Synthesis of some 3,7-Disubstituted Quino[3,2-*c*][1,8]naphthyridines

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The preparation of some 3,7-disubstituted-5,6-dihydroquino[3,2-*c*][1,8]naphthyridines (**6**) by the condensation of 7-substituted-2,3-dihydro-1,8-naphthyridin-4-(1*H*)ones (**5**) with *o*-aminoacetophenone or *o*-aminobenzophenone is described. All the 5,6-dihydroderivatives **6** were transformed into the fully aromatic compounds **7** by heating with nitrobenzene. Only a few quino[3,2-*c*][1,8]naphthyridines were previously described.

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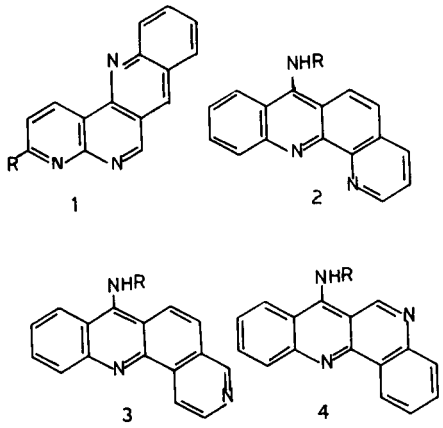
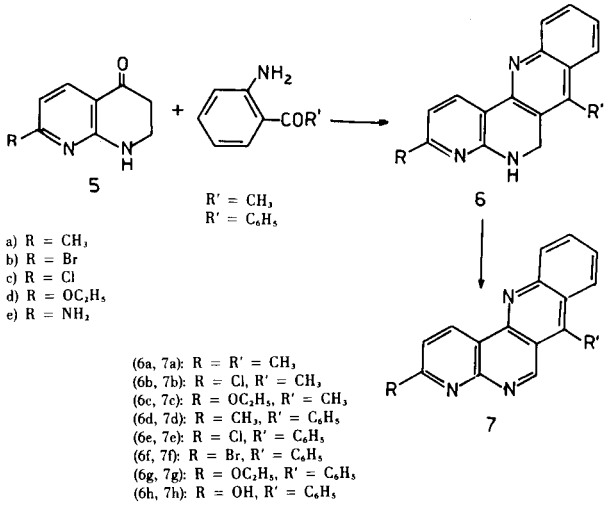
Earlier, we reported the synthesis of some 3-substituted quino[3,2-*c*][1,8]naphthyridines (**1**), a new heterocyclic ring system (1), having a structural resemblance to some compounds **2**, **3**, **4** with good antiamebic activity (2a-c).



Compounds **1** were obtained by the reaction of *o*-aminobenzaldehyde and appropriately substituted ketones **5** (3a-c) in alkaline or acidic medium in yields ranging from 59.1 to 82.9% (1). Only a few of these compounds were described in the previous paper. Therefore, the simple reaction conditions, the favorable yields and the desire to prepare substituted quino[3,2-*c*][1,8]naphthyridines prompted us to investigate the reaction of ketones **5** and other *o*-aminocarbonyl compounds such as *o*-aminoacetophenone and *o*-aminobenzophenone, which are easily available commercially. The reaction conditions were essentially the same as described in previous papers for the reaction of **5a,b,d** with *o*-aminobenzaldehyde (1). Thus, compound **6a** was obtained in 34.1% yield when the ketone **5a** and *o*-aminoacetophenone were heated in alkaline ethanolic solution. When the reaction was carried out with anhydrous hydrogen chloride in absolute ethanol, the yield was 60.5%. Compound **6a**, a yellow crystalline solid (m.p. 209-213°), was converted into the fully aromatic 3,7-dimethylquino[3,2-*c*][1,8]naphthyridine (**7a**) by refluxing in nitrobenzene (yield 84.2%).

The structure of these compounds (**6a** and **7a**) were assigned based on analytical data and spectral evidence. The nmr spectrum in trifluoroacetic acid (25°) of **6a** shows two singlets at δ 2.78 and at δ 3.03 (three protons each) due to methyl groups, a singlet at δ 5.48 (two protons) assigned



to the CH_2 in the 6 position and two proton signals at δ 9.08 and δ 7.18 due to H_1 and H_2, respectively (J = 8.25 Hz). The absorption range for the phenyl protons is δ 8.0-8.75. The nmr spectrum of **7a** (deuteriochloroform, 25°) shows two singlets at δ 2.85 and at δ 3.13 (three protons each) due to methyl groups, a singlet at δ 9.75 assigned to H_6 and two proton signals at δ 9.28 and δ 7.38 due to H_1 and H_2, respectively (J = 8.25 Hz). The absorption range for the phenyl protons is δ 7.55 to δ 8.25.

