A New Heterocyclic Ring System

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Isatoic acid reacts with 7-methyl-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**8**) to give 3-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridin-7-carboxylic acid (**9a**), which was transformed into the 3-methylquino[3,2-*c*][1,8]naphthyridine (**7a**) by refluxing with copper chromite in quinoline. The same product (**7a**) was also obtained by aromatization of the 3-methyl-5,6-dihydroquino-[3,2-*c*][1,8]naphthyridine (**10a**), prepared by condensation of the ketone (**8**) and *o*-amino-benzaldehyde. Other 3-substituted quino[3,2-*c*][1,8]naphthyridines (**7b,c,d,e**), which contain a new heterocyclic ring structure, have been prepared using *o*-aminobenzaldehyde and 7-substituted-2,3-dihydro-1,8-naphthyridin-4(1*H*)ones (**12** and **13**) as starting materials. Also, the preparation of the parent nucleus (**7f**) is described.

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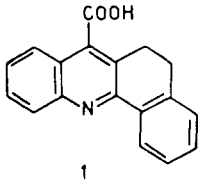
Previously, Von Braun and Wolf (1) have shown that α-tetralone condenses readily with isatoic acid to yield the 5,6-dihydrobenzo[*c*]acridine-7-carboxylic acid (**1**) and Clemo and Perkin (2) obtained the condensation product (**2**) from the same acid and 4-tetrahydroquinolone.



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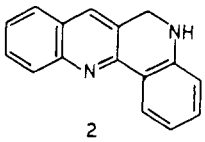

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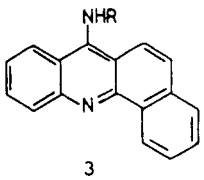
More recently, a number of *N*-substituted 7-aminobenzo-[*c*]acridines (**3**), benzo[*b*][1,8]phenanthrolines (**4**), benzo-[*b*][1,10]phenanthrolines (**5**) and dibenzo[*b,h*][1,6]-naphthyridines (**6**) have been prepared by E. F. Elslager and coworkers (3a-d). Several of these compounds exhibited good antiamebic activity.



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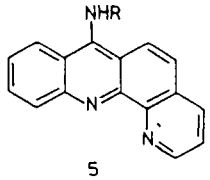

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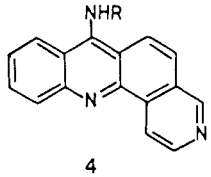

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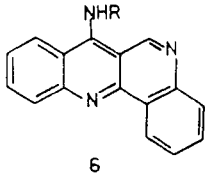

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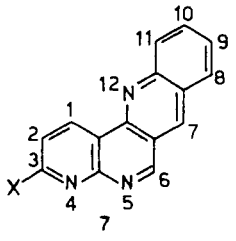
Pursuing our interest in heteropolycyclic compounds (4a-c) which might exhibit pharmacological activity because of their structural resemblance to the above substances and to some very important alkaloids as olivacine, ellipticine, lysergic acid, *etc.*, we describe in this paper the synthesis and the characterization of some 3-substituted quino[3,2-*c*][1,8]naphthyridines (**7**), which represent a new heterocyclic ring structure.



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7a: X = CH_3
7b: X = Br
7c: X = OC_2H_5
7d: X = OH
7e: X = SH
7f: X = H

The route employed for the synthesis of **7a** was essentially the same as described by Clemo and Perkin for the preparation of compound **2** (2). Thus, when isatin and 7-methyl-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**8**) (5) were heated in alkaline ethanolic solution the acid **9a** was obtained in 73.9% yield (see Scheme I). This compound is a high melting yellow crystalline solid (m.p. above 320°), slightly soluble in all usual organic solvents. It was converted into the acetyl derivative (**9b**) (80.3% yield) by heating with acetic anhydride and into the fully aromatic 3-methylquino[3,2-*c*][1,8]naphthyridine (**7a**) by refluxing with copper chromite in quinoline (83.1% yield). The structure of these compounds were assigned based upon analytical data, nmr spectra of compounds **9b** and **7a** and chemical evidence. The nmr spectrum (DMSO-d_6, 25°) of **9b** shows two singlets at δ 2.40 and at δ 2.54 (three protons each) due to CH_3 groups, a singlet at δ 5.33 (two protons) assigned to CH_2 in the 6 position and two proton signals at δ 8.68 and δ 7.32 due to H_1 and H_2 respectively (J = 8.0 Hz). The absorption range for phenyl protons is δ 8.27 to δ 7.57. The nmr spectrum of **7a** (deuteriochloroform, 25°) shows a singlet at δ 2.90 (three protons) assigned to CH_3, a singlet at δ 8.92 assigned to H_7, a singlet at δ 9.67 assigned to H_6 and two proton signals at δ 9.50 and δ

