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Synthesis of Meridine, Cystodamine, and Related Compounds Including Iminoquinolinequinone Structure

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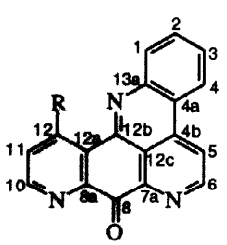
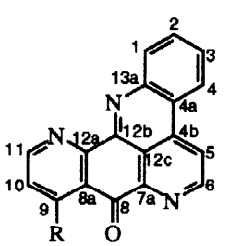
Abstract: Two aromatic alkaloids, meridine (**1**) and cystodamine (**3**), and related compounds (**2, 4, 5**) were synthesized by hetero Diels-Alder reaction between 4-methoxy- (or 4-chloro-)5,8-quinolinedione and 2-nitrocinnamaldehyde dimethylhydrazone.

A series of biologically active fused polycyclic aromatic alkaloids possessing iminoquinolinequinone structure have been isolated from marine organisms.[1] In 1991 Schmidtz *et al.* reported the isolation and structural elucidation of new pentacyclic alkaloids, meridine and 11-hydroxyascididemin from *Amphicarpa meridiana* and from a *Leptoclinides* sp., respectively.[2] They determined the structure of meridine as 12-hydroxybenzo[*b*]pyrido[4,3,2-*de*][1,7]phenanthrolin-8(8*H*)-one (**1**) by X-ray analysis.[2] McCarthy *et al.* found antifungal activity of **1** against *Trichophyton mentagrophytes* and *Epidermophyton floccosum*.[3] Cystodamine (**3**) was isolated from a Mediterranean ascidian *Cystodytes delle chiajei* (Polycitoridae), and showed activity against human leukemic lymphoblasts.[4]

In connnection with our synthetic studies on fused aromatic alkaloids, we have carried out the total synthesis of kuanoniamine A, 11-hydroxyascididemin and eupomatidines 1–3 including the iminoquinolinequinone structure.[5] Now we report the full details[6] of the synthesis of meridine (**1**), cystodamine (**3**) and related compounds (**2, 4, 5**) by hetero Diels-Alder reaction.



1: R = OH
2: R = OCH_3
3: R = NH_2



4: R = OCH_3
5: R = NH_2

The hetero Diels-Alder reaction between 4-methoxy-5,8-quinolinedione[7] (**11a**) and 2-nitrocinnamaldehyde dimethylhydrazone (**12**) in chloroform or acetonitrile (reflux, 48 h) gave no expected products (**13, 14**). In contrast, the cycloaddition was carried out in the presence of acetic anhydride[8] (and

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silica gel) for the purpose of preventing a nucleophilic attack of liberated dimethylamine to the quinone (**11a** or **13**) to give 1,4-dihydropyrido[3,2-*g*]quinoline-5,10-dione (**13**) and pyrido[3,2-*g*]quinoline-5,10-dione (**14**), regioselectively. Addition of boron trifluoride diethyl etherate was also effective; the quinones (**13**, **14**) were obtained.

To improve the yields of **13** and **14** we studied the hetero Diels-Alder reaction using haloquinone.[9] The required 7-bromo-4-methoxy-5,8-quinolinedione (**11b**) was obtained by oxidative demethylation of 4,5,8-trimethoxyquinoline (**10**, prepared from 3-bromo-2,5-dimethoxyaniline[10] (**6**), Meldrum's acid and trimethyl orthoformate *via* 4(1*H*)-quinolinone[11] (**8**) in four steps) with cerium(IV) ammonium nitrate (CAN) in aqueous acetonitrile. The reaction of **11b** and aza-diene (**12**) in refluxing chloroform (144 h) or acetonitrile (48 h) in the presence of acetic anhydride gave **13** and **14** in better

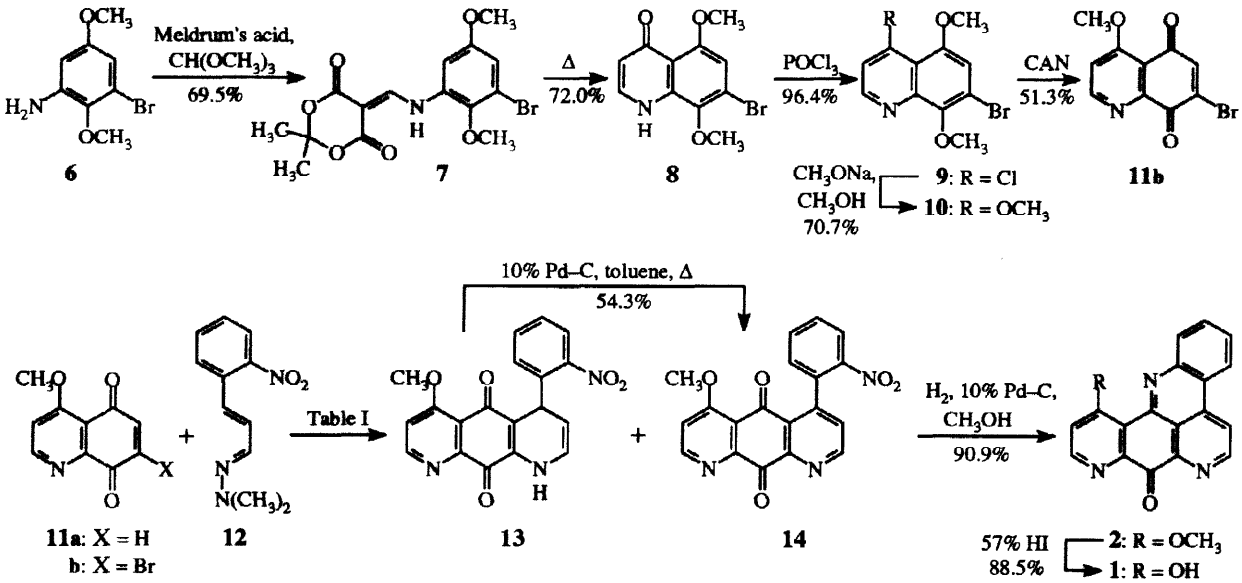

Table I. Hetero Diels-Alder Reaction between Quinone (**11a**, **b**) and Diene (**12**).

Entry	Quinone	Diene (**12**)	Solvent	Additive(s)	Temp.	Time	Yield [%]	
		[equiv.]			[°C]	[h]	**13**	**14**
1	**11a**	1.2	$CHCl_3$	—	reflux	48	—	—
2	**11a**	1.2	$CHCl_3$	$(CH_3CO)_2O$	reflux	48	2.7	—
3	**11a**	1.2	$CHCl_3$	$(CH_3CO)_2O$, SiO_2	reflux	15	7.8	6.1
4	**11a**	1.2	$CHCl_3$	$(CH_3CO)_2O$, SiO_2	reflux	30	—	7.3
5	**11a**	1.2	CH_2Cl_2	$(CH_3CO)_2O$, SiO_2	reflux	30	5.4	8.7
6	**11a**	1.2	CH_2Cl_2	$(CH_3CO)_2O$, SiO_2	reflux	60	—	13.1
7	**11a**	1.2	CH_3CN	—	reflux	48	—	—
8	**11a**	1.2	$CHCl_3$	$(CF_3CO)_2O$	reflux	30	—	—
9	**11a**	1.2	CH_2Cl_2	$BF_3{\cdot}O(CH_2CH_3)_2$	25	43	9.6	1.0
10	**11b**	1.2	$CHCl_3$	$(CH_3CO)_2O$	reflux	144	4.4	10.2
11	**11b**	1.2	CH_3CN	$(CH_3CO)_2O$	reflux	48	13.9	12.8
12	**11b**	28	$CHCl_3$	$(CH_3CO)_2O$	50	65	14.5	17.1

yields. The use of a large excess[12] of aza-diene (**12**) slightly improved the yield. The dihydro compound (**13**) was treated with 10% palladium on carbon in refluxing toluene to give **14** in 54% yield. The reaction of quinone (**11a, b**) and aza-diene (**12**) is summarized in Table I.

