 2 H, H(9,10)); 8.00—8.35 (m, 4 H, H(5,6,8,11)). IR, ν/cm^{-1}: 1680 (C=O). UV, λ_{max}/nm (ε): 256 (35811), 263 (38514), 282 (20270), 315 (14805), 425 (4054).

B. The reaction of 4-diethylaminonaphtho[2,3-*h*]quinoline-2(1*H*),7,12-trione (**11a**) (0.10 g, 0.3 mmol) and $POCl_3$ (0.13 g,

0.9 mmol) in 10 mL of dioxane under the same conditions gave 0.07 g (66.7%) of 4-diethylamino-2-chloronaphtho[2,3-*h*]quinoline-7,12-dione (**10a**).

4-Piperidino-2-chloronaphtho[2,3-*h*]quinoline-7,12-dione (10b) was synthesized similarly to **10a** from **3b** (0.16 g, 0.4 mmol); yield 0.10 g (67.1%), m.p. 222—224 °C (from a benzene—pentane mixture). Found (%): C, 70.06; H, 4.48; Cl, 9.42. $C_{22}H_{17}ClN_2O_2$. Calculated (%): C, 70.12; H, 4.55; Cl, 9.41. ^{1}H NMR, δ: 1.60—2.10 (m, 6 H, $-(CH_2)_3-$); 3.10—3.45 (m, 4 H, CH_2NCH_2); 6.93 (s, 1 H, H(3)); 7.65—7.95 (m, 2 H, H(9,10)); 8.15—8.45 (m, 4 H, H(5,6,8,11)). IR, ν/cm^{-1}: 1675 (C=O). UV, λ_{max}/nm (ε): 257 (39316), 263 (37607), 283 (20513), 305 (14103), 417 (4188).

4-Butylamino-2-chloronaphtho[2,3-*h*]quinoline-7,12-dione (10c). A solution of **3c** (0.16 g, 0.4 mmol) and $POCl_3$ (0.38 g, 2.5 mmol) in 16 mL of dioxane was heated for 5.5 h at 80 °C and quenched with aqueous $NaHCO_3$. The product was extracted with $CHCl_3$. The extract was concentrated *in vacuo* to a volume of 3 mL and diluted with 20 mL of pentane. The resulting precipitate was filtered off. Chromatography on silica gel (with a 3 : 1 benzene—ether mixture as the eluent) gave 0.06 g (40.5%) of **10c**, m.p. 245—247 °C (from a benzene—pentane mixture). Found (%): C, 68.98; H, 4.69; Cl, 9.65. $C_{21}H_{17}ClN_2O_2$. Calculated (%): C, 69.14; H, 4.70; Cl, 9.72. ^{1}H NMR, δ: 0.97 (m, 3 H, CH_3); 1.20—1.95 (m, 4 H, CH_2CH_2); 3.10—3.40 (m, 2 H, NCH_2); 5.40 (br.m, 1 H, NH); 6.45 (s, 1 H, H(3)); 7.60—7.90 (m, 2 H, H(9,10)); 7.95—8.35 (m, 4 H, H(5,6,8,11)). IR, ν/cm^{-1}: 1680 (C=O), 3475 (NH). UV, λ_{max}/nm (ε): 278 (18215), 313 (18761), 430 (4372).

3-Piperidino-2-chloronaphtho[2,3-*h*]quinoline-7,12-dione (9). A solution of **8b** (0.14 g, 0.4 mmol) and $POCl_3$ (0.60 g, 4.0 mmol; 0.36 mL) in 28 mL of anhydrous dioxane was stirred at 100 °C. After 4 h and then after every 7 h, an additional amount of $POCl_3$ (a total of 5.0 g, 32.8 mmol; 3 mL) was added in equal portions. The total heating time was 39 h. The reaction mixture was carefully poured into a solution of $NaHCO_3$ (30.0 g) in 0.5 L of water, and the product was extracted with $CHCl_3$ (2×200 mL). Chromatography on Al_2O_3 (toluene as the eluent) gave 0.05 g (34.0%) of **9**, m.p. 204—206 °C (from a benzene—hexane mixture). Found (%): C, 70.09; H, 4.66; Cl, 9.19. $C_{22}H_{17}ClN_2O_2$. Calculated (%): C, 70.12; H, 4.55; Cl, 9.41. ^{1}H NMR, δ: 1.50—2.20 (m, 6 H, C—$(CH_2)_3$—C); 3.15 (br.s, 4 H, CH_2NCH_2); 7.50 (s, 1 H, H(4)); 7.65—8.70 (m, 6 H, H(5—10)). IR, ν/cm^{-1}: 1675 (C=O).

