Studies on Quinoline Derivatives and Related Compounds. VI. A Novel Displacement Reaction of 1-Ethylquinolinium Iodides with Nucleophiles (1)

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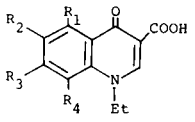
The reaction of 4-amino- (**3a**) and 4-anilino-3-carbethoxy-1-ethyl-6,7-methylenedioxyquinolinium iodide (**3b**) with nucleophilic reagents produced 7-substituted 4-amino-3-carboxy-1-ethyl-6-hydroxyquinolinium betaines (**5b-d**) and 7-substituted 1-ethyl-1,4-dihydro-6-hydroxy-4-phenylimino-3-quinolinecarboxylic acid (**6b-d**), respectively, which led to 7-substituted 1-ethyl-1,4-dihydro-6-hydroxy-4-oxo-3-quinolinecarboxylic acids (**1b-d**) by alkaline hydrolysis. With a variety of 1-ethyl-1,4-dihydroquinoline carboxylates (**16a-e**) these novel displacement reactions were attempted.

J. Heterocyclic Chem., **16**, 1353 (1979).

Many investigations on the displacement reaction of quinoline derivatives with nucleophiles have been limited to those occurring on the pyridine moiety of the quinoline skeleton, except the reaction of 7-halogenoquinolines with nucleophiles (2).

In the course of a study on 1-alkyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid (3), we found that treatment of 4-amino-3-carbethoxy-1-ethyl-6,7-methylenedioxyquinolinium iodide (**3a**) (4) with methanolic potassium hydroxide results in 4-amino-3-carbethoxy-6-hydroxy-7-methoxyquinolinium betaine (**5b**). We have become interested in this novel displacement reaction, because 1-ethyl-1,4-dihydro-6-hydroxy-7-methoxy-4-oxo-3-quinolinecarboxylic acid (**1b**) (5), which might readily be derived from **5b**, has been known as one of the metabolites of oxolinic acid (**1a**) (6). This paper describes the reaction of 1-ethylquinolinium iodides with alcoholic or thioethanolic potassium hydroxide, and discusses the mechanism of the reaction.



1a-1

a: R_1=R_4=H, R_2=R_3=OCH_2O
b: R_1=R_4=H, R_2=OH, R_3=OMe
c: R_1=R_4=H, R_2=OH, R_3=OEt
d: R_1=R_4=H, R_2=OH, R_3=SEt
e: R_1=R_4=H, R_2=OMe, R_3=OH
f: R_1=R_4=H, R_2=R_3=OMe
g: R_1=R_3=H, R_2=R_4=OMe
h: R_1=R_3=OMe, R_2=R_4=H
i: R_1=R_2=R_4=H, R_3=Cl
j: R_1=R_2=R_4=H, R_3=SMe
k: R_1=R_4=H, R_2=OMe, R_3=OEt
l: R_1=R_4=H, R_2=OMe, R_3=SEt

When compound **3a** was refluxed in methanolic potassium hydroxide for 50 hours, there was obtained a mixture of a phenolic compound **5b** and 1-ethyl-1,4-dihydro-6,7-methylenedioxy-4-oxo-3-quinoline carboxylic acid (**1a**), which was separated into the respective pure forms, **5b**, m.p. 319-320° dec and **1a**, m.p. 315-316° dec in 70 and 4% yields, respectively, on the basis of differing solubility in dimethylformamide. The nuclear magentic resonance spectrum of **5b** indicates the absence of OCH_2O and OEt, the presence of OMe, NEt, and three aromatic protons. In order to determine the structure of **5b**, compound **5b** was converted to the corresponding 4-oxo-3-quinolinecarboxylic acid (**1b**). On the other hand, 1-ethyl-1,4-dihydro-7-hydroxy-6-methoxy-4-oxo-3-quinolinecarboxylic acid (**1e**) (7) was synthesized in a four step sequence starting with 3-benzyloxy-4-