The reaction of the ketones **5b,d,e** previously described (3b,c) with *o*-aminoacetophenone in ethanolic alkaline solution failed; the starting materials were recovered unchanged in the case of **5d** and **5e**. The ketone **5b** was only transformed into **5d**. Some attempts to condense the ketones **5d** and **5e** with anhydrous hydrogen chloride in ethanolic solution were also unsuccessful. Under the same conditions, compound **5b** was converted into 3-chloro-7-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6b**) in 28.6% yield.

The substitution of the bromine atom in the 3 position

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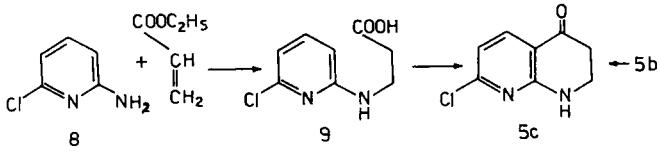
with the chlorine is not unusual, because similar substitutions are already described (4a,b) for several bromopyridines. The structure of **6b** was proved by analytical and nmr spectral data (see Experimental and Table II) and chemical evidence. In fact, when the 7-chloro-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one (**5c**), obtained as described below, was allowed to react at room temperature with *o*-aminoacetophenone and anhydrous hydrogen chloride in ethanolic solution, 3-chloro-7-methyl-5,6-dihydroquino-[3,2-*c*][1,8]naphthyridine (**6b**) was obtained in poor yield (13.0%). Compound **6b**, a yellow crystalline solid (m.p. 243-244°) was converted into the fully aromatic 3-chloro-7-methyl derivative (**7b**) by refluxing in nitrobenzene (yield 81.5%) (nmr see Table II).

The route employed to obtain the ketone **5c** was essentially the same as described by us for the preparation of ketones **5a,b,e** (3). The starting 2-amino-6-chloropyridine was obtained in a different way from that previously described in literature (5), by the reaction of 3-hydroxyglutaronitrile with anhydrous hydrogen chloride. Compound **8** gives in 44.2% yield, 3-(6-chloro-2-pyridilimino)-propionic acid (**9**), by heating with ethyl acrylate and



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alkaline hydrolysis. As in the similar preparation, the isomeric amide was not isolated (3b). When compound **9** was heated at 120° with polyphosphoric acid, 7-chloro-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one (**5c**) was obtained in 34.6% yield. Its structure was assigned based on analytical and spectral data. Its nmr spectrum (DMSO-d_6) shows two triplets at δ 2.63 and at δ 3.53 assigned to the two protons H_3 and to the two protons H_2, respectively, and a broad signal at δ 7.8 due to NH, that disappears after treatment with deuterium oxide. Two proton signals at δ 8.03 and at δ 6.8 are due to H_5 and H_6, respectively (J = 8.25 Hz).

The ketone **5c** was also obtained in 73.1% yield by treatment of the bromoketone **5b** (3b) with anhydrous hydrogen chloride in benzene solution.

An attempt to obtain the 3-bromo-7-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine by condensation of 7-bromo-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one (**5b**) (3b) and *o*-aminoacetophenone with hydrobromic acid was unsuccessful. Compound **6b** was converted into the 7-ethoxy derivative **6c** by reaction in autoclave with sodium ethoxide at 120° for 18 hours in 84.6% yield. The fully aromatic product **7c** was prepared from **6c** by reflux in nitrobenzene (89.0% yield).

Better results were obtained in the reaction of the ketones **5a-d** and *o*-aminobenzophenone in acidic medium. Only the ketone **5e** does not give definite products and some starting material was recovered unchanged.

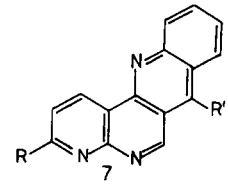
When an ethanolic solution of ketones **5a,c,d** was allowed to react at room temperature for 24 hours with *o*-aminobenzophenone and anhydrous hydrogen chloride the three 3-substituted-7-phenyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridines (**6d,e,g**) were obtained in 88.0%, 48.7% and 36.4% yields, respectively.

Elemental analyses (see Experimental) and nmr spectra of **6d,e,g** are all consistent with the assigned structures (see Table II).