The pyridoquinolinequinone (**14**) was catalytically reduced in methanol to afford pentacyclic compound (**2**) in 91% yield. Finally, **2** was heated with 57% hydroiodic acid to furnish the demethylated product (**1**) in 89% yield. The spectral data of **1** was identical to the natural meridine.

Similarly, a regioisomer (**4**) was prepared from 6-bromo-4-methoxy-5,8-quinolinedione (**17**). The hetero Diels-Alder reaction between **17** (obtained from 6-bromo-4-chloro-5,8-dimethoxyquinoline[13] (**15**) in two steps) and aza-diene (**12**) in refluxing chloroform, acetonitrile or toluene in the presence of acetic anhydride (and silica gel) proceeded regioselectively to afford pyrido[2,3-*g*]quinoline-5,10-dione (**18**) in 10-28% yields, but no 1,4-dihydropyrido[2,3-*g*]quinoline-5,10-dione (Table II). Catalytic reduction of **18** furnished **4** in 36% yield.

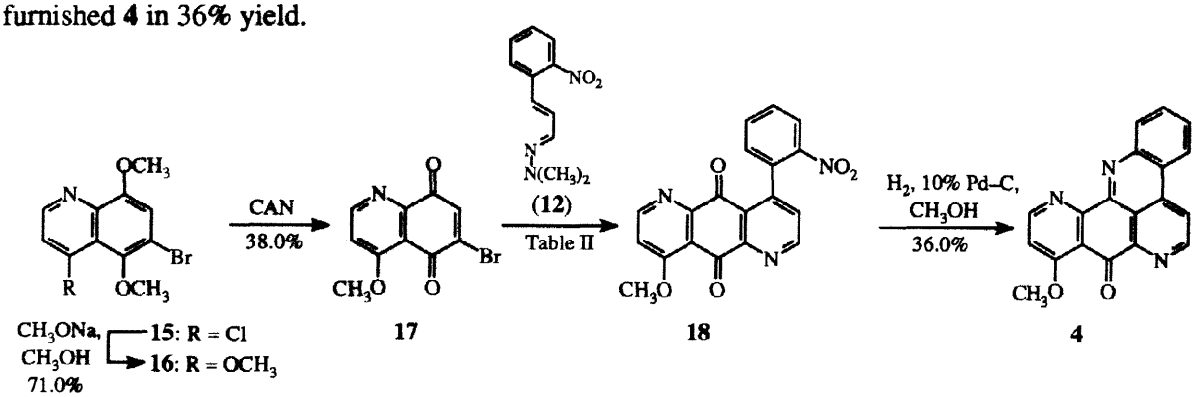

Table II. Hetero Diels-Alder Reaction between Quinone (**17**) and Diene (**12**).

Entry	Diene (**12**) [equiv.]	Solvent	Additive(s)	Temp.	Time [d]	Yield of **18** [%]
1	1.2	$CHCl_3$	$(CH_3CO)_2O$, SiO_2	reflux	6	13.0
2	1.2	CH_2Cl_2	$(CH_3CO)_2O$, SiO_2	reflux	5	—
3	1.2	CH_3CN	$(CH_3CO)_2O$	reflux	2	28.3
4	1.2	$CHCl_3$	$(CH_3CO)_2O$	reflux	5	18.9
5	1.2	$C_6H_5CH_3$	$(CH_3CO)_2O$	reflux	9	10.2

We then synthesized cystodamine (**3**) and its isomer (**5**). The hetero Diels-Alder reaction between 7-bromo-4-chloro-5,8-quinolinedione (**19**) and aza-diene (**12**) in chloroform containing acetic anhydride afforded 1,4-dihydropyrido[3,2-*g*]quinoline-5,10-dione (**20**, 21% yield) and pyrido[3,2-*g*]-quinoline-5,10-dione (**21**, 34% yield), regioselectively. The dihydro compound (**20**) was dehydrogenated with 10% palladium on carbon in refluxing toluene to give **21** (69% yield). Treatment of **21** with sodium methoxide in methanol gave methoxyquinone (**14**, 75% yield), a synthetic intermediate of meridine (**1**). The fact showed that 4-chloro-5,8-quinolinedione (**19**) is more efficient starting material for the synthesis of **1** and **2**. The chloroquinone (**21**) was heated with sodium azide in aqueous *N,N*-dimethylformamide to afford aminoquinone (**22**) in 58% yield. Catalytic reduction of **22** in methanol furnished cystodamine (**3**) in 88% yield. The hetero Diels-Alder reaction between 6-bromo-4-chloro-5,8-quinolinedione[5a] (**23**) and aza-diene (**12**) in chloroform containing acetic anhydride afforded pyrido[2,3-*g*]quinoline-5,10-dione (**24**,

28% yield), regioselectively. The isomer (5) was obtained from **24** in 46% yield (two steps). The ^{13}C-NMR chemical shift data for **1–5** are given in Table III.

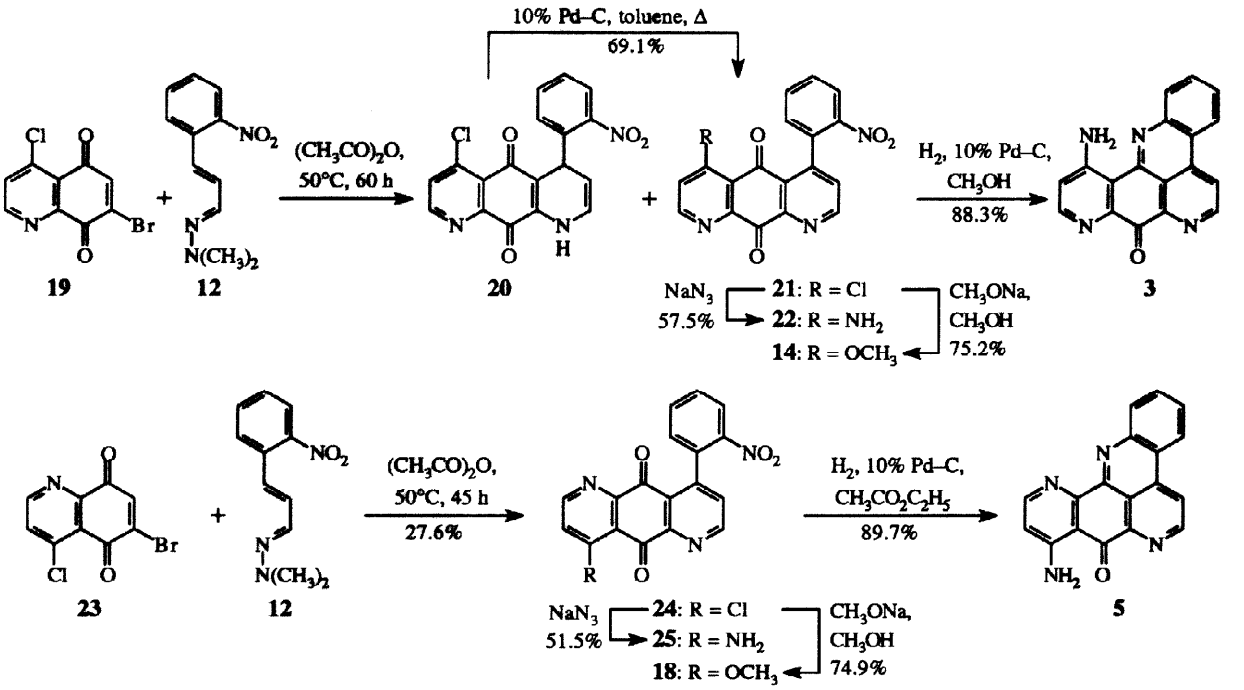

Table III. ^{13}C-NMR Chemical Shift Data for Meridine (1), 2, Cystodamine (3), 4, and 5[a]