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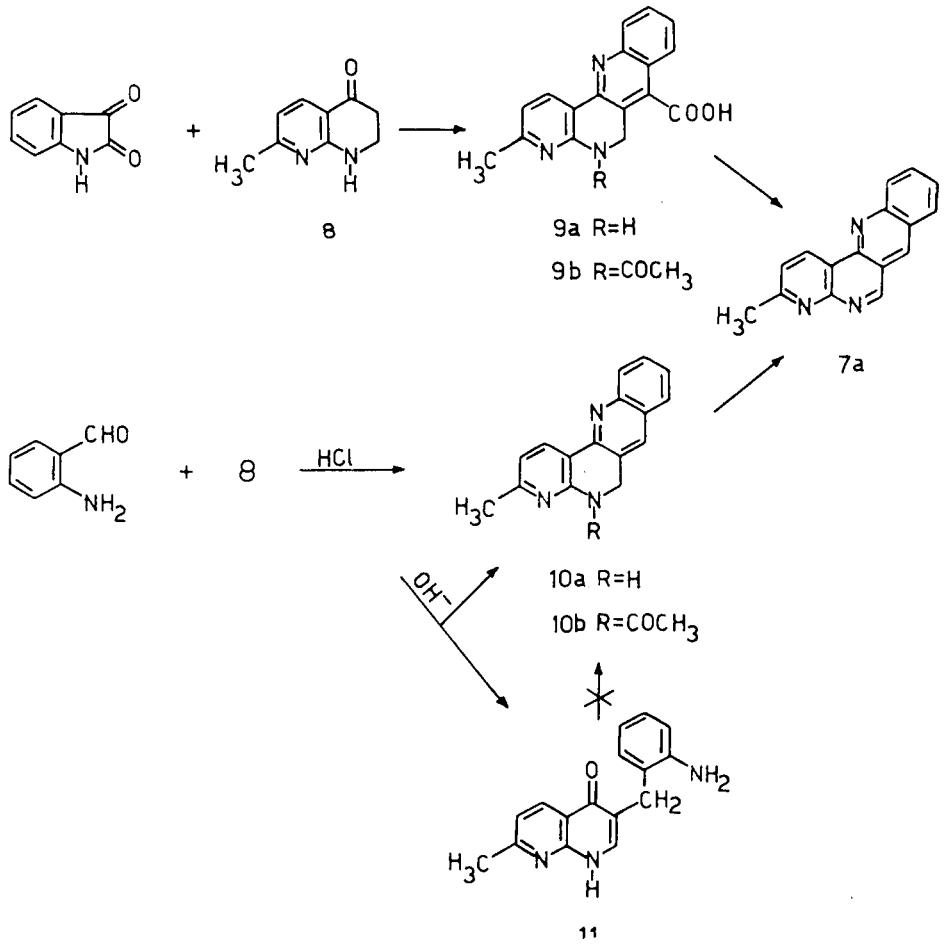
SCHEME I

