Streptonigrin and Related Compounds. I. Some 2-Phenyl- and 2,2-Pyridylquinoline-5,8-diones

Koppaka V. Rao

College of Pharmacy, J. Hillis Miller Health Center, University of Florida, Gainesville, Florida 32610

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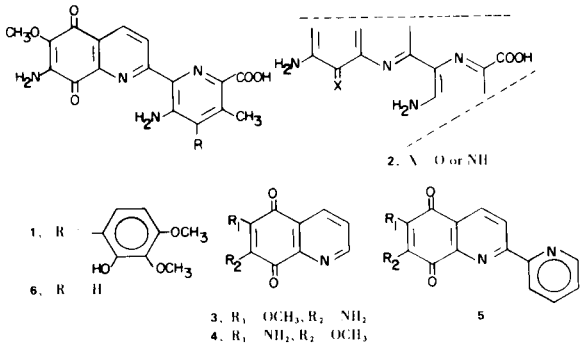
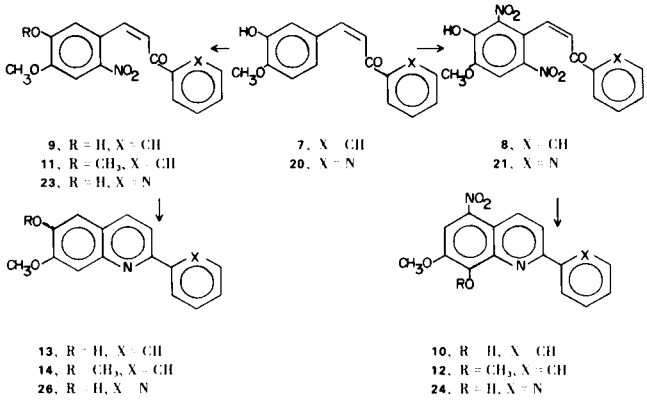
Methods for the synthesis of 6-amino-7-methoxy- and 7-amino-6-methoxy-2,2-pyridylquinoline-5,8-diones and the corresponding 2-phenylquinoline-5,8-diones are described. The 6-aminoquinone system was generated by direct amination with sodium azide and the 7-aminoquinone system *via* the novel 6-hydroxy-7-nitroquinone intermediates. The basic skeleton was derived by the application of the Friedlander quinoline synthesis.

The antitumor antibiotic streptonigrin (**1**, 1-5) is of interest as a potential chemotherapeutic agent in certain forms of lymphoma (6,7). Although Kametani *et. al.*, (8) reported a number of synthetic efforts in this area, no details on the biological activity of the analogues they prepared are available. In a systematic structure-activity study, it is desirable to define the structural elements essential for activity and arrive at a minimum structure consistent with this activity. Based on a study of selected analogues of **1**, it was suggested that **2** might be such a minimum structure (9). One way of checking this is to test the activity of a series of analogues of increasing complexity. Thus, although neither **3** nor **4** was active *in vivo*, **3** showed activity in the He La cell-culture system (9). The next step is to test the 2,2-pyridylquinoline-5,8-dione system (**5**) followed by other tricyclic analogues such as **6**.

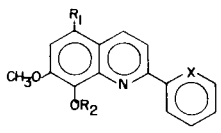


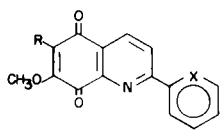
The 2-arylquinoline system was generated by the application of a modified Friedlander quinoline synthesis (10). Thus, nitration of the chalcone **7** gave a 3:1 mixture of the 2,6-dinitro (**8**) and the 6-nitro (**9**) derivatives, and on treatment of the mixture with ammonium sulfide, **8** underwent selective reductive cyclization to form **10** while **9** remained unchanged. Methylation of the mother liquor and chromatography gave **11** and **12**. Cyclization of **9** and **11** was best effected by sodium dithionite to form **13** and **14**, the latter being identical with the known 6,7-dimethoxy-2-phenylquinoline (11).



Reduction of **10** to the amine **15**, followed by oxidation gave the quinone **16** which was converted to the 6-amino-7-methoxy-2-phenylquinoline-5,8-dione **17** by reaction with sodium azide (12). This was confirmed by the formation of **17** *via* the 6-bromoquinone **18** and the 6-azidoquinone **19** followed by reduction and spontaneous oxidation.