Carbon	1	2	3	4	5
C_1	129.33	131.50	131.64	131.13	132.98
C_2	132.55	131.79	134.23	131.87	134.84
C_3	129.62	129.35	132.17	129.40	133.46
C_4	123.34	122.61	124.18	123.96	124.68
C_{4a}	121.74	120.42	121.40	121.80	123.02
C_{4b}	137.91	137.85	139.68[b]	137.06	140.06
C_5	119.73	120.28	124.18	119.91	123.32
C_6	151.55	149.72	150.39	149.74	149.00
C_{7a}	147.58	145.69	139.48[b]	146.86	143.90
C_8	180.43	180.70	175.42	179.85	186.07
C_{8a}	148.91	149.39	138.97	119.09	110.94
C_9				166.61	159.90
C_{10}	153.70	152.77	139.44	110.13	114.46
C_{11}	116.95	111.38	114.93	155.07	141.41
C_{12}	167.26	166.21	160.37		
C_{12a}	116.49	122.08	113.90	153.19	146.87
C_{12b}	152.17	148.42	143.38	148.76	140.45
C_{12c}	117.69	117.90	118.58	117.61	117.65
C_{13a}	142.51	145.22	144.32	145.19	145.53
OCH_3		56.67		56.73	

a) Assignments confirmed by direct and long-range C-H correlations. *b*) Assignments may be interchanged.

Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were obtained with a Hitachi 260-10 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were measured in $CDCl_3$ (unless otherwise noted) at 270.05 (or 500) MHz and 125.65 MHz, respectively, with JEOL JNM-EX 270 and JEOL JNM-LA 500 spectrometers, and chemical shifts were recorded in δ values relative to an internal standard, tetramethylsilane. Mass spectra were recorded on a JMS-DX 302 mass spectrometer. Elemental analyses were obtained by a Perkin-Elmer Model 240B elemental analyzer. All reactions were run with magnetic stirring. Anhydrous sodium sulfate was used for drying organic solvent extracts, and the solvent was removed with a rotary evaporator and finally under high vacuum. Column chromatography was carried out on E. Merck silica gel 60 (230–400 mesh) with the flash technique.

5-[[(3'-Bromo-2',5'-dimethoxyphenyl)amino]methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (7) A solution of Meldrum's acid (170 mg, 1.18 mmol) in trimethyl orthoformate (2 ml) was refluxed for 1 h, and then a solution of 3-bromo-2,5-dimethoxyaniline (**6**) (229 mg, 0.99 mmol) in trimethyl orthoformate (2 ml) was added. The whole was refluxed for 1 h, then cooled, and evaporated. The residue was chromatographed (CH_2Cl_2) to afford **7** (265 mg, 69.5%). mp 171 °C (yellow powder from ethyl acetate). MS *m/z* (%): 387 (M^++2, 27), 385 (M^+, 28), 329 (34), 327 (33), 254 (98), 252 (100). *Anal.* Calcd for $C_{15}H_{16}BrNO_6$: C, 46.65; H, 4.18; N, 3.63. Found: C, 46.66; H, 4.20; N, 3.56. IR (KBr): 1728, 1686 cm^{-1} (C=O). ^{1}H-NMR δ: 1.76 (6H, s, $C(CH_3)_2$), 3.82 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 6.82 (1H, d, J = 2.6 Hz, C_4'-H or C_6'-H), 6.95 (1H, d, J = 2.6 Hz, C_4'-H or C_6'-H), 8.61 (1H, d, J = 14.2 Hz, =CH-N), 11.65 (1H, d, J = 14.2 Hz, NH).

7-Bromo-5,8-dimethoxy-4(1*H*)-quinolinone (8) A solution of **7** (200 mg, 0.518 mmol) in diphenyl ether (4.5 ml) was refluxed for 30 min. After cooling the whole was poured into hexane (17 ml). The precipitated solid was collected, washed with hexane, and chromatographed (CH_2Cl_2-methanol, 9:1) to afford **8** (106 mg, 72.0%). mp 250-252 °C (colorless powder from $CHCl_3$). MS *m/z* (%): 285 (M^++2, 23), 283 (M^+, 23), 270 (97), 268 (100). *Anal.* Calcd for $C_{11}H_{10}BrNO_3 \cdot 1/4\ H_2O$: C, 45.78; H, 3.67; N, 4.85. Found: C, 45.63; H, 3.49; N, 4.83. IR (KBr): 1620 cm^{-1} (C=O). ^{1}H-NMR δ: 3.93 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 6.25 (1H, dd, J = 7.6, 1.7 Hz, C_3-H), 6.78 (1H, s, C_6-H), 7.51 (1H, dd, J = 7.6, 5.6 Hz, C_2-H), 8.70 (1H, br d, J = 5.6 Hz, NH).

7-Bromo-4-chloro-5,8-dimethoxyquinoline (9) A mixture of **8** (300 mg, 1.06 mmol) and phosphorus oxychloride (6.2 ml) was refluxed for 30 min. The reaction mixture was cooled, poured into ice-water (45 ml), neutralized with 5 N NaOH solution, and extracted with CH_2Cl_2 (3 x 50 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **9** (308 mg, 96.4%). mp 113 °C (colorless powder from ether). MS *m/z* (%): 303 (M^++2, 36), 301 (M^+, 28), 290 (26), 288 (100), 286 (79). *Anal.* Calcd for $C_{11}H_9BrClNO_2$: C, 43.67; H, 3.00; N, 4.63. Found: C, 43.65; H, 3.00; N, 4.62. ^{1}H-NMR δ: 3.96 (3H, s, OCH_3), 4.05 (3H, s, OCH_3), 7.05 (1H, s, C_6-H), 7.45 (1H, d, J = 4.6 Hz, C_3-H), 8.73 (1H, d, J = 4.6 Hz, C_2-H).

7-Bromo-4,5,8-trimethoxyquinoline (10) A solution of 28% sodium methoxide in methanol (7.52 ml) was added to **9** (188 mg, 0.621 mmol). The whole was heated at 65 °C for 30 min, then cooled, diluted with water (30 ml), neutralized with 10% HCl, and extracted with CH_2Cl_2 (3 x 100 ml). The

extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **10** (131 mg, 70.7%). mp 154 °C (colorless powder from ether). MS *m/z* (%): 299 (M^++2, 50), 297 (M^+, 50), 284 (97), 282 (100). *Anal.* Calcd for $C_{12}H_{12}BrNO_3$: C, 48.34; H, 4.06; N, 4.70. Found: C, 48.24; H, 4.05; N, 4.76. ^{1}H-NMR δ: 3.94 (3H, s, OCH_3), 4.02 (3H, s, OCH_3), 4.04 (3H, s, OCH_3), 6.78 (1H, d, J = 5.3 Hz, C_3-H), 6.96 (1H, s, C_6-H), 8.75 (1H, d, J = 5.3 Hz, C_2-H).