When an ethanolic solution of the ketone **5b** and *o*-aminobenzophenone, saturated with anhydrous hydrogen chloride, was allowed to react at room temperature, the substitution of the bromine atom with

Table I

3,7-Disubstituted Quino[3,2-*c*][1,8]naphthyridines



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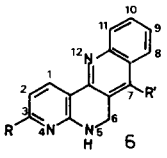
Compound No.	R	R'	Reaction Time	Yield %	Crystallization Solvent	M.p. °C	Empirical Formula	Elemental Analyses Calcd. % C	H	N	Found % C	H	N
7a	CH_3	CH_3	20 minutes	84.2	benzene-petroleum ether	189-193 dec.	$C_{17}H_{13}N_3$	78.7	5.0	16.2	78.4	5.1	15.9
7b	Cl	CH_3	1 hour	81.5	DMFA	244-247	$C_{16}H_{10}ClN_3$	68.7	3.6	15.0	69.0	3.8	14.8
7c	OC_2H_5	CH_3	15 minutes	89.0	benzene	198-202	$C_{18}H_{15}N_3O$	74.7	5.2	14.5	75.0	5.3	14.3
7d	CH_3	C_6H_5	40 minutes	84.8	DMFA	254-256	$C_{22}H_{15}N_3$	82.2	4.7	13.0	82.1	4.7	13.0
7e	Cl	C_6H_5	2 hours	86.1	DMFA	290-291	$C_{21}H_{12}ClN_3$	73.8	3.5	12.3	73.9	3.7	12.4
7f	Br	C_6H_5	2.5 hours	82.1	DMFA	300-302	$C_{21}H_{12}BrN_3$	65.3	3.1	10.9	65.4	3.1	10.8
7g	OC_2H_5	C_6H_5	1 hour	84.5	DMFA	175-177	$C_{23}H_{17}N_3O$	78.6	4.9	11.9	78.4	4.8	11.8
7h	OH	C_6H_5	1 hour	83.4	DMFA	>320	$C_{21}H_{13}N_3O$	78.0	4.0	13.0	77.8	4.1	13.2

Table II

Nmr Spectral Data of Some 3,7-Disubstituted-5,6-dihydroquino[3,2-*c*][1,8]naphthyridines (**6**) and Fully Aromatic Derivatives (**7**) (observed chemical shift, temperature 25°)



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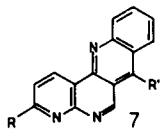

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Compound No.	R	R'	H_1	H_2	3-CH_3	O-CH_2-CH_3 -CH_2	-CH_3	H_6	7-CH_3	Phenyl Protons	$J_{1,2}$ (Hz)	Solvent
6b	Cl	CH_3	9.15 (d)	7.3 (d)	—	—	—	5.53 (s)	3.0 (s)	8.1-8.7 (m)	8.25	trifluoroacetic acid
6d	CH_3	C_6H_5	9.2 (d)	7.2 (d)	2.8 (s)	—	—	5.12 (s)	—	7.35-8.6 (m)	8.25	trifluoroacetic acid
6e	Cl	C_6H_5	9.25 (d)	7.35 (d)	—	—	—	5.15 (s)	—	7.43-8.58 (m)	8.25	trifluoroacetic acid
6g	OC_2H_5	C_6H_5	9.2 (d)	6.8 (d)	—	4.7 (q)	1.7 (t)	5.07 (s)	—	7.32-8.50 (m)	9.0	trifluoroacetic acid
7b	Cl	CH_3	9.55 (d)	7.7 (d)	—	—	—	10.25 (s)	3.25 (s)	7.61-8.53 (m)	8.25	deuteriochloroform
7d	CH_3	C_6H_5	10.55 (d)	(a)	3.42 (s)	—	—	10.0 (s)	—	7.75-9.1 (m)	8.25	trifluoroacetic acid
7e	Cl	C_6H_5	10.1 (d)	(a)	—	—	—	10.38 (s)	—	7.75-9.2 (m)	8.25	trifluoroacetic acid
7g	OC_2H_5	C_6H_5	9.8 (d)	(a)	—	4.9 (q)	1.67 (t)	10.1 (s)	—	7.7-9.1 (m)	9.0	trifluoroacetic acid

(a) Included among phenyl protons.