For the 2,2-pyridylquinoline system, nitration of **20** gave a 1:2:2 mixture of the 2,6-dinitro (**21**), the 2-nitro (**22**) and the 6-nitro (**23**) derivatives which were cyclized respectively to **24**, **25** and **26**. Oxidation of **25** with Fremy's salt gave the quinone **27** which rapidly underwent amination to **28** when treated with sodium azide. Similar oxidation of 8-hydroxy-2,2-pyridylquinoline (**29**) to the corresponding 5,8-dione (**30**) and amination with azide

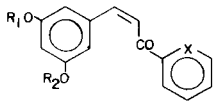


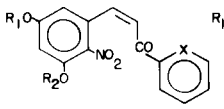


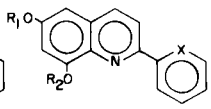
15. R_1 NH_2, R_2 H, X CH 16. R = H, X = CH 19. R N_3, X = CH
25. R_1 R_2 H, X N 17. R = NH_2, X CH 27. R = H, X = N
18. R = Br, X = CH 28. R = NH_2, X = N

gave the 6-amino-2,3-pyridylquinoline-5,8-dione (**31**), together with the 6-azido derivative.

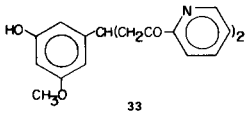
For the synthesis of the 2-aryl-7-amino-6-methoxyquinoline-5,8-diones, 3-acetoxy-5-methoxybenzaldehyde **32**, prepared by the direct partial methylation of 3,5-diacetoxybenzaldehyde (13) was first condensed with 2-acetylpyridine. This gave essentially a bimolecular condensation product **33** (14) while the desired product **34** was formed in low yield. In contrast, acetophenone and **32** readily gave the chalcone **35**. Similarly 3,5-dimethoxybenzaldehyde gave good yields of **36** and **37** respectively with 2-acetylpyridine and acetophenone. Nitration of **35**, **36** and **37** to the respective mononitro derivatives **38**, **39** and **40** and cyclization to the 2-arylquinolines **41**, **42** and **43** proceeded smoothly.





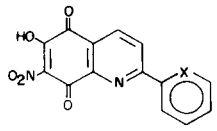


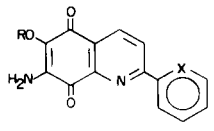
34. R_1 H, R_2 CH_3, X N 38. R_1 H, R_2 CH_3, X CH 41. R_1 = H, R_2 = CH_3, X CH
35. R_1 H, R_2 CH_3, X CH 39. R_1 = R_2 = CH_3, X = CH 42. R_1 = R_2 = CH_3, X = N
36. R_1 = R_2 CH_3, X N 40. R_1 R_2 = CH_3, X = CH 43. R_1 = R_2 = CH_3, X = CH
37. R_1 R_2 CH_3, X CH



33

Nitration of **42** gave in addition to a mono-nitro derivative **44**, an acidic product $C_{14}H_7N_3O_5$ (ir: 3580, 3420, 1700, 1570 and 1320 cm^{-1}) for which structure **45** is proposed. On reduction and spontaneous oxidation, **45** gave an acidic purple quinone **46** (m/e 267), which on methylation with diazomethane gave a neutral maroon quinone **47** (m/e 281) with spectral properties similar to those of **28**.



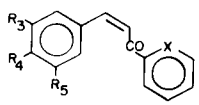


45. X = N 46. R = H, X = N; 47. R = CH_3, X N
48. X = CH 51. R = H, X CH; 52. R = CH_3, X CH

Nitration of **43** similarly gave a mixture which contained the hydroxynitroquinone **48**, a mononitro (**49**) and a dinitro (**50**) derivative. Partial separation and reduction of **48** gave the aminohydroxy quinone (**51**) which was readily isolated and converted to the aminomethoxy quinone (**52**) by methylation. One might speculate that **45** and **48** arose from the corresponding dinitro derivatives although this is not a common reaction. Jones and Kenner (15) reported a somewhat related conversion of 2,6-diaryl-4-nitrophenols