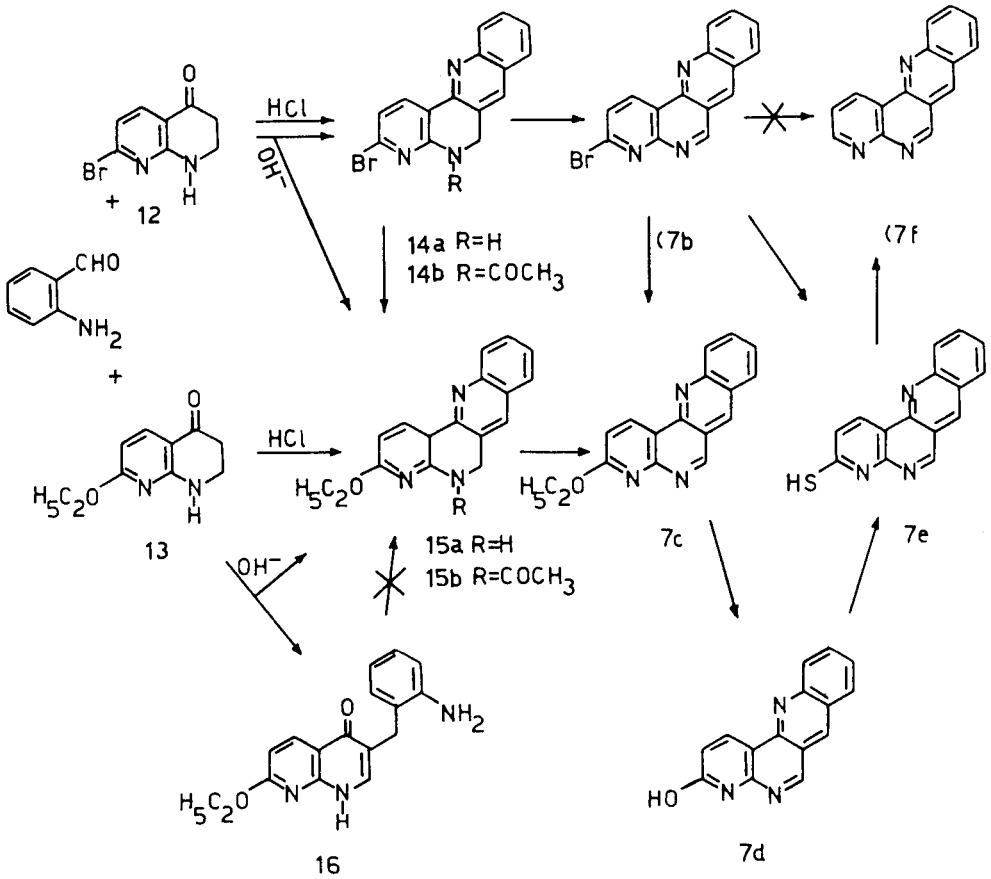


7.50 due to H_1 and H_2 respectively (J = 8.0 Hz). The absorption range for phenyl protons is δ 8.51 to δ 7.70.

It was impossible to obtain the nmr spectrum of **9a** because of its insolubility. The structures of **7a** and consequently of **9** were confirmed by chemical evidence as follows: compound **7a** was synthesized besides as described above (**9a⇒7a**), also by aromatization of 3-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**10a**), obtained in 82.9% yield by treating the ketone (**8**) and *o*-aminobenzaldehyde with anhydrous hydrochloric acid in absolute ethanolic solution. When the reaction was carried out in aqueous alcoholic alkaline solution, little amount of condensation product (**11**) was obtained from the mother liquors of **10**. An attempt to cyclize **11** to **10** by treatment with anhydrous hydrochloric acid was unsuccessful. The acetyl derivative **10b** of **10a** was also prepared (see Scheme I). Elemental analyses and nmr spectral data are all consistent with the assigned structures **10a, 10b** and **11** (see Table 1).