4-Diethylamino-2-ethoxynaphtho[2,3-*h*]quinoline-7,12-dione (12a). Concentrated H_2SO_4 (0.2 mL) was added to a solution of ester **3a** (0.21 g, 0.5 mmol) in 35 mL of anhydrous benzene. The mixture was stirred for 1.5 h at 20 °C and neutralized with aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with benzene. Chromatography on Al_2O_3 ($CHCl_3$ as the eluent) gave 0.11 g (59.5%) of **11a** (see above) and 0.06 g (30%) of **12a**, m.p. 124—125 °C (from a benzene—pentane mixture). Found (%): C, 73.86; H, 5.85; N, 7.60. $C_{23}H_{22}N_2O_3$. Calculated (%): C, 73.78; H, 5.92; N, 7.48. ^{1}H NMR, δ: 1.12 (m, 6 H, CH_3—CH_2—N); 1.50 (m, 3 H, CH_3CH_2O); 3.30 (q, 4 H, CH_2N, J = 7.7 Hz); 4.73 (q, 2 H, CH_2O, J = 7.7 Hz); 6.50 (s, 1 H, H(3)); 7.65—7.90 (m, 2 H, H(9,10)); 8.10—8.40 (m, 4 H, H(5,6,8,11)). IR, ν/cm^{-1}: 1680 (C=O). UV, λ_{max}/nm (ε): 256 (35088), 261 (36257), 286 (16374), 306 (11696), 388 (4211), 425 (4269).

4-Piperidino-2-ethoxynaphtho[2,3-*h*]quinoline-7,12-dione (12b). *A.* Ester **3b** (0.23 g, 0.6 mmol) in 38 mL of benzene was cyclized in the presence of H_2SO_4 (0.15 mL) as described above for **3a**; the reaction time was 35 min. The reaction gave 0.12 g (58.8%) of **11b** (see above) and 0.07 g (31.8%) of **12b**, m.p. 181—182 °C (from a benzene—pentane mixture). Found (%): C, 74.49; H, 5.89; N, 7.22. $C_{24}H_{22}N_2O_3$. Calculated (%): C, 74.59; H, 5.74; N, 7.25. ^{1}H NMR, δ: 1.50 (t, 3 H, CH_3 J = 6.9 Hz); 1.60—2.00 (m, 6 H, C—$(CH_2)_3$—C); 3.00—3.20 (m, 4 H, CH_2NCH_2); 4.70 (q, 2 H, OCH_2, J = 6.9 Hz); 6.45 (s, 1 H, H(3)); 7.65—7.85 (m, 2 H, H(9,10)); 8.10—8.35 (m, 4 H, H(5,6,8,11)). IR, ν/cm^{-1}: 1675 (C=O). UV, λ_{max}/nm (ε): 255 (39013), 260 (39462), 287 (18834), 305 sh (13004), 389 (4484), 425 (4888).

B. A mixture of **11b** (0.12 g, 0.3 mmol), $HC(OEt)_3$ (15 mL), 15 mL of anhydrous benzene, and H_2SO_4 (0.15 mL) was heated at reflux for 27 h and carefully poured in an aqueous solution of $NaHCO_3$, and the product was extracted with benzene. After the solvent and excess orthoformic ester had been removed *in vacuo*, the residue was chromatographed on Al_2O_3 (with $CHCl_3$ as the eluent) to give 0.07 g (54.3%) of **12b**.