Table I

Chalcones

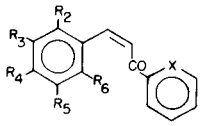


	R_3	R_4	R_5	X	Yield %	Crystallization Solvent	M.P. °C	Formula	Anal. Calcd./Found C	H	N
1	OH	OMe	H	CH	80	C	108-109	$C_{16}H_{14}O_3$	75.57 75.62	5.55 5.62	--- ---
2	OH	H	OMe	CH	60	C	135-136	$C_{16}H_{14}O_3$	75.57 75.33	5.55 5.69	--- ---
3	OMe	H	OMe	CH	78	B	79-80	$C_{17}H_{16}O_3$	76.10 75.90	6.01 5.99	--- ---
4	OH	H	H	N	65	A	141-142	$C_{14}H_{11}NO_2$	74.65 74.53	4.92 4.90	6.22 6.17
5	OH	OMe	H	N	65	A	156-158	$C_{15}H_{13}NO_3$	70.58 70.49	5.13 4.94	5.49 5.27
6	OH	H	OMe	N	15	C	145-146	$C_{15}H_{13}NO_3$	70.58 70.22	5.13 5.35	5.49 5.71
7	OMe	H	OMe	N	82	B	126-127	$C_{15}H_{13}NO_3$	71.36 70.98	5.01 5.29	5.20 4.99

Crystallization solvents: A, ethanol; B, ethanol-ether (1:4); C, ether.

Table II

Nitrochalcones



	R_2	R_3	R_4	R_5	R_6	X	Yield %	Crystallizing Solvent	M.P. °C	Formula	Anal. C	Calcd./Found H	N
1	H	OH	OMe	H	NO_2	CH	20 (a)	A	170-171	$C_{16}H_{13}NO_5$	64.21 64.48	4.38 4.40	4.68 4.37
2	H	OMe	OMe	H	NO_2	CH	95	B	184-185	$C_{17}H_{15}NO_5$	65.17 65.43	4.82 4.66	4.47 4.36
3	NO_2	OH	OMe	H	NO_2	CH	60 (a)	B	193-195	$C_{16}H_{12}N_2O_7$	55.82 55.58	3.51 3.31	8.14 7.84
4	NO_2	OMe	OMe	H	NO_2	CH	95	B	131-132	$C_{17}H_{14}N_2O_7$	56.98 57.12	3.94 3.74	7.82 7.54
5	H	OH	H	OMe	NO_2	CH	50	C	152-153	$C_{16}H_{13}NO_5$	64.21 63.91	4.38 4.52	4.68 4.62
6	H	OMe	H	OMe	NO_2	CH	55	C	129-130	$C_{17}H_{15}NO_5$	65.17 65.36	4.82 4.90	4.47 4.21
7	H	OH	H	H	NO_2	N	30 (b)	A	161-162	$C_{14}H_{10}N_2O_4$	62.22 62.07	3.73 3.82	10.37 10.31
8	NO_2	OH	H	H	H	N	30 (b)	A	216-218	$C_{14}H_{10}N_2O_4$	62.22 61.93	3.73 3.84	10.37 10.11
9	NO_2	OH	OMe	H	H	N	30 (c)	D	153-154	$C_{15}H_{12}N_2O_5$	60.00 60.30	4.03 4.12	9.33 9.54
10	H	OH	OMe	H	NO_2	N	30 (c)	E	246-247	$C_{15}H_{12}N_2O_5$	60.00 59.82	4.03 3.98	9.33 9.22
11	H	OMe	OMe	H	NO_2	N	90	B	161-162	$C_{16}H_{14}N_2O_5$	61.14 60.86	4.49 4.50	8.91 8.62
12	NO_2	OH	OMe	H	NO_2	N	15 (c)	D	192-193	$C_{15}H_{11}N_3O_7$	52.18 52.39	3.21 3.23	12.17 11.84
13	NO_2	OMe	OMe	H	NO_2	N	95	B	158-159	$C_{16}H_{13}N_3O_7$	53.48 53.38	3.65 3.62	11.70 11.71
14	H	OMe	H	OMe	NO_2	N	45	B	174-175	$C_{16}H_{14}N_2O_5$	61.14 60.81	4.49 4.64	8.91 8.64

1. Crystallization solvents: D, methanol-chloroform (1:1); E, pyridine. 2. (a) Formed together; (b) and (c), same.

to the corresponding quinones by lead tetraacetate.