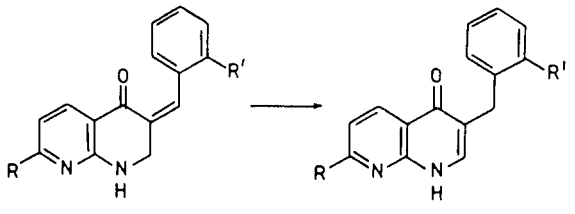
It was also of interest to prepare other quino[3,2-*c*][1,8]naphthyridines having oxygen functions (OH or OC_2H_5) in the 3 position, for pharmacological evaluation. A possible route to obtain these compounds, analogous to that employed to prepare **10a**, appears to be the condensation of the bromo ketone (**12**) or ethoxy ketone (**13**) previously described (6), with *o*-aminobenzaldehyde. When ketones **12** or **13** were allowed to react at room temperature with *o*-aminobenzaldehyde and anhydrous hydrochloric acid in ethanolic solution, the two 3-substituted-5,6-dihydroquino[3,2-*c*][1,8]naphthyridines **14a** and **15a** were obtained in 59.1% and 74.1% yields, respectively. The reaction between ethoxy ketone (**13**) and *o*-aminobenzaldehyde in aqueous alcoholic alkaline solution, gives the non cyclized compound (**16**) in low yield, together with **15a**. In the same reaction conditions, a mixture of **14a** (47.3% yield) and **15a** (25.4% yield) was obtained from the ketone (**12**). Compound **16** doesn't cyclize to **15a** by treatment with anhydrous hydrochloric acid. Compound **15a** was also directly prepared in 56.3% yield by treating **14a** with sodium ethoxide in absolute ethyl alcohol. Elemental analyses and nmr spectra of **14a, 15a** and **16** are all consistent with the assigned structures (nmr spectral data see Table 1). Additional support for the above structures was obtained by convert-

SCHEME II



ing compounds **14a** and **15a** into the *N*-acetyl derivatives **14b** and **15b** (nmr spectrum of **14b** see Table I).

The same compounds **14a** and **15a** were also converted in satisfactory yield into the fully aromatic substances **7b** and **7c** respectively, by refluxing with nitrobenzene (nmr spectral data of **7c** see Table I). Compound **7c** was also obtained in 80% yield by heating **7b** with sodium ethoxide in ethanol. The desired derivative (**7d**), having the hydroxyl group in the 3 position as in natural steroidal compounds, was obtained from **7c** by hydrolysis with hydrogen iodide in 91.3% yield (see Scheme II). Compounds **11** and **16** obtained in the reaction of the ketones **8** and **13** with *o*-aminobenzaldehyde in alkaline solution, were very probably formed from the non isolated con-



17a: R = CH_3, R' = NH_2
17b: R = OC_2H_5, R' = NH_2
17c: R = CH_3, R' = H

11: R = CH_3, R' = NH_2
16: R = OC_2H_5, R' = NH_2
18: R = CH_3, R' = H

densation products **17a** and **17b** initially formed. This transposition of the double bond is well known. In fact the ready conversion of compound **17c** into the isomer **18** in alkaline solution (98% yield) is described (7). Therefore, compounds **11** and **16** don't cyclize to **10a** and **15a**, because of their vinylogous amidelike structure.

Considerable interest had the preparation of the parent nucleus (**7f**) that, to the best of our knowledge, has never been reported. Attempts to obtain quino[3,2-c][1,8]-naphthyridine (**7f**) by catalytic reduction of bromo derivative (**7b**) or by oxidation of the methyl group of **7a** and decarboxylation failed. However, substitution of oxygen by sulfur using phosphorus pentasulfide as the thiating agent has been widely reported in heterocyclic chemistry when the hydroxyl structure is tautomeric with the cyclic amidelike or lactamic structure (4c,6,8); the sulfur is then replaced by hydrogen using Raney nickel (4c,6,9). Therefore, we have converted the 3-hydroxyquino[3,2-c][1,8]naphthyridine (**7d**) with phosphorus pentasulfide in pyridine into the thio derivative (**7e**) (67.1% yield), also obtained in 64.3% yield from **7b** by treatment with sodium hydrosulfide in ethanol. Compound **7e** was then desulfurized to the parent nucleus (**7f**) by means of sponge nickel catalyst. Ele-

Table 1
^{1}H Nmr Spectral Data (δ values; solvent DMSO-d_6)
Observed Chemical Shifts