2,4-Dipiperidinonaphtho[2,3-*h*]quinoline-7,12-dione (13). A solution of quinone **10b** (0.15 g, 0.4 mmol) in 5 mL of piperidine was stirred for 5 min at 100 °C, diluted with 100 mL of benzene, washed with water several times, and concentrated *in vacuo* to a volume of 3 mL, and the residue was diluted with 20 mL of hexane to give 0.14 g (82.8%) of **13**, m.p. 252—254 °C (from a benzene—hexane mixture). Found (%): C, 76.01; H, 6.31; N, 10.14. $C_{27}H_{27}N_3O_2$. Calculated (%): C, 76.21; H, 6.40; N, 9.87. ^{1}H NMR (δ: 1.55—2.00 (m, 12 H, C—$(CH_2)_3$—C); 2.90—3.15 and 3.70—4.00 (m, 8 H, CH_2NCH_2); 6.45 (s, 1 H, H(3)); 7.55—7.80 (m, 2 H, H(9,10)); 7.90—8.35 (m, 4 H, H(5,6,8,11)). IR, ν/cm^{-1}: 1675 (C=O).

2-Butylthio-4-piperidinonaphtho[2,3-*h*]quinoline-7,12-dione (14). BuSH (0.17 g, 1.9 mmol; 0.2 mL) and Na_2CO_3 (0.3 g, 2.8 mmol) was added to a solution of quinone **10b** (0.14 g, 0.4 mmol) in 10 mL of dioxane at 90 °C, and the mixture was stirred at the same temperature for 2 h and poured into 200 mL of water. The product was extracted with toluene. Chromatography on silica gel in toluene gave 0.09 g (56.3%) of **14**, m.p. 112—113 °C (from a benzene—hexane mixture). Found (%): C, 72.46; H, 6.03; S, 6.64. $C_{26}H_{26}N_2O_2S$. Calculated (%): C, 72.53; H, 6.09; S, 7.45. ^{1}H NMR, δ: 0.90 (t, 3 H, CH_3, J = 7.2 Hz); 1.50—2.10 (m, 10 H, $-C(CH_2)_3C-$ and β-, γ-CH_2); 3.00—3.30 (m, 4 H, CH_2NCH_2); 3.50 (t, 2 H, SCH_2, J = 7.2 Hz); 6.70 (s, 1 H, H(3)); 7.70—7.95 (m, 2 H, H(8,9)); 8.15—8.50 (m, 4 H, H(5—7,10)). IR, ν/cm^{-1}: 1675 (C=O).

2-[Di(ethoxycarbonyl)methyl]-4-piperidinonaphtho[2,3-*h*]-quinoline-7,12-dione (15). A mixture of sodium diethyl malonate, prepared from sodium (0.06 g, 2.6 mmol) in 5 mL of diethyl malonate, and quinone **10b** (0.15 g, 0.4 mmol) was stirred for 3 h at 100 °C, diluted for 50 mL of benzene, washed with 300 mL of water, and concentrated *in vacuo* to a volume of 5 mL. Hexane (20 mL) was added. The precipitated product **15** was filtered off; yield 0.13 g (65.0%), m.p. 203—205 °C (from benzene—hexane a mixture). Found (%): C, 69.31; H, 5.57; N, 5.66. $C_{29}H_{28}N_2O_6$. Calculated (%): C, 69.59; H, 5.64; N, 5.60. ^{1}H NMR, δ: 1.35—1.45 (m, 6 H, CH_3); 1.75—1.90 (m, 6 H, C—$(CH_2)_3$—C); 3.05—3.15 (m, 4 H, CH_2NCH_2); 4.25—4.50 (m, 4 H, OCH_2); 7.07 (s, 1 H, H(3)); 7.75—7.85 (m, 2 H, H(9,10)); 8.04 and 8.12 (both d, 2 H, H(5,6), J = 8.5 Hz); 8.25 and 8.53 (both m, 2 H, H(8,11)); 13.48 (s, 1 H, OCCHCO). IR, ν/cm^{-1}: 1670, 1705 sh (C=O).

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