Table III

Ultraviolet Absorption Spectra of 3,7-Disubstituted Quino[3,2-*c*][1,8]naphthyridines (**7**)

Compound No.	λ max mμ	log ε	λ max mμ	log ε	λ max mμ	log ε	λ max mμ	log ε	λ max mμ	log ε
7a	212	4,420	253	4,460	266	4,452	291	4,367 (a)	300	4,450
7b	212	4,489	255	4,529 (a)	264	4,536	294	4,339 (a)	304	4,435
7c	210	4,380	262	4,752	271	4,639	294	4,472 (a)	304	4,620
7d	213	4,580	256	4,498 (a)	272	4,512	293	4,464 (a)	301	4,517
7e	212	4,548	259	4,555 (a)	266	4,577	296	4,401 (a)	304	4,473
7f	211	4,575	260	4,607 (a)	267	4,619	296	4,471 (a)	305	4,584
7g	210	4,551	264	4,771	271	4,687 (a)	295	4,510	306	4,632
7h	211	4,506	267	4,962	312	4,313 (a)	321	4,433		

(a) Inflection.

chlorine takes place and the compound **6e** was again obtained in 65.7% yield. The same product **6e** was also prepared, in 61.1% yield, by treating with anhydrous hydrogen chloride the 3-bromo derivative **6f**, synthesized from **5b** and *o*-aminobenzophenone by condensation with anhydrous hydrogen bromide in ethanolic solution (37.9% yield).

Compound **6f** was converted into the 3-ethoxy-7-phenyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6g**) by refluxing with sodium ethoxide in absolute ethyl alcohol (91.5% yield). The 3-hydroxy derivative **6h** was prepared from **6g** by hydrolysis with 57% hydrogen iodide (95.0% yield).

The solutions of **6**, even when very diluted, exhibit a green fluorescence in Wood's light, which disappears in the fully aromatic compounds **7**, easily obtained from **6** by heating with nitrobenzene. The uv spectra in ethanol of compounds **7** are reported in Table III. It was impossible to record the uv spectra of **6**, because of their easy aromatization to **7**.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. Ir spectra in nujol mulls were recorded on a Perkin-Elmer Model 197 spectrophotometer and were consistent with the assigned structure in all cases. Uv spectra in ethanol were measured with a Perkin-Elmer Model 575 spectrophotometer. ^1H nmr spectra were obtained with a JEOL Model C 60 HL spectrometer for solutions indicated in Table II and an internal TMS standard.

3-(6-Chloro-2-pyridylimino)propionic acid (**9**).

A mixture of 8.0 g. of 2-amino-6-chloropyridine (0.062 mole), 11.7 ml. of ethyl acrylate (0.108 mole) and 2.7 ml. of glacial acetic acid was heated at 120° for 72 hours. After cooling, 30 ml. of a 6N aqueous sodium hydroxide solution were added and the mixture refluxed for 60 minutes. The solution was cooled to room temperature and extracted three times with diethyl ether. The combined extracts were dried over anhydrous magnesium sulfate and evaporated to dryness; the starting 2-amino-6-chloropyridine (0.54 g.) was recovered. The aqueous solution was acidified with hydrochloric acid (*p*H 4-5) and the precipitate was collected, washed with water and crystallized from benzene to give 5.15 g. of pure **9** (44.2% yield), m.p. 105-108°.

Anal. Calcd. for $C_8H_9ClN_2O_2$: C, 47.9; H, 4.5; N, 13.9. Found: C, 48.1; H, 4.4; N, 13.6.

7-Chloro-2,3-dihydro-1,8-naphthyridin-4(1*H*)one (**5c**).

A) From **9**.

A mixture of **9** (2.0 g.) and 30 g. of polyphosphoric acid was heated at 120° for 30 minutes. After cooling the mixture was poured into crushed ice and made basic (*p*H 9) with cold concentrated ammonium hydroxide.

The solid was collected by filtration, washed with water and crystallized from ethanol to give 0.63 g. of **5c** (34.6% yield) m.p. 177-179°.

Anal. Calcd. for $C_8H_7ClN_2O$: C, 52.6; H, 3.8; N, 15.3; Cl, 19.4. Found: C, 52.8; H, 3.9; N, 15.0; Cl, 19.2.

B) From **5b**.

A cooled and stirred solution of 1.0 g. of **5b** in dry benzene (100 ml.) was saturated with anhydrous hydrochloric acid. After standing at room temperature for 24 hours, the solution was concentrated at reduced pressure to a small volume. The yellow precipitate was collected, treated with dilute sodium hydroxide solution and collected again to give 0.59 g. (73.1%) of **5c**.