For the preparation of the 7-amino-2,2-pyridylquinoline-5,8-dione, 8-hydroxy-2,2-pyridylquinoline (**29**) was first subjected to nitration. In addition to the expected 5,7-dinitro derivative (**53**), a second product was separated and identified as **45**. This is an unusual reaction in which a monohydric phenol is directly converted to a disubstituted quinone and emphasizes the reactivity of the 6-position of quinoline-5,8-diones. It also opens an alternative route for the 2-aryl-7-amino-6-methoxyquinoline-5,8-dione system.

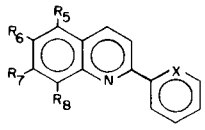
Tables I-III list the various chalcones, their nitro derivatives and the 2-arylquinolines. The various amino- and the aminomethoxyquinones showed significant antibacterial activity when tested by a simple disc-plate procedure against *Bacillus subtilis* in the concentration range 25-100 μg./ml. In comparison with streptonigrin **17**, **47** and **52** were approximately 25% as active and **28** was 10% as active in this system. The aminohydroxyquinones **46** and **51** and the hydroxynitroquinones **45** and **48** were inactive.

EXPERIMENTAL

The melting points were obtained using a Thomas-Hoover apparatus in open-ended capillary tubes and were uncorrected. The spectra were obtained using the following instruments: Beckman Model 25 (uv); Beckman Acculab 3 (ir), Varian A60A (nmr) and Perkin-Elmer-Hitachi SMU-6E (mass spectra).

Table III

2-Phenyl and 2,2-Pyridylquinolines



	R_5	R_6	R_7	R_8	X	Yield %	Crystallization Solvent	M.P. °C	Formula	Anal. Calcd./Found C	H	N
1	H	OH	OMe	H	CH	75	C	178-179	$C_{16}H_{13}NO_2$	76.47 76.27	5.26 5.15	5.57 5.31
2	H	OMe	OMe	H	CH	88	C	133-134	$C_{17}H_{15}NO_2$	76.96 76.67	5.70 5.69	5.28 5.09
3	NO_2	H	OMe	OH	CH	80	D	184-185	$C_{16}H_{12}N_2O_4$	64.86 64.63	4.08 3.86	9.46 9.30
4	NO_2	H	OMe	OMe	CH	90	B	132-133	$C_{17}H_{14}N_2O_4$	65.80 65.55	4.40 4.47	9.03 9.07
5	H	OH	H	OMe	CH	83	B	147-148	$C_{16}H_{13}NO_2$	76.47 76.18	5.22 5.32	5.57 5.47
6	H	OMe	H	OMe	CH	74	F	162-163	$C_{17}H_{15}NO_2$ HCl	67.66 67.56	5.34 5.22	4.63 4.84
7	H	H	H	OH	N	72	C	119-121	$C_{14}H_{10}N_2O$	75.65 75.46	4.54 4.74	12.61 12.68
8	H	OH	H	H	N	78	C	168-170	$C_{14}H_{10}N_2O$	75.65 75.46	4.54 4.74	12.61 12.68
9	H	H	OMe	OH	N	64	C	108-109	$C_{15}H_{12}N_2O_2$	71.41 71.53	4.80 4.86	11.11 11.08
10	H	OH	OMe	H	N	85	F	228-229	$C_{15}H_{12}N_2O_2$ HCl	62.40 62.18	4.53 4.67	9.69 9.91
11	H	OMe	OMe	H	N	78	C	157-158	$C_{16}H_{14}N_2O_2$	71.41 71.53	4.80 4.86	11.11 11.08
12	NO_2	H	OMe	OH	N	75	E	240-242	$C_{15}H_{11}N_3O_4$	60.60 60.32	3.73 3.78	14.40 14.01
13	NO_2	H	OMe	OMe	N	95	C	179-181	$C_{16}H_{13}N_3O_4$	61.73 61.51	4.21 4.08	13.50 13.69
14	H	OMe	H	OMe	N	61	C	96-98	$C_{16}H_{14}N_2O_2$	72.16 72.18	5.30 5.40	10.52 10.45

Thin-layer chromatography (tlc) was carried out using silica gel plates prepared from Merck Silica gel HF254 and 366. Column chromatography, where needed, was performed using a mixture of silicic acid (Mallinckrodt 275-325 mesh) and cellulose powder (Brown & Co.), with benzene as solvent and acetone-benzene mixtures for elution.