Compound	H-1	H-2	CH_3	$O\text{-}CH_2\text{-}CH_3$ CH_2	$O\text{-}CH_2\text{-}CH_3$ $-CH_3$	$COCH_3$	H-5	H-6	H-7	CH_2	NH_2	Phenyl Protons	J Values (Hz)	Temperature (°C)
7c	9.50 (d)	7.30 (d)	–	4.68 (q)	1.47 (t)	–	–	9.82 (s)	9.43 (s)	–	–	8.48-7.70 (m)	$J_{1,2}$ 8.0	110
10a	8.50 (d)	6.72 (d)	2.38 (s)	–	–	–	6.90 br	4.80 (2H, s)	8.17 (s)	–	–	8.10-7.40 (m)	$J_{1,2}$ 8.0	25
10b	8.92 (d)	7.47 (d)	2.45 (s)	–	–	2.62 (s)	–	5.36 (2H, s)	8.50 (s)	–	–	8.40-7.72 (m)	$J_{1,2}$ 8.0	110
11	12.10 br	7.33 br	2.60 (s)	–	–	–	8.38 (d)	7.22 (d)	–	3.66 (s)	5.17 br	7.07-6.40 (m)	$J_{5,6}$ 8.0	25
14a	8.45 (d)	6.98 (d)	–	–	–	–	7.25 br	4.94 (2H, s)	8.18 (s)			8.12-7.49 (m)	$J_{1,2}$ 8.0	100
14b	8.44 (d)	7.44 (d)	–	–	–	2.34 (s)	–	5.10 (2H, s)	8.13 (s)	–	–	7.95-7.47 (m)	$J_{1,2}$ 8.0	100
15a	8.41 (d)	6.15 (d)	–	4.30 (q)	1.32 (t)	–	6.90 br	4.75 (2H, s)	8.01 (s)	–	–	7.95-7.26 (m)	$J_{1,2}$ 8.0	25
16	12.00 br	7.68 br	–	4.42 (q)	1.37 (t)	–	8.40 (d)	6.77 (d)	–	3.63 (s)	5.22 br	7.20-6.32 (m)	$J_{5,6}$ 8.0	25

mental analysis and ir and nmr spectra are all consistent with the assigned structure (**7f**). Its nmr spectrum shows two singlets at δ 9.64 and at δ 9.25 due to H_6 and H_7, respectively, three proton signals at δ 9.46 at δ 7.74 and at δ 9.05 assigned to H_1, H_2 and H_3, respectively ($J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 4.7 Hz: $J_{1,3}$ = 2.0 Hz). The absorption range for phenyl protons is δ 8.36 to δ 7.61.

A wide range screening was carried out with some of the above compounds in collaboration with the Bristol Myers Laboratories, Syracuse (U.S.A.), in order to assay their microbiological and pharmacological properties, but none of such compounds was found to be active.

EXPERIMENTAL

Melting points were determined with a Kofler apparatus. Ir spectra were determined with a Perkin-Elmer Infracord Model 137 spectrophotometer in Nujol mulls. ^{1}H nmr spectra were obtained with a JEOL Model C 60 HL spectrometer for solutions in DMSO-d_6 unless otherwise stated (see Table 1) and an internal TMS standard.

3-Methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridin-7-carboxylic Acid (**9a**).

A solution of 5.8 g. (35.8 mmoles) of 7-methyl-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**8**), isatin (5.8 g., 39.4 mmoles) and potassium hydroxide (4 g.) in ethanol (30 ml.) and water (5 ml.) was refluxed for 6 hours. After cooling, the yellow-orange precipitate was collected, suspended in water and acidified (*p*H 4-5) with diluted hydrochloric acid; the obtained solid was collected again, washed with water and dried to give 7.7 g. (73.9%) of **9a**. An analytical sample was obtained by crystallisation from ethanol, m.p. > 320°; ir max (Nujol): 1670, 1460, 1340, 1300, 1110, 760 and 735 cm^{-1}.

Anal. Calcd. for $C_{17}H_{13}N_3O_2$: C, 70.1; H, 4.5; N, 14.4. Found: C, 70.4; H, 4.7; N, 14.2.

5-Acetyl-3-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridin-7-carboxylic Acid (**9b**).