7-Bromo-4-methoxy-5,8-quinolinedione (11b) A solution of cerium(IV) ammonium nitrate (CAN) (1.47 g, 2.68 mmol) in water (8 ml) was added to **10** (200 mg, 0.67 mmol) dissolved in acetonitrile (20 ml) at 0-5 °C. The mixture was stirred at 0-5 °C for 1 h, diluted with water (50 ml), and extracted with CH_2Cl_2 (4 x 100 ml). The extract was washed with water, dried, and evaporated. The residue was recrystallized from ethyl acetate to afford **11b** (92.2 mg, 51.3%). mp 210 °C (decomp.) (yellow powder from ethyl acetate). MS *m/z* (%): 269 (M^++2, 98), 267 (M^+, 100), 188 (32). *Anal.* Calcd for $C_{10}H_6BrNO_3 \cdot 1/3\ H_2O$: C, 43.82; H, 2.45; N, 5.11. Found: C, 43.65; H, 2.16; N, 5.26. IR (KBr): 1692, 1658 cm^{-1} (C=O). ^{1}H-NMR δ: 4.08 (3H, s, OCH_3), 7.20 (1H, d, J = 5.6 Hz, C_3-H), 7.46 (1H, s, C_6-H), 8.86 (1H, d, J = 5.6 Hz, C_2-H).

***trans*-2-Nitrocinnamaldehyde Dimethylhydrazone (12)** *N,N*-Dimethylhydrazine (0.56 ml, 7.37 mmol) was added to a solution of *trans*-2-nitrocinnamaldehyde (1.0 g, 5.6 mmol) in CH_2Cl_2 (50 ml). The whole was stirred at 25 °C for 5 h, and then evaporated to dryness. The residue was chromatographed (CH_2Cl_2) to afford **12** (915 mg, 73.9%). mp 39 °C (red powder from hexane). MS *m/z* (%): 219 (M^+, 100). *Anal.* Calcd for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.12; H, 6.02; N, 19.15. ^{1}H-NMR δ: 2.99 (6H, s, $N(CH_3)_2$), 6.97 (1H, dd, J = 15.2, 8.6 Hz, CH=C<u>H</u>-CH), 7.10 (1H, d, J = 15.2 Hz, C<u>H</u>=CH-CH), 7.13 (1H, d, J = 8.6 Hz, CH=CH-C<u>H</u>), 7.32 (1H, ddd, J = 7.9, 7.3, 1.3 Hz, C_4-H), 7.53 (1H, ddd, J = 7.9, 7.3, 1.3 Hz, C_5-H), 7.70 (1H, dd, J = 7.9, 1.3 Hz, C_6-H), 7.89 (1H, dd, J = 7.9, 1.3 Hz, C_3-H).

1,4-Dihydro-6-methoxy-4-(2'-nitrophenyl)pyrido[3,2-*g*]quinoline-5,10-dione (13) and 4-Methoxy-6-(2'-nitrophenyl)pyrido[3,2-*g*]quinoline-5,10-dione (14) (a) Table I, Entry 3: Acetic anhydride (0.1 ml, 1.06 mmol), silica gel (E. Merck silica gel 60, 70–230 mesh, 1.14 g), and **12** (139.2 mg, 0.635 mmol) in $CHCl_3$ (5 ml) were added to a solution of **11a** (100 mg, 0.529 mmol) in $CHCl_3$ (15 ml), and the whole was refluxed for 15 h. Silica gel was filtered off and the filtrate was evaporated to dryness. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **13** (14.9 mg, 7.8%) and **14** (11.6 mg, 6.1%).

13: mp 210 °C (purple powder from $CHCl_3$-methanol). MS *m/z* (%): 363 (M^+, 11), 346 (35), 315 (100), 301 (38). High-resolution MS Calcd for $C_{19}H_{13}N_3O_5$: 363.0855. Found: 363.0853. IR (KBr): 3432 cm^{-1} (NH); 1682, 1662 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$–DMSO-d_6) δ: 3.96 (3H, s, OCH_3), 5.2-5.3 (1H, m, C_3-H), 5.41 (1H, d, J = 4.0 Hz, C_4-H), 6.34 (1H, dd, J = 7.6, 4.3 Hz, C_2-H), 7.16 (1H, d, J = 5.9 Hz, C_7-H), 7.2-7.4 (1H, m, $C_{4'}$-H), 7.5-7.6 (2H, m, $C_{5'}$-H, $C_{6'}$-H), 7.81 (1H, d, J = 8.5 Hz, $C_{3'}$-H), 8.60 (1H, br, NH), 8.73 (1H, d, J = 5.9 Hz, C_8-H). ^{13}C-NMR ($CDCl_3$–DMSO-d_6) δ: 33.09 (C_4), 56.21 (CH_3), 106.26 (C_3), 111.76 (C_7), 112.91 (C_{4a}), 118.13 (C_{5a}), 123.35 (C_2 or $C_{3'}$), 123.37 (C_2 or $C_{3'}$), 126.58 ($C_{4'}$), 130.84 ($C_{6'}$), 132.95 ($C_{5'}$), 139.19 (C_{10a}), 141.31 ($C_{1'}$), 146.88 ($C_{2'}$), 148.29 (C_{9a}), 153.38 (C_8), 164.76 (C_6), 178.96 (C_{10}), 180.76 (C_5).

14: mp 293-296 °C (decomp.) (colorless powder from ethyl acetate). MS *m/z* (%): 361 (M^+, 0.4), 316 (33), 315 (100). High-resolution MS Calcd for $C_{19}H_{11}N_3O_5$: 361.0699. Found: 361.0696. IR (KBr): 1700, 1676 cm^{-1} (C=O). ^{1}H-NMR δ: 3.98 (3H, s, OCH_3), 7.16 (1H, d, J = 5.8 Hz, C_3-H), 7.28 (1H, dd, J = 7.6, 1.2 Hz, $C_{6'}$-H), 7.44 (1H, d, J = 4.6 Hz, C_7-H), 7.67 (1H, ddd, J = 8.2, 7.6, 1.2 Hz, $C_{4'}$-H), 7.77 (1H, td, J = 7.6, 1.2 Hz, $C_{5'}$-H), 8.34 (1H, dd, J = 8.2, 1.2 Hz, $C_{3'}$-H), 8.92 (1H, d, J = 5.8 Hz, C_2-H), 9.11 (1H, d, J = 4.6 Hz, C_8-H). ^{13}C-NMR δ: 56.89 (CH_3), 111.52 (C_3), 120.01 (C_{4a}), 125.05 ($C_{3'}$), 128.58 (C_{5a}), 128.95 (C_7), 129.27 ($C_{4'}$), 129.92 ($C_{6'}$), 134.00 ($C_{5'}$), 135.25 ($C_{1'}$), 146.51 ($C_{2'}$), 148.14 (C_{9a}), 149.22 (C_6), 150.36 (C_{10a}), 154.07 (C_8), 155.81 (C_2), 166.36 (C_4), 180.41 (C_5 or C_{10}), 181.58 (C_5 or C_{10}).

(b) Table I, Entry 9: Boron trifluoride diethyl etherate (65 μl, 0.529 mmol) was added to an ice-cooled solution of **11a** (100 mg, 0.529 mmol) and **12** (139.2 mg, 0.635 mmol) in CH_2Cl_2 (30 ml) with stirring, and the whole was stirred at 25 °C for 30 h. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution, dried, and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **13** (18.4 mg, 9.6%) and **14** (2.0 mg, 1.0%).