General Procedures.

a)

The chalcones of Table I were prepared by base-catalyzed condensation (aqueous 2*N* potassium hydroxide) of the appropriate aldehyde with acetophenone at 25° for 3-5 hours or with 2-acetylpyridine at 0-5° for 2 hours.

The bimolecular condensation product **33** was recovered from the neutralized reaction mixture by filtration and crystallized from methanol-chloroform, m.p. 220-222°.

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 70.45; H, 5.13; N, 7.11.

b)

The nitro compounds listed in Table II were prepared by reaction of the appropriate chalcone (1 g.) in acetic acid (5 ml.) with nitric acid (16*N*, 1-2 ml.) at 5-10°. Separation of the mono and dinitro derivatives was effected by partition between ethyl acetate and aqueous sodium bicarbonate. The dinitro derivatives favored the aqueous phase.

c)

Methylation was carried out by stirring the phenolic compounds in acetone with 1.5 equivalents of methyl sulfate and 3 equivalents of anhydrous potassium carbonate at 25° for 20 hours.

d)

Reductive cyclization of the mononitrochalcones to form the 2-arylquinolines (Table III) was effected by boiling under reflux in 50% aqueous methanol with 3-5 equivalents of sodium dithionite for 1 hour. Concentration of methanol, neutralization, extraction

with chloroform and crystallization gave the products.

For the cyclization of the dinitrochalcones (*eg.* **8**, **21**) the sample (1 g.) was stirred in methanol (20 ml.) with ammonium sulfide (2-3 ml.) for 1 hour. The crystalline ammonium salt of the hydroxynitroquinoline which separated out was filtered, suspended in 1*N* hydrochloric acid and refiltered. It was purified by crystallization.

3-Acetoxy-5-methoxybenzaldehyde (**32**).

A mixture of 3,5-diacetoxybenzaldehyde (**13**, 22.2 g.), methyl sulfate (15 g.) in dimethylformamide (100 ml.) was stirred for 24-30 hours. It was filtered and the filtrate concentrated to an oil. Purification by chromatography on a silicic acid-cellulose column using benzene-hexane (1:1) gave **32** as a colorless oil, yield, 15.5 g. (80%); nmr (deuteriochloroform): τ 0.09, s, 1H; τ 2.75, m, 2H; τ 3.10, m, 1H; τ 6.7, s, 3H; τ 7.70, s, 3H.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 62.01; H, 5.04.

When the above reaction was carried out using acetone as a solvent, a by-product was formed in varying yields. It was separated by chromatography and crystallized from ether-hexane; m.p. 70-71°; nmr (deuteriochloroform): τ -2.40, 2.69, 3.20, 3.49, q, J = 17 Hz, 2H; τ 3.09, m, 2H; τ 3.25, m, 1H; τ 6.7, s, 3H; τ 7.65, s, 3H; τ 7.70, s, 3H. It is shown to be 3-acetoxy-5-methoxybenzalacetone.

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.30; H, 6.06.

5-Amino-8-hydroxy-7-methoxy-2-phenylquinoline (**15**).

A solution of **10** (0.6 g.) in 1:1 tetrahydrofuran-water (20 ml.) was boiled (nitrogen) with sodium dithionite (1.2 g.) for 15 minutes. Partial concentration and cooling gave a crystalline solid which was recrystallized from methanol-chloroform; yield, 0.45 g. (85%); m.p. 171-173°.

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.24; H, 5.51; N, 10.34.

7-Methoxy-2-phenylquinoline-5,8-dione (**16**).

A solution of **15** (0.8 g.) in 2*N* sulfuric acid (25 ml.) was stirred with the addition of 5% sodium dichromate until there was a slight excess of the reagent (starch-iodide paper). After 10 minutes it was neutralized with aqueous sodium bicarbonate and extracted with chloroform twice. Concentration of the extract and crystallization from methanol-ether gave **16** as a yellow crystalline solid, yield, 0.3 g. (38%), m.p. 215-217°, m/e, 265.