Compound **9a** (0.37 g.) was refluxed with acetic anhydride (5 ml.) for 2 hours. After cooling the white crystalline solid was collected (0.34 g., 80.3%) and crystallised from acetic acid, m.p. 261-263° dec.

Anal. Calcd. for $C_{19}H_{15}N_3O_3$: C, 68.5; H, 4.5; N, 12.6. Found: C, 68.7; H, 4.3; N, 12.6.

Reaction of *o*-Aminobenzaldehyde with 7-Methyl-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**8**).

a) In Acidic Solution.

An ice cooled suspension of 0.162 g. (0.001 mole) of **8** and 0.121 g. (0.001 mole) of *o*-aminobenzaldehyde in 15 ml. of dry ethanol was saturated with anhydrous hydrochloric acid. From the obtained solution, after standing at room temperature overnight, an orange solid was formed that was filtered off and treated with diluted ammonia. The solid was collected and crystallised from ethanol to give 0.205 g. (82.9%) of 3-methyl-5,6-dihydroquino-[3,2-*c*][1,8]naphthyridine (**10a**) as yellow crystals, m.p. 210-212°.

Anal. Calcd. for $C_{16}H_{13}N_3$: C, 77.7; H, 5.2; N, 17.0. Found: C, 77.5; H, 5.1; N, 16.9.

b) In Alkaline Solution.

To a mixture of 0.648 g. (0.004 mole) of **8** and *o*-amino-benzaldehyde (0.484 g., 0.004 mole) a solution of 0.2 g. of

potassium hydroxide in ethanol (25 ml.) was added and the mixture was refluxed for 15 hours. The obtained solution was concentrated to about half volume; the precipitated solid was collected and crystallised from ethanol to give 0.58 g. (58.7%) of pure **10a**. From the initial mother liquors, concentrated to a small volume, there was obtained 0.055 g. (5.2%) of 3-(*o*-aminobenzyl)-7-methyl-1,8-naphthyridin-4(1*H*)one (**11**). Crystallisation from ethanol afforded analytically pure **11** as white solid, m.p. 271-273°.

Anal. Calcd. for $C_{16}H_{15}N_3O$: C, 72.4; H, 5.6; N, 15.8. Found: C, 72.7; H, 5.8; N, 15.6.

5-Acetyl-3-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**10b**).

This compound was obtained by refluxing **10a** with acetic anhydride under the same conditions used for the preparation of **9b**. The crude product was crystallised from acetic acid to give pure **10b** (85% yield) as white prisms, m.p. 230-232°.

Anal. Calcd. for $C_{18}H_{15}N_3O$: C, 74.7; H, 5.2; N, 14.5. Found: C, 74.4; H, 5.2; N, 14.3.

3-Methylquino[3,2-*c*][1,8]naphthyridine (**7a**).

a) From **9a**.

A mixture of the acid (**9a**) (3.0 g.), copper chromite (0.6 g.) and freshly distilled quinoline (15 ml.) was refluxed for 1.5 hours. The mixture was filtered, the filtrate was evaporated to 6-7 ml. at reduced pressure and the residue was diluted with light petroleum (120-150 ml.). The precipitated red brown solid was collected and crystallised from benzene to give **7a** (2.1 g., 83.1%), m.p. 251-253°

Anal. Calcd. for $C_{16}H_{11}N_3$: C, 78.4; H, 4.5; N, 17.1. Found: C, 78.7; H, 4.7; N, 16.9.

b) From **10a**.

A solution of **10a** (0.6 g.) in 12 ml. of nitrobenzene was refluxed for 15 minutes. After evaporation to a small volume, compound **7a** was obtained by addition of light petroleum to nitrobenzene (0.32 g., 53.7%).

Reaction of *o*-Aminobenzaldehyde with 7-Bromo-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**12**).

a) In Acidic Solution.

Anhydrous hydrochloric acid was bubbled into a chilled suspension of **12** (0.197 g., 0.867 mmole) and *o*-aminobenzaldehyde (0.105 g., 0.868 mmole) in 20 ml. of absolute ethanol. After saturation the solution was concentrated to a small volume. The separated solid was then filtered, treated with dilute ammonia and collected. Crystallisation from ethanol gave pure 3-bromo-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**14a**) (0.16 g. 59.1%) as yellow needles, m.p. 230-231° dec.