(c) Table I, Entry 11: Acetic anhydride (70 μl, 0.746 mmol), and **12** (98.1 mg, 0.447 mmol) in acetonitrile (5 ml) were added to a solution of **11b** (100 mg, 0.373 mmol) in acetonitrile (5 ml), and the whole was refluxed for 48 h. The reaction mixture was evaporated to dryness, and the residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **13** (18.8 mg, 13.9%) and **14** (17.3 mg, 12.8%).

(d) Table I, Entry 12: Acetic anhydride (35 μl, 0.374 mmol) and **11b** (50 mg, 0.187 mmol) were added to a solution of **12** (1.18 g, 5.38 mmol) in $CHCl_3$ (2 ml), and the whole was heated at 50 °C for 65 h. The reaction mixture was cooled and chromatographed ($CHCl_3$-methanol, 19:1) to afford **13** (9.8 mg, 14.5%) and **14** (11.5 mg, 17.1%).

(e) Palladium on carbon (10%, 60 mg) was added to a solution of **13** (20 mg, 0.055 mmol) in toluene (4 ml). The mixture was refluxed for 4 h, then cooled and filtered. The filtrate was evaporated and the residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **14** (10.8 mg, 54.3%).

Meridine Methyl Ether (2) The nitro compound **14** (25 mg, 0.069 mmol) in methanol (6 ml) was hydrogenated at 1 atm for 1.5 h using 10% palladium on carbon (20 mg) as a catalyst. The catalyst was filtered off and the filtrate was evaporated. The residue was chromatographed (CH_2Cl_2-methanol, 19:1) to afford **2** (19.7 mg, 90.9%). mp >300 °C (yellow powder from $CHCl_3$). MS *m/z* (%): 313 (M^+, 100), 284 (26), 255 (32). High-resolution MS Calcd for $C_{19}H_{11}N_3O_2$: 313.0851. Found: 313.0852. IR (KBr): 1686 (C=O), 1598, 1572, 1330, 1304, 1066, 984, 758 cm^{-1}. ^{1}H-NMR δ: 4.25 (3H, s, OCH_3), 7.30 (1H, d, J = 5.6 Hz, C_{11}-H), 7.84 (1H, ddd, J = 8.3, 7.9, 1.0 Hz, C_3-H), 7.96 (1H, ddd, J = 8.3, 7.9, 1.0 Hz, C_2-H), 8.36 (1H, dd, J = 8.3, 1.0 Hz, C_1-H), 8.62 (1H, dd, J = 8.3, 1.0 Hz, C_4-H), 8.69 (1H, d, J = 5.6 Hz, C_5-H), 8.91 (1H, d, J = 5.6 Hz, C_{10}-H), 9.34 (1H, d, J = 5.6 Hz, C_6-H). ^{1}H-NMR (500 MHz, $CDCl_3$–DMSO-d_6) δ: 4.22 (3H, s, OCH_3), 7.32 (1H, d, J = 5.6 Hz, C_{11}-H), 7.83 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, C_3-H), 7.94 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, C_2-H), 8.27 (1H, dd, J = 8.2, 1.2 Hz, C_1-H), 8.58 (1H, dd, J = 8.2, 1.2 Hz, C_4-H), 8.67 (1H, d, J = 5.6 Hz, C_5-H), 8.83 (1H, d, J = 5.6 Hz, C_{10}-H), 9.25 (1H, d, J = 5.6 Hz, C_6-H). ^{13}C-NMR ($CDCl_3$–DMSO-d_6): see Table III.

Meridine (1) Hydroiodic acid (57%, 20 ml) was added to a suspension of **2** (100 mg, 0.317 mmol) in acetic acid (8 ml), and the whole was heated at 100 °C for 30 min. The reaction mixture was

cooled, diluted with ice-water (200 ml), neutralized with $NaHCO_3$, and extracted with $CHCl_3$ (containing 3% methanol, 3 x 100 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **1** (84.5 mg, 88.5%). mp >250 °C (yellow powder from $CHCl_3$-methanol). MS *m/z* (%): 299 (M^+, 100), 271 (20), 243 (43). High-resolution MS Calcd for $C_{18}H_9N_3O_2$: 299.0695. Found: 299.0695. IR (KBr): 3444 (OH), 1690 (C=O), 1606, 1478, 1468, 1336, 1322, 1296, 1216, 1106, 866, 772 cm^{-1}. ^{1}H-NMR (500 MHz) δ: 7.28 (1H, d, J = 5.5 Hz, C_{11}-H), 7.89 (1H, ddd, J = 8.1, 7.3, 1.1 Hz, C_3-H), 8.00 (1H, ddd, J = 8.1, 7.3, 1.1 Hz, C_2-H), 8.26 (1H, dd, J = 8.1, 1.1 Hz, C_1-H), 8.66 (1H, dd, J = 8.1, 1.1 Hz, C_4-H), 8.69 (1H, d, J = 5.5 Hz, C_5-H), 8.81 (1H, d, J = 5.5 Hz, C_{10}-H), 9.41 (1H, d, J = 5.5 Hz, C_6-H), 15.30 (1H, s, OH). ^{13}C-NMR: see Table III.

6-Bromo-4,5,8-trimethoxyquinoline (16) A solution of 28% sodium methoxide in methanol (2 ml) was added to **15** (50 mg, 0.165 mmol). The whole was refluxed for 30 min, then cooled, diluted with water (30 ml), neutralized with 10% HCl, and extracted with CH_2Cl_2 (3 x 50 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **16** (35.0 mg, 71.0%). mp 142 °C (colorless powder from $CHCl_3$). MS *m/z* (%): 299 (M^++2, 38), 297 (M^+, 39), 284 (98), 282 (100). *Anal.* Calcd for $C_{12}H_{12}BrNO_3$: C, 48.34; H, 4.06; N, 4.70. Found: C, 48.08; H, 3.99; N, 4.67. ^{1}H-NMR δ: 3.85 (3H, s, OCH_3), 4.04 (3H, s, OCH_3), 4.06 (3H, s, OCH_3), 6.85 (1H, d, J = 5.3 Hz, C_3-H), 7.17 (1H, s, C_7-H), 8.75 (1H, d, J = 5.3 Hz, C_2-H).

6-Bromo-4-methoxy-5,8-quinolinedione (17) A solution of CAN (920 mg, 1.68 mmol) in water (4 ml) was added to **16** (100 mg, 0.335 mmol) dissolved in acetonitrile (12 ml) at 0-5 °C. The mixture was stirred at 25 °C for 1 h, diluted with water (100 ml), and extracted with CH_2Cl_2 (3 x 150 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **17** (34.2 mg, 38.0%). mp 180 °C (yellow powder from ethyl acetate). MS *m/z* (%): 269 (M^++2, 14), 267 (M^+, 15), 223 (100). IR (KBr): 1672 cm^{-1} (C=O). ^{1}H-NMR δ: 4.10 (3H, s, OCH_3), 7.20 (1H, d, J = 5.6 Hz, C_3-H), 7.29 (1H, s, C_7-H), 8.87 (1H, d, J = 5.6 Hz, C_2-H).