Anal. Calcd. for $C_{16}H_{11}NO_3$: C, 72.44; H, 4.18; N, 5.28. Found: C, 72.14; H, 4.18; N, 5.03.

6-Amino-7-methoxy-2-phenylquinoline-5,8-dione (**17**).

A solution of **16** (0.2 g.) in DMF (2 ml.) was stirred with sodium azide (0.1 g.) and acetic acid (0.2 ml.) for 24 hours. Dilution with water, filtration and crystallization from methanol gave **17** as a maroon crystalline solid, yield, 0.15 g. (75%), m.p. 185-187°; m/e, 280.

Anal. Calcd. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.73; H, 4.61; N, 9.81.

6-Bromo-7-methoxy-2-phenylquinoline-5,8-dione (**18**).

When **16** (0.13 g.) in chloroform (2 ml.) was allowed to stand with bromine (0.2 ml.) for 2 hours, **18** separated as a crystalline solid. It was filtered and recrystallized from methanol-chloroform, yield, 0.12 g. (70%); m.p. 162-164°.

Anal. Calcd. for $C_{16}H_{10}BrNO_3$: C, 55.83; H, 2.93; Br, 23.22; N, 4.71. Found: C, 56.02; H, 3.12; Br, 23.56; N, 4.98.

6-Azido-7-methoxy-2-phenylquinoline-5,8-dione (**19**).

A mixture of **18** (0.17 g.) in DMF (2 ml.) was stirred with sodium azide (0.1 g.) for 20 hours. After dilution with water, the solid was filtered and crystallized from acetone-methanol, yield, 0.12 g. (80%), m.p. 137-139°. The compound was highly sensitive to light.

Anal. Calcd. for $C_{16}H_{10}N_4O_3$: C, 62.74; H, 3.29; N, 18.29. Found: C, 62.95; H, 3.02; N, 17.95.

When **19** was heated with sodium dithionite in aqueous methanol, the solution extracted with ethyl acetate, and the purple extract concentrated to dryness, a reddish-brown crystalline solid was obtained which was identical with **17** by melting point, spectral and chromatographic comparison.

7-Methoxy-2,2-pyridylquinoline-5,8-dione (**27**).

Potassium nitrosodisulfonate (2.5 g.) was added in portions to a solution of **25** (0.5 g.) in methanol (10 ml.) and 0.5*M* potassium dihydrogen phosphate (50 ml.). After 1 hour, the mixture was extracted with chloroform, the extract concentrated to dryness and the orange-red solid crystallized from methanol-chloroform; yield, 0.32 g. (60%); m.p. 155-157°; m/e 266.

Anal. Calcd. for $C_{15}H_{10}N_2O_3$: C, 67.66; H, 3.79; N, 10.52. Found: C, 67.51; H, 3.95; N, 10.82.

6-Amino-7-methoxy-2,2-pyridylquinoline-5,8-dione (**28**).

A mixture of **27** (0.2 g.) sodium azide (0.1 g.) and acetic acid (0.2 ml.) in acetone (10 ml.) was stirred for 30 minutes. The deep purple solution was diluted with water, extracted with chloroform and the extract concentrated to dryness. The purple solid was crystallized from methanol, yield, 0.19 g. (90%), m.p. 256-258°; m/e, 281.

Anal. Calcd. for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 64.23; H, 4.10; N, 15.21.

6-Amino-2,2-pyridylquinoline-5,8-dione (**31**).

A sample of **29** (0.45 g.) (Table III) was oxidized with potassium nitrosodisulfonate as described under **27**. The product (0.25 g.) was taken up in DMF (2 ml.) and stirred with sodium azide (0.2 g.) and acetic acid (0.2 ml.) for 2 hours. Addition of water, filtration and crystallization gave a purple solid, yield, 0.11 g. (23%), m.p. 256-258°.

Anal. Calcd. for $C_{14}H_9N_3O_2$: C, 66.92; H, 3.61; N, 16.73. Found: C, 67.11; H, 3.42; N, 17.04.