Anal. Calcd. for $C_{15}H_{10}BrN_3$: C, 57.7; H, 3.2; N, 13.5. Found: C, 57.9; H, 3.2; N, 13.1.

b) In Alkaline Solution.

To a mixture of **12** (2 g., 0.0088 mole) and *o*-aminobenzaldehyde (1.07 g., 0.0088 mole), a solution of 0.6 g. of potassium hydroxide in ethanol (60 ml.) was added. After 15 hours of refluxing, the solution was concentrated to about half volume and the precipitate collected and crystallised from ethanol. Pure **14a** (1.3 g., 47.3%) was obtained, m.p. 230-231°. The initial mother liquors were concentrated to a small volume and the separated solid was collected and crystallised from ethanol to give 0.62 g. (25.4%) of 3-ethoxy-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**15a**) as yellow crystals, m.p. 161-164°.

Anal. Calcd. for $C_{17}H_{15}N_3O$: C, 73.6; H, 5.4; N, 15.1. Found: C, 74.0; H, 5.6; N, 15.1.

Reaction of *o*-Aminobenzaldehyde with 7-Ethoxy-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**13**).

a) In Acidic Solution.

When a suspension of **13** (0.29 g., 0.0015 mole) and *o*-aminobenzaldehyde (0.19 g., 0.0015 mole) in absolute ethanol (30 ml.) was saturated with anhydrous hydrochloric acid, a solution was obtained from which, by concentration, an orange solid precipitated. Compound **15a** (0.31 g., 74.1%) was obtained by treatment of this solid with diluted ammonia, m.p. 161-164° (see above).

b) In Alkaline Solution.

The compound **13** (0.5 g., 0.0026 mole), *o*-aminobenzaldehyde (0.315 g., 0.0026 mole) and a solution of 0.126 g. of potassium hydroxide in ethanol (10 ml.) were treated as described above for the preparation of **10a** or **14a** in alkaline solution. Compound **15a** was obtained in 34% yield, m.p. 161-164°. By concentration to a small volume of the ethanolic mother liquors of **15a**, 0.2 g. (26%) of 3-(*o*-aminobenzyl)-7-ethoxy-1,8-naphthyridin-4(1*H*)one (**16**) was obtained. Crystallisation from ethanol afforded analytically pure **16** as white crystals, m.p. 269-271°.

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.1; H, 5.8; N, 14.2. Found: C, 68.9; H, 5.8; N, 13.8.

5-Acetyl-3-bromo-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**14b**).

Acetylation of **14a** with acetic anhydride under the same conditions used for the preparation of **9b** and **10b** (see above) gave the acetyl derivative (**14b**) in 64% yield. An analytical sample was obtained by crystallization from acetic acid as white crystals, m.p. 232-235°.

Anal. Calcd. for $C_{17}H_{12}N_3OBr$: C, 57.6; H, 3.4; N, 11.9. Found: C, 58.0; H, 3.6; N, 12.0.

5-Acetyl-3-ethoxy-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**15b**).

This compound was obtained by refluxing **15a** with acetic anhydride under the same conditions used for the preparation of **9b**, **10b** or **14b**. The product was purified by crystallisation from benzene-light petroleum (70% yield), white prisms with m.p. 220-223°.

Anal. Calcd. for $C_{19}H_{17}N_3O_2$: C, 71.5; H, 5.3; N, 13.2. Found: C, 71.2; H, 5.5; N, 13.1.

3-Bromoquino[3,2-*c*][1,8]naphthyridine (**7b**).

A mixture of **14a** (0.5 g.) and nitrobenzene (7 ml.) was refluxed for 3 hours. The filtered solution was diluted with light petroleum (100 ml.). The obtained solid was collected and crystallised from benzene to give 7b (0.3 g., 60.4%), m.p. 300-303° dec.