4-Methoxy-9-(2'-nitrophenyl)pyrido[2,3-*g*]quinoline-5,10-dione (18) (a) Table II, Entry 1: Acetic anhydride (70 μl, 0.746 mmol), silica gel (E. Merck silica gel 60, 70–230 mesh, 0.81 g), and **12** (98.1 mg, 0.447 mmol) in $CHCl_3$ (5 ml) were added to a solution of **17** (100 mg, 0.373 mmol) in $CHCl_3$ (15 ml), and the whole was refluxed for 6 days. Silica gel was filtered off and the filtrate was evaporated to dryness. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **18** (17.5 mg, 13.0%). mp 271-275 °C (decomp.) (yellow powder from ethyl acetate-$CHCl_3$). MS *m/z* (%): 315 (M^+-NO_2, 100), 285 (18). FABMS: 362 (M^++1). High-resolution MS Calcd for $C_{19}H_{11}N_2O_3$ (M^+-NO_2): 315.0770. Found: 315.0775. IR (KBr): 1684 cm^{-1} (C=O). ^{1}H-NMR δ: 4.13 (3H, s, OCH_3), 7.20 (1H, d, J = 5.9 Hz, C_3-H), 7.25 (1H, dd, J = 7.6, 1.7 Hz, $C_{6'}$-H), 7.47 (1H, d, J = 5.0 Hz, C_8-H), 7.66 (1H, ddd, J = 7.9, 7.6, 1.7 Hz, $C_{4'}$-H), 7.74 (1H, td, J = 7.6, 1.3 Hz, $C_{5'}$-H), 8.34 (1H, dd, J = 7.9, 1.3 Hz, $C_{3'}$-H), 8.81 (1H, d, J = 5.9 Hz, C_2-H), 9.14 (1H, d, J = 5.0 Hz, C_7-H). ^{13}C-NMR δ: 56.97 (CH_3), 111.37 (C_3), 119.82 (C_{4a}), 124.79 ($C_{3'}$), 126.33 (C_{9a}), 127.94 (C_8), 129.34 ($C_{4'}$), 129.90 ($C_{6'}$), 133.87 ($C_{5'}$), 134.50 ($C_{1'}$), 146.81 ($C_{2'}$), 149.53 (C_{5a} or C_9), 149.60 (C_{5a} or C_9), 150.66 (C_{10a}), 154.67 (C_7), 155.72 (C_2), 166.45 (C_4), 179.80 (C_5 or C_{10}), 181.66 (C_5 or C_{10}).

(b) Table II, Entry 3: Acetic anhydride (35 μl, 0.374 mmol), and **12** (49.1 mg, 0.224 mmol) in acetonitrile (3 ml) were added to a solution of **17** (50 mg, 0.187 mmol) in acetonitrile (8 ml), and the

whole was refluxed for 2 days. The reaction mixture was evaporated to dryness and the residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **18** (19.1 mg, 28.3%).

9-Methoxybenzo[*b*]pyrido[4,3,2-*de*][1,10]phenanthrolin-8(8*H*)-one (4) The nitro compound **18** (25 mg, 0.069 mmol) in methanol (14 ml) was hydrogenated at 1 atm for 30 h using 10% palladium on carbon (20 mg) as a catalyst. The catalyst was filtered off and the filtrate was evaporated. The residue was chromatographed (CH_2Cl_2-methanol, 19:1) to afford **4** (7.8 mg, 36.0%). mp 293-295 °C (decomp.) (yellow powder from ethyl acetate-$CHCl_3$). MS *m/z* (%): 313 (M^+, 100), 284 (30). High-resolution MS Calcd for $C_{19}H_{11}N_3O_2$: 313.0851. Found: 313.0844. IR (KBr): 1672 (C=O), 1574, 1464, 1358, 1302, 1264, 1082, 1058, 774 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 4.09 (3H, s, OCH_3), 7.51 (1H, d, J = 5.9 Hz, C_{10}-H), 7.94 (1H, ddd, J = 8.3, 7.3, 1.3 Hz, C_3-H), 8.05 (1H, ddd, J = 8.3, 7.3, 1.3 Hz, C_2-H), 8.41 (1H, dd, J = 8.3, 1.3 Hz, C_1-H), 8.96 (1H, d, J = 5.9 Hz, C_{11}-H), 8.98 (1H, dd, J = 8.3, 1.3 Hz, C_4-H), 9.07 (1H, d, J = 5.6 Hz, C_5-H), 9.29 (1H, d, J = 5.6 Hz, C_6-H). ^{13}C-NMR (DMSO-d_6): see Table III.

7-Bromo-4-chloro-5,8-quinolinedione (19) A solution of CAN (2.71 g, 4.95 mmol) in water (20 ml) was added to **9** (300 mg, 0.99 mmol) dissolved in acetonitrile (25 ml) at 0-5 °C. The mixture was stirred at 25 °C for 30 min, diluted with water (100 ml), and extracted with CH_2Cl_2 (4 x 150 ml). The extract was washed with water, dried, and evaporated. The residue was recrystallized from $CHCl_3$ to afford **19** (180 mg, 66.6%). mp 170-176 °C (yellow powder from $CHCl_3$). MS *m/z* (%): 275 (M^++4, 25), 273 (M^++2, 100), 271 (M^+, 76), 245 (15), 243 (12), 194 (15), 192 (43). *Anal.* Calcd for $C_9H_3BrClNO_2$: C, 39.67; H, 1.11; N, 5.14. Found: C, 39.40; H, 1.13; N, 5.13. IR (KBr): 1688, 1660 cm^{-1} (C=O). ^{1}H-NMR δ: 7.58 (1H, s, C_6-H), 7.73 (1H, d, J = 5.3 Hz, C_3-H), 8.89 (1H, d, J = 5.3 Hz, C_2-H).

1,4-Dihydro-6-chloro-4-(2'-nitrophenyl)pyrido[3,2-*g*]quinoline-5,10-dione (20) and 4-Chloro-6-(2'-nitrophenyl)pyrido[3,2-*g*]quinoline-5,10-dione (21) (a) Acetic anhydride (35 μl, 0.374 mmol) and **19** (50 mg, 0.183 mmol) were added to a solution of **12** (1.13 g, 5.15 mmol) in $CHCl_3$ (2 ml), and the whole was heated at 50 °C for 60 h. The reaction mixture was cooled and chromatographed ($CHCl_3$-methanol, 19:1) to afford **20** (14.2 mg, 21.0%) and **21** (22.7 mg, 33.8%).

20: mp >300 °C (purple powder from $CHCl_3$-ether). MS *m/z* (%): 369 (M^++2, 4), 367 (M^+, 12), 352 (24), 350 (67), 319 (100). High-resolution MS Calcd for $C_{18}H_{10}ClN_3O_4$: 367.0360. Found: 367.0363. IR (KBr): 3176 cm^{-1} (NH); 1694, 1660 cm^{-1} (C=O). ^{1}H-NMR δ: 5.31-5.36 (1H, m, C_3-H), 5.55 (1H, d, J = 4.3 Hz, C_4-H), 6.34 (1H, dd, J = 7.6, 4.3 Hz, C_2-H), 7.01 (1H, br, NH), 7.28-7.55 (3H, m, $C_{4'}$-H, $C_{5'}$-H, $C_{6'}$-H), 7.58 (1H, d, J = 5.3 Hz, C_7-H), 7.86 (1H, d, J = 8.3 Hz, $C_{3'}$-H), 8.72 (1H, d, J = 5.3 Hz, C_8-H).