6-Hydroxy-7-nitro-2,2-pyridylquinoline-5,8-dione (**45**) and 6,8-Dimethoxy-5-nitro-2,2-pyridylquinoline (**44**).

A mixture of 1:1 sulfuric acid-nitric acid (2 ml.) was added to **42** (0.5 g.) in acetic acid (2 ml.) and the mixture stirred for 10 minutes at 40-50°. After addition of water and filtration, the solid was purified by fractional crystallization from DMF. The first fraction was mostly **45**. Addition of methanol gave the second fraction which was mostly **44**. They were each recrystallized from DMF, yield of 45, 0.22 g. (40%), m.p. 223-225°; yield of **44**, 0.3 g. (50%), m.p. 214-216°.

Anal. Calcd. for $C_{14}H_7N_3O_5 \cdot 2H_2O$: C, 50.45; H, 3.33; N, 12.60. Found: C, 50.45; H, 3.33; N, 12.61.

Anal. Calcd. for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: C, 61.45; H, 4.05; N, 13.85.

7-Amino-6-hydroxy-2,2-pyridylquinoline-5,8-dione (**46**).

A suspension of **45** (0.1 g.) in 1:1 aqueous methanol (5 ml.) was heated with sodium dithionite (0.2 g.) until a clear light brown solution resulted. It was cooled, diluted with water (25 ml.) and extracted twice with ethyl acetate. Concentration of the extract

gave a purple solid which was recrystallized from methanol-chloroform, yield, 0.06 g. (75%), m.p. 272-274°; m/e 267.

Anal. Calcd. for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.73. Found: C, 63.12; H, 3.11; N, 15.46.

7-Amino-6-methoxy-2,2-pyridylquinoline-5,8-dione (**47**).

To a solution of **46** (0.15 g.) in methanol-chloroform (10 ml.) was added a slight excess of diazomethane. After one minute the reddish brown solution was concentrated to dryness and the solid crystallized from methanol-ether, yield, 0.15 g. (90%), m.p. 172-174°; m/e, 281.

Anal. Calcd. for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 64.25; H, 4.12; N, 14.68.

6,8-Dimethoxy-5(7)-nitro-2-phenylquinoline (**49**) and 7-Amino-6-hydroxy-2-phenylquinoline-5,8-dione (**51**).

Nitration of **43** (0.5 g.) was carried out as described under **45**. Fractional crystallization of the product from DMF gave as the major product, a mixture of **49** and **50**. A second crystallization gave essentially pure **49**, yield 0.25 g. (42%), m.p. 198-200°.

Anal. Calcd. for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.52; H, 4.32; N, 9.38.

Mother liquor from the crystallization of **49** and **50** was heated with sodium dithionite (0.3 g.) until the initial reddish brown color changed to pale brown. Dilution with water (25 ml.) and extraction with ethyl acetate followed by concentration of the extract gave a purple solid. It was crystallized from methanol-chloroform, yield, 0.15 g. (30%), m.p. 218-220°.

Anal. Calcd. for $C_{15}H_{10}N_2O_3$: C, 67.66; H, 3.79; N, 10.52. Found: C, 67.51; H, 3.85; N, 10.82.

7-Amino-6-methoxy-2-phenylquinoline-5,8-dione (**52**).

Methylation of **51** (0.1 g.) in methanol-chloroform (10 ml.) with diazomethane followed by crystallization from acetone gave **52** as a maroon crystalline solid, yield, 0.1 g., m.p. 176-178°; m/e, 280.

Anal. Calcd. for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.33; H, 4.52; N, 10.25.

8-Hydroxy-5,7-dinitro-2,2-pyridylquinoline **53** and 6-Hydroxy-7-nitro-2,2-pyridylquinoline-5,8-dione (**45**).

Nitration of **29** (0.5 g.) was carried out as described under **44**. The product was purified by fractional crystallization from DMF. The first fraction was **53**, yield, 0.36 g. (57%), m.p. 266-268°.

Anal. Calcd. for $C_{14}H_8N_4O_5$: C, 53.85; H, 2.58; N, 17.95. Found: C, 54.11; H, 2.75; N, 18.27.

The second fraction from the crystallization was identical with **45** on the basis of melting point, spectral and chromatographic comparison, yield, 0.15 g. (25%).

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