3,7-Dimethyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6a**).

A) In Acidic Solution.

Anhydrous hydrochloric acid was bubbled into a chilled solution of **5a** (1.6 g., 9.9 mmoles) and *o*-aminoacetophenone (1.45 ml., 12 mmoles) in 100 ml. of absolute ethanol. After saturation and standing at room temperature for 24 hours, an orange solid was formed which was filtered off, treated with dilute aqueous sodium hydroxide solution, collected again and washed with water. Crystallization from ethanol gave pure **6a** (1.13 g.) as yellow crystals, m.p. 209-213°. From the initial ethanolic mother liquors, concentrated at reduced pressure to a small volume, some other **6a** (0.43 g.) was obtained by alkalinization (total yield 60.5%).

Anal. Calcd. for $C_{17}H_{13}N_3$: C, 78.1; H, 5.8; N, 16.1. Found: C, 78.5; H, 5.9; N, 16.2.

B) In Alkaline Solution.

To a solution of 3.0 g. (18.5 mmoles) of 7-methyl-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one (**5a**) and *o*-aminoacetophenone (2.3 ml., 19.0 mmoles) in hot ethanol (60 ml.), a solution of 0.75 g. of sodium hydroxide in water (3 ml.) was added. After 20 hours of refluxing, the solution was concentrated to about half volume and the precipitate collected and crystallized from ethanol. Pure **6a** was obtained (1.65 g., 34.1%).

3-Chloro-7-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6b**).

A) From **5c**.

An ice cooled solution of 0.35 g. (1.92 mmoles) of 7-chloro-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one (**5c**) and 0.28 ml. (2.31 mmoles) of *o*-aminoacetophenone in 80 ml. of dry ethanol was saturated with anhydrous hydrochloric acid. After standing at room temperature 24 hours, the solution was evaporated to dryness at reduced pressure, the red residue treated with 10% sodium hydroxide solution and extracted several times with chloroform. The combined extracts were dried over anhydrous magnesium sulfate and evaporated to dryness. A yellow precipitate formed which was collected and crystallized from DMFA to give 0.07 g. (13.0% yield) of pure **6b**, m.p. 243-244°.

Anal. Calcd. for $C_{16}H_{12}ClN_3$: C, 68.2; H, 4.3; N, 14.9; Cl, 12.6. Found: C, 68.6; H, 4.3; N, 15.1; Cl, 12.4.

B) From **5b**.

Anhydrous hydrochloric acid was bubbled to saturation into a chilled solution of **5b** (0.58 g., 2.5 mmoles) and *o*-aminoacetophenone (0.37 ml., 3.06 mmoles) in 50 ml. of dry ethanol. After standing at room temperature 24 hours, the solution was treated as described in method A. Compound **6b** was obtained pure by crystallization from DMFA (0.2 g., 28%).

3-Ethoxy-7-methyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6c**).

To a suspension of 0.2 g. (0.7 mmoles) of **6b** in absolute ethanol (60 ml.), 0.16 g. (6.9 mmoles) of sodium metal dissolved in 20 ml. of the same solvent was added and the mixture was heated in autoclave at 120° for 18 hours. The ethanol was evaporated and water was added. A precipitate formed which was collected and crystallized from ethanol to give 0.18 g. (84.6%) of pure **6c** as yellow brown crystals, m.p. 198-201°.

Anal. Calcd. for $C_{18}H_{17}N_3O$: C, 74.2; H, 5.8; N, 14.4. Found: C, 73.9; H, 5.5; N, 14.5.

3-Methyl-7-phenyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6d**).

An ice cooled solution of 2.5 g. (15.4 mmoles) of **5a** and 3.04 g. (15.4 mmoles) of *o*-aminobenzophenone in 150 ml. of dry ethanol was saturated with anhydrous hydrochloric acid. After standing at room temperature 24 hours an orange solid was formed which was collected and treated with 10% aqueous sodium hydroxide solution. The solid was filtered off and crystallized from ethanol to give 3.58 g. of **6d** as yellow crystals, m.p. 263-265°.

Anal. Calcd. for $C_{22}H_{17}N_3$: C, 81.7; H, 5.3; N, 13.0. Found: C, 81.7; H, 5.2; N, 12.7.

The initial ethanolic mother liquors were concentrated to a small volume at reduced pressure and the separated orange solid was collected, alkalinized with diluted sodium hydroxide solution, collected again and crystallized from DMFA. There was obtained another 0.8 g. of **6a** (total yield 88.0%).