21: mp 252-255 °C (yellow powder from $CHCl_3$-ether). MS *m/z* (%): 365 (M^+, 1), 319 (100). High-resolution MS Calcd for $C_{18}H_8ClN_3O_4$: 365.0203. Found: 365.0208. IR (KBr): 1698, 1678 cm^{-1} (C=O). ^{1}H-NMR δ: 7.31 (1H, dd, J = 7.6, 1.3 Hz, $C_{6'}$-H), 7.51 (1H, d, J = 4.6 Hz, C_7-H), 7.71 (1H, d, J = 4.6 Hz, C_3-H), 7.72 (1H, ddd, J = 8.3, 7.3, 1.3 Hz, $C_{4'}$-H), 7.81 (1H, ddd, J = 7.6, 7.3, 1.3 Hz, $C_{5'}$-H), 8.36 (1H, dd, J = 8.3, 1.3 Hz, $C_{3'}$-H), 8.94 (1H, d, J = 4.6 Hz, C_2-H), 9.17 (1H, d, J = 4.6 Hz, C_8-H). ^{13}C-NMR δ: 125.07 ($C_{3'}$), 127.55 (C_{4a}), 128.62 (C_{5a}), 129.15 (C_7), 129.66 ($C_{4'}$), 130.01 ($C_{6'}$), 131.14 (C_3), 134.14 ($C_{5'}$), 134.45 ($C_{1'}$), 145.54 (C_4), 146.64 ($C_{2'}$), 148.06 (C_{9a}), 149.39 (C_6), 150.07 (C_{10a}), 154.07 (C_2), 154.65 (C_8), 179.35 (C_5 or C_{10}), 181.14 (C_5 or C_{10}).

(b) Palladium on carbon (10%, 30 mg) was added to a solution of **20** (9.6 mg, 0.026 mmol) in toluene (3 ml). The mixture was refluxed for 2 h, then cooled and filtered. The filtrate was evaporated and the residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **21** (6.6 mg, 69.1%).

4-Methoxy-6-(2'-nitrophenyl)pyrido[3,2-*g*]quinoline-5,10-dione (14) from 21 A solution of 28% sodium methoxide in methanol (1 ml) was added to **21** (30 mg, 0.082 mmol). The whole was stirred at 25 °C for 30 min, diluted with water (50 ml), and extracted with $CHCl_3$ (3 x 50 ml). The extract was washed with water, dried, and evaporated. The residue was recrystallized from $CHCl_3$ to afford **14** (22.3 mg, 75.2%).

4-Amino-6-(2'-nitrophenyl)pyrido[3,2-*g*]quinoline-5,10-dione (22) Sodium azide (22.1 mg, 0.34 mmol) was added to a solution of **21** (25 mg, 0.068 mmol) in *N,N*-dimethylformamide–water (1:1, 0.5 ml), and the whole was heated at 90 °C for 1 h. The reaction mixture was cooled, diluted with water (30 ml), and extracted with $CHCl_3$ (3 x 50 ml). The extract was washed with water, dried and evaporated. The residue was chromatographed ($CHCl_3$-methanol, 19:1) to afford **22** (13.6 mg, 57.5%). mp >300 °C (red powder from $CHCl_3$-ether). MS *m/z* (%): 346 (M^+, 1), 300 (100), 272 (16). High-resolution MS Calcd for $C_{18}H_{10}N_4O_4$: 346.0702. Found: 346.0703. IR (KBr): 3416, 3284 cm^{-1} (NH_2); 1692, 1644 cm^{-1} (C=O). ^{1}H-NMR δ: 6.75 (1H, d, *J* = 5.9 Hz, C_3-H), 7.28 (1H, dd, *J* = 7.6, 1.7 Hz, $C_{6'}$-H), 7.45 (1H, d, *J* = 5.0 Hz, C_7-H), 7.68 (1H, ddd, *J* = 7.9, 7.6, 1.7 Hz, $C_{4'}$-H), 7.78 (1H, td, *J* = 7.6, 1.3 Hz, $C_{5'}$-H), 8.34 (1H, dd, *J* = 7.9, 1.3 Hz, $C_{3'}$-H), 8.51 (1H, d, *J* = 5.9 Hz, C_2-H), 9.12 (1H, d, *J* = 5.0 Hz, C_8-H). ^{13}C-NMR ($CDCl_3$ + DMSO-d_6) δ: 112.64 (C_{4a}), 115.32 (C_3), 124.42 ($C_{3'}$), 127.74 (C_{5a}), 129.08 (C_7 or $C_{4'}$), 129.09 (C_7 or $C_{4'}$), 129.87 ($C_{6'}$), 133.98 ($C_{5'}$), 135.53 ($C_{1'}$), 146.62 ($C_{2'}$), 148.47 (C_{9a}), 149.06 (C_6), 149.75 (C_{10a}), 151.36 (C_2), 153.74 (C_8), 156.13 (C_4), 180.70 (C_5 or C_{10}), 185.22 (C_5 or C_{10}).

Cystodamine (3) The nitro compound **22** (63.1 mg, 0.182 mmol) in methanol (35 ml) was hydrogenated at 1 atm for 24 h using 10% palladium on carbon (64 mg) as a catalyst. The catalyst was filtered off and the filtrate was evaporated. The residue was chromatographed (CH_2Cl_2-methanol, 9:1) to afford **3** (48.0 mg, 88.3%). mp >250 °C (red powder from $CHCl_3$-CH_3OH). MS *m/z* (%): 298 (M^+, 100), 270 (47), 243 (16). High-resolution MS Calcd for $C_{18}H_{10}N_4O$: 298.0855. Found: 298.0856. IR (KBr): 3336, 1686 (C=O), 1610, 1330, 1294 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 7.09 (1H, d, *J* = 5.6 Hz, C_{11}-H), 7.86 (1H, td, *J* = 7.3, 1.0 Hz, C_3-H), 7.98 (1H, td, *J* = 7.3, 1.0 Hz, C_2-H), 8.34 (1H, d, *J* = 5.6 Hz, C_{10}-H), 8.41 (1H, dd, *J* = 7.3, 1.0 Hz, C_1-H), 8.91 (1H, dd, *J* = 7.3, 1.0 Hz, C_4-H), 9.07 (1H, d, *J* = 5.6 Hz, C_5-H), 9.28 (1H, d, *J* = 5.6 Hz, C_6-H), 7.8-7.9, 10.1-10.2 (each 1H, br, NH_2). ^{1}H-NMR (DMSO-d_6 + 1 drop of HCl) δ: 7.54 (1H, d, *J* = 7.3 Hz, C_{11}-H), 7.99 (1H, ddd, *J* = 8.3, 6.9, 1.0 Hz, C_3-H), 8.09 (1H, td, *J* = 6.9, 1.0 Hz, C_2-H), 8.34 (1H, d, *J* = 7.3 Hz, C_{10}-H), 8.70 (1H, dd, *J* = 6.9, 1.0 Hz, C_1-H), 9.03 (1H, dd, *J* = 8.3, 1.0 Hz, C_4-H), 9.25 (1H, d, *J* = 5.6 Hz, C_5-H), 9.39 (1H, d, *J* = 5.6 Hz, C_6-H). ^{1}H-NMR (500 MHz, CD_2Cl_2 + 2 drops of CF_3CO_2D) δ: 7.38 (1H, d, *J* = 7.0 Hz, C_{11}-H), 7.97 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz, C_3-H), 8.06 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz, C_2-H), 8.24 (1H, d, *J* = 7.0 Hz, C_{10}-H), 8.37 (1H, dd, *J* = 8.2, 1.2 Hz, C_1-H), 8.70 (1H, dd, *J* = 8.2, 1.2 Hz, C_4-H), 8.97 (1H, d, *J* = 5.5 Hz, C_5-H), 9.43 (1H, d, *J* = 5.5 Hz, C_6-H). ^{13}C-NMR (CD_2Cl_2 + 2 drops of CF_3CO_2D): see Table III.