Anal. Calcd. for $C_{15}H_8BrN_3$: C, 58.1; H, 2.6; N, 13.5. Found: C, 58.4; H, 2.8; N, 13.7.

3-Ethoxy-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**15a**).

This compound was also obtained by treating **14a** with sodium ethoxide. A solution of **14a** (0.2 g., 0.64 mmole) in absolute ethanol (50 ml.) and sodium ethoxide (0.14 g. of sodium, 6.1 mmoles) was heated under reflux for 24 hours. The solution was evaporated to dryness and the residue was diluted with water to give pure **15a** (0.1 g., 56.3%).

3-Ethoxyquino[3,2-*c*][1,8]naphthyridine (**7c**).

A mixture of **15a** (1.2 g.) and nitrobenzene (24 ml.) was refluxed for 15 minutes. The filtered solution was evaporated to a small volume and the residue diluted with light petroleum

(100 ml.). The precipitate was collected and crystallised from benzene-light petroleum 1:1 to yield **15a** (0.8 g., 67.1%) as yellow solid, m.p. 220-222°.

Anal. Calcd. for $C_{17}H_{13}N_3O$: C, 74.2; H, 4.7; N, 15.3. Found: C, 73.9; H, 4.6; N, 15.2.

b) From **7b**.

Compound **7c** was obtained from **7b** in 80% yield by treatment with sodium ethoxide as described above for the preparation of **15a** from **14a**.

3-Hydroxyquino[3,2-*c*][1,8]naphthyridine (**7d**).

A mixture of **7c** (0.5 g.) and 57% hydrogen iodide (5 ml.) was refluxed for 3 hours. After cooling the obtained solid was collected, neutralized with 10% sodium hydroxide solution and washed with water. The crude product was purified by crystallization from DMF to give 0.41 g. of yellow crystals of **7d** (91.3%), m.p. >320°.

Anal. Calcd. for $C_{15}H_9N_3O$: C, 72.9; H, 3.6; N, 17.0. Found: C, 72.5; H, 3.9; N, 16.9.

3-Mercaptoquino[3,2-*c*][1,8]naphthyridine (**7e**).

a) From Hydroxy derivative (**7d**).

A mixture of 0.3 g. (1.21 mmoles) of **7d** and 0.3 g. (1.35 mmoles) of phosphorus pentasulfide in 30 ml. of anhydrous pyridine was refluxed for 2 hours. The resulting warm solution was filtered and diluted with water (200 ml.). The obtained crude product was collected and purified by extraction with boiling carbon disulfide to remove a small quantity of sulfur and crystallised from DMF to give pure **7e** (0.21 g., 65.7%) as red needles, m.p. >310°.

Anal. Calcd. for $C_{15}H_9N_3S$: C, 68.4; H, 3.4; N, 15.9. Found: C, 68.7; H, 3.5; N, 15.9.

b) From Bromo Derivative **7b**.

A sodium hydrosulfide-ethanol solution was prepared by bubbling hydrogen sulfide for 30 minutes through a solution of 0.1 g. (4.35 mmoles) of sodium metal in absolute ethanol (250 ml.). To this solution, 0.22 g. (0.71 mmole) of **7b** was added and the suspension was refluxed for 8 hours. After standing overnight a precipitate was formed that was collected and treated with dilute hydrochloric acid and water. Compound **7e** was obtained (0.12 g., 64.3%).

Quino[3,2-*c*][1,8]naphthyridine (**7f**).

A suspension of **7e** (0.5 g.) and Raney nickel catalyst (3 g.) in ethanol (750 ml.) was refluxed with stirring for 10 hours. The catalyst was separated by filtration and extracted several times with boiling ethanol. The combined extracts and solution were evaporated at reduced pressure to small volume to give **7f**, that was crystallised from benzene (0.14 g., 31.8%), m.p. 234-235°; ir mas (Nujol): 1600, 1460, 1360, 795 and 755 cm^{-1}.

Anal. Calcd. for $C_{15}H_9N_3$: C, 77.9; H, 3.9; N, 18.2. Found: C, 78.1; H, 4.2; N, 18.0.

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