3-Chloro-7-phenyl-2,3-dihydroquino[3,2-*c*][1,8]naphthyridine (**6e**).

A) From **5c**.

A solution of 0.23 g. (1.26 mmoles) of **5c** and 0.3 g. (1.5 mmoles) of *o*-aminobenzophenone in 60 ml. of absolute ethanol was saturated with anhydrous hydrochloric acid. Compound **6e** was obtained operating as described for the preparation of **6d** (total yield 48.7%). The melting point of analytical sample, yellow crystals from DMFA, is 264-265°.

Anal. Calcd. for $C_{21}H_{14}ClN_3$: C, 73.4; H, 4.1; N, 12.2; Cl, 10.3. Found: C, 73.2; H, 4.1; N, 12.2; Cl, 10.0.

B) From **5b**.

A solution of 0.58 g. (2.5 mmoles) of **5b** and 0.61 g. (3.1 mmoles) of *o*-aminobenzophenone in 60 ml. of dry ethanol was saturated with anhydrous hydrochloric acid. Operating as described for the preparation of **6d**, compound **6e** was obtained in 65.7% yield.

C) From **6f**.

The 3-bromo derivative (**6f**) was transformed into the 3-chloro derivative (**6e**) by treatment of its absolute ethanolic solution with anhydrous hydrochloric acid as described in A) (61.1% yield).

3-Bromo-7-phenyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6f**).

A solution of 1.06 g. (4.67 mmoles) of 7-bromo-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one (**5b**) and 1.216 g. (6.1 mmoles) of *o*-aminobenzophenone in 90 ml. of absolute ethanol was saturated with anhydrous hydrogen bromide. Operating as described for the preparation of **6d** there was obtained crude **6f**, that was purified by crystallization from DMFA; yellow crystals, m.p. 274-276° (0.69 g., 37.9%).

Anal. Calcd. for $C_{21}H_{14}BrN_3$: C, 64.9; H, 3.6; N, 10.8. Found: C, 65.2; H, 3.7; N, 10.7.

3-Ethoxy-7-phenyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6g**).

A) From **5d**.

From 0.5 g. (2.6 mmoles) of 7-ethoxy-2,3-dihydro-1,8-naphthyridin-4-(1*H*)one and 0.62 g. (3.15 mmoles) of *o*-aminobenzophenone in absolute ethanol (60 ml.), operating as described for **6d**, there was obtained crude **6g**. This product was extracted with hot ethanol (50 ml.) and the insoluble residue was crystallized from DMFA, to give 0.33 g. (36.0% yield) of pure **6g**, as yellow crystals, m.p. 222-225°.

Anal. Calcd. for $C_{23}H_{19}N_3O$: C, 78.2; H, 5.4; N, 11.9. Found: C, 78.2; H, 5.3; N, 11.9.

B) From **6f**.

To a suspension of 0.2 g. (0.51 mmoles) of **6f** in 120 ml. of absolute ethanol, 0.15 g. of sodium metal dissolved in 10 ml. of the same solvent was added and the mixture was refluxed for 28 hours. Starting material (0.08 g. of **6f**) was collected by filtration; the solution was evaporated and water was added. The solid was collected and crystallized from DMFA to

give pure **6g** (0.1 g., 91.5%).

3-Hydroxy-7-phenyl-5,6-dihydroquino[3,2-*c*][1,8]naphthyridine (**6h**).

A mixture of **6g** (0.49 g.) and 57% hydrogen iodide (6 ml.) was refluxed for 4.5 hours. After cooling the obtained red solid was collected, neutralized with 10% sodium hydroxide solution and washed with water. The crude product was purified by crystallization from DMFA to give 0.43 g. of yellow crystals of **6h** (95.0%), m.p. > 320°.

Anal. Calcd. for $C_{21}H_{15}N_3O$: C, 77.5; H, 4.6; N, 12.9. Found: C, 77.8; H, 4.5; N, 12.7.

General Procedure for the Preparation of 3-Substituted-7-methyl- (**7a-c**) and 7-phenylquino[3,2-*c*][1,8]naphthyridines (**7d-h**).

A mixture of 0.3 g. of **6a-h** and 4 ml. of nitrobenzene was refluxed for different time (see Table I) and, after cooling, the solution was diluted with light-petroleum (~80 ml.). The solid thus obtained was collected and crystallized. Yields, crystallization solvents, melting points, analytical data and reaction times for compounds **7a-h** are given in Table I.

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