4-Chloro-9-(2'-nitrophenyl)pyrido[2,3-*g*]quinoline-5,10-dione (24) (a) Acetic anhydride (30 μl, 0.32 mmol), and **12** (60 mg, 0.274 mmol) were added to a solution of **23** (30 mg, 0.11 mmol) in CH_2Cl_2 (0.6 ml), and the whole was refluxed for 5 h. The reaction mixture was evaporated to dryness

and the residue was chromatographed (CH_2Cl_2-ethyl acetate, 19:1) to afford **24** (8.2 mg, 20.4%). mp 222-225 °C (decomp.) (yellow powder from ethyl acetate-ether). MS *m/z* (%): 365 (M^+, 2), 321 (36), 319 (100). IR (KBr): 1694 cm^{-1} (C=O). ^{1}H-NMR δ: 7.26 (1H, dd, *J* = 7.3, 1.3 Hz, C_6-H), 7.52 (1H, d, *J* = 5.0 Hz, C_8-H), 7.68 (1H, ddd, *J* = 8.3, 7.6, 1.3 Hz, C_4-H), 7.75 (1H, d, *J* = 5.3 Hz, C_3-H), 7.76 (1H, ddd, *J* = 7.6, 7.3, 1.3 Hz, C_5-H), 8.36 (1H, dd, *J* = 8.3, 1.3 Hz, C_3-H), 8.85 (1H, d, *J* = 5.3 Hz, C_2-H), 9.18 (1H, d, *J* = 5.0 Hz, C_7-H). ^{13}C-NMR δ: 124.96 (C_3), 126.65 (C_{9a}), 127.13 (C_{4a}), 128.45 (C_8), 129.60 (C_4), 129.87 (C_6), 131.07 (C_3), 134.03 (C_5), 134.20 (C_1), 145.98 (C_4), 146.81 (C_2), 149.40 (C_{5a}), 149.87 (C_9), 150.40 (C_{10a}), 154.07 (C_2), 155.04 (C_7), 179.44 (C_5 or C_{10}), 180.54 (C_5 or C_{10}).

(b) Acetic anhydride (35 μl, 0.374 mmol) and **23** (50 mg, 0.183 mmol) were added to a solution of **12** (1.13 g, 5.15 mmol) in $CHCl_3$ (2 ml), and the whole was heated at 50 °C for 45 h. The reaction mixture was cooled and chromatographed ($CHCl_3$-methanol, 19:1) to afford **24** (18.5 mg, 27.6%).

4-Methoxy-9-(2'-nitrophenyl)pyrido[2,3-*g*]quinoline-5,10-dione (18) from 24 A solution of 28% sodium methoxide in methanol (0.6 ml) was added to **24** (15 mg, 0.041 mmol). The whole was stirred at 25 °C for 30 min, diluted with water (9 ml), and extracted with CH_2Cl_2 (3 x 10 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed (CH_2Cl_2-methanol, 99:1) to afford **18** (11.1 mg, 74.9%).

4-Amino-9-(2'-nitrophenyl)pyrido[2,3-*g*]quinoline-5,10-dione (25) Sodium azide (15 mg, 0.23 mmol) was added to a solution of **24** (20.5 mg, 0.056 mmol) in *N,N*-dimethylformamide–water (1:1, 1.0 ml), and the whole was heated at 90 °C for 1 h. The reaction mixture was cooled, diluted with water (30 ml), and extracted with $CHCl_3$ (3 x 30 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed (CH_2Cl_2-methanol, 97:3) to afford **25** (10.0 mg, 51.5%). mp 181-184 °C (yellow powder from ethyl acetate-ether). MS *m/z* (%): 346 (M^+, 1), 300 (100), 273 (16). High-resolution MS Calcd for $C_{18}H_{10}N_4O_4$: 346.0702. Found: 346.0706. IR (KBr): 3412, 3292 cm^{-1} (NH_2); 1686, 1652 cm^{-1} (C=O). ^{1}H-NMR δ: 6.80 (1H, d, *J* = 5.6 Hz, C_3-H), 7.23 (1H, dd, *J* = 7.3, 1.6 Hz, C_6-H), 7.47 (1H, d, *J* = 5.0 Hz, C_8-H), 7.65 (1H, ddd, *J* = 8.2, 7.6, 1.6 Hz, C_4-H), 7.73 (1H, ddd, *J* = 7.6, 7.3, 1.3 Hz, C_5-H), 8.35 (1H, dd, *J* = 8.2, 1.3 Hz, C_3-H), 8.41 (1H, d, *J* = 5.6 Hz, C_2-H), 9.13 (1H, d, *J* = 5.0 Hz, C_7-H).

9-Aminobenzo[*b*]pyrido[4,3,2-*de*][1,10]phenanthrolin-8(8*H*)-one (5) The nitro compound **25** (11 mg, 0.032 mmol) in ethyl acetate (7 ml) was hydrogenated at 1 atm for 2 h using 10% palladium on carbon (11 mg) as a catalyst. The catalyst was filtered off and the filtrate was evaporated. The residue was chromatographed (CH_2Cl_2-methanol, 19:1) to afford **5** (8.5 mg, 89.7%). mp >250 °C (red powder from $CHCl_3$-ether). MS *m/z* (%): 298 (M^+, 100), 270 (53), 243 (14). High-resolution MS Calcd for $C_{18}H_{10}N_4O$: 298.0855. Found: 298.0854. IR (KBr): 3388, 3276, 1640 (C=O), 1620, 1598, 1288 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 6.97 (1H, d, *J* = 5.9 Hz, C_{10}-H), 7.93 (1H, ddd, *J* = 7.3, 6.9, 1.3 Hz, C_3-H), 8.04 (1H, ddd, *J* = 7.3, 6.9, 1.3 Hz, C_2-H), 8.38 (1H, dd, *J* = 7.3, 1.3 Hz, C_1-H), 8.44 (1H, d, *J* = 5.9 Hz, C_{11}-H), 8.97 (1H, dd, *J* = 7.3, 1.3 Hz, C_4-H), 9.06 (1H, d, *J* = 5.6 Hz, C_5-H), 9.28 (1H, d, *J* = 5.6 Hz, C_6-H), 7.8-8.2, 8.8-9.1 (each 1H, br, NH_2). ^{1}H-NMR (DMSO-d_6 + 1 drop of HCl) δ: 7.43 (1H, d, *J* = 7.3 Hz, C_{10}-H), 8.10 (1H, ddd, *J* = 7.9, 6.9, 1.3 Hz, C_3-H), 8.19 (1H, ddd, *J* = 7.9, 6.9, 1.3 Hz, C_2-H), 8.41 (1H, d, *J* = 7.3 Hz, C_{11}-H), 8.49 (1H, dd, *J* = 7.9, 1.3 Hz, C_1-H), 9.12 (1H, dd, *J* = 7.9, 1.3 Hz, C_4-H), 9.22 (1H, d, *J* = 5.6 Hz, C_5-H), 9.40 (1H, d, *J* = 5.6 Hz, C_6-H). ^{1}H-NMR (500 MHz, CD_2Cl_2 + 2 drops of

CF_3CO_2D) δ: 7.29 (1H, d, J = 7.0 Hz, C_{10}-H), 8.14 (1H, ddd, J = 7.9, 7.0, 1.2 Hz, C_3-H), 8.22 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, C_2-H), 8.46 (1H, d, J = 7.0 Hz, C_{11}-H), 8.53 (1H, dd, J = 8.2, 1.2 Hz, C_1-H), 8.83 (1H, dd, J = 7.9, 1.2 Hz, C_4-H), 9.04 (1H, d, J = 5.8 Hz, C_5-H), 9.51 (1H, d, J = 5.8 Hz, C_6-H). ^{13}C-NMR (CD_2Cl_2 + 2 drops of CF_3CO_2D): see Table III.

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