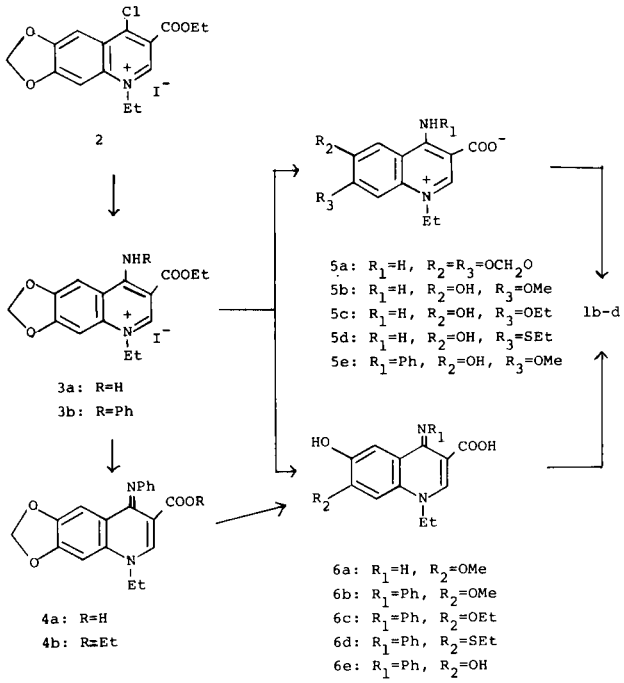


Chart 1

0022-152X/79/071353-08$02.25

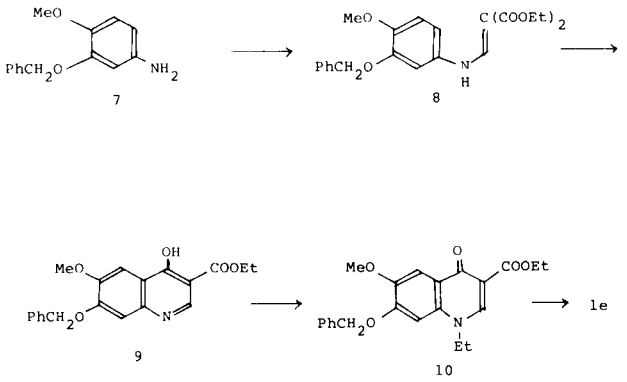


Chart 2

methoxyaniline (7) (8), as shown in Chart 2. Condensation of 7 with diethyl ethoxymethylenemalonate gave diethyl 3-benzyloxy-4-methoxyailinomethylenemalonate (**8**) in 88% yield, which led to ethyl 7-benzyloxy-4-hydroxy-6-methoxy-3-quinolinecarboxylate (**9**) in 89% yield by thermal cyclization with Dowtherm A. Ethylation of **9** with ethyl iodide and potassium carbonate in dimethylformamide afforded ethyl 7-benzyloxy-1-ethyl-1,4-dihydro-6-methoxy-4-oxo-3-quinolinecarboxylate (**10**) in 69% yield. The compound **10** thus obtained was converted into **1e** by refluxing in concentrated hydrochloric acid.

The samples of **1b** and **1e** were not identical with each other. Thus the structures of **1b** and **5b** were unambigously decided. Then the ultraviolet spectrum of **5b** was taken in order to determine whether the structure exists in the betaine form or in the imino form. As Figure 1 shows, the similarity between the ultraviolet spectra of **5b** and of 4-amino-3-carboxy-1-ethyl-6,7-methylendioxyquinolinium betaine (**5a**) (4) rather than **1b** suggests that compound **5b** may exist in the betaine form rather than in the tautomeric imino form (**6a**).

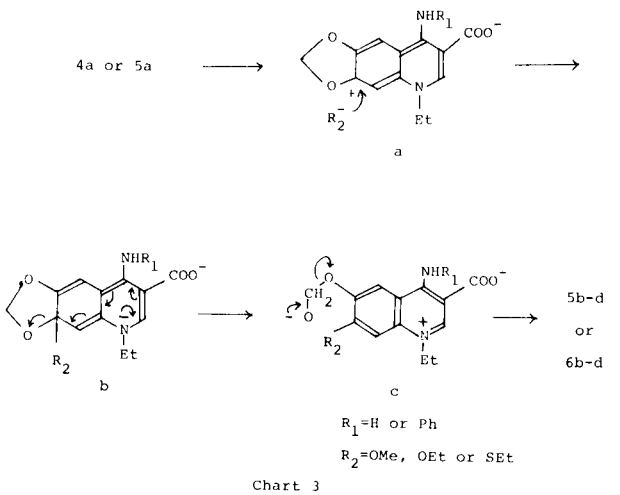


Chart 3

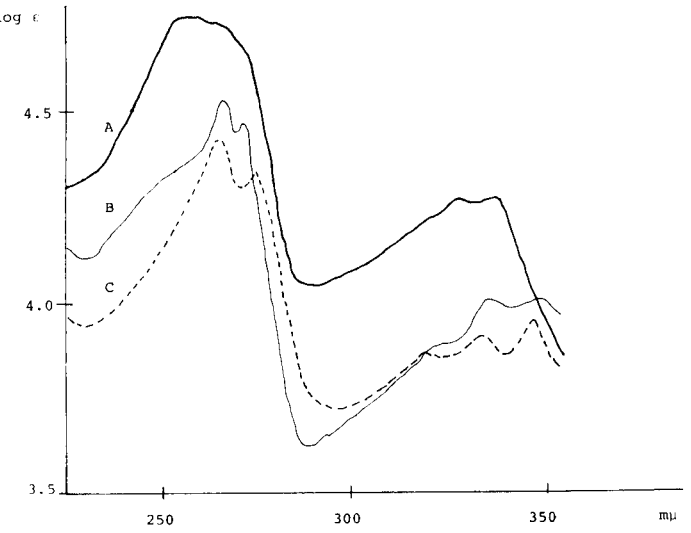


Figure 1. Uv spectra in methanol of compounds, (1b)(A); (5b)(B); (5a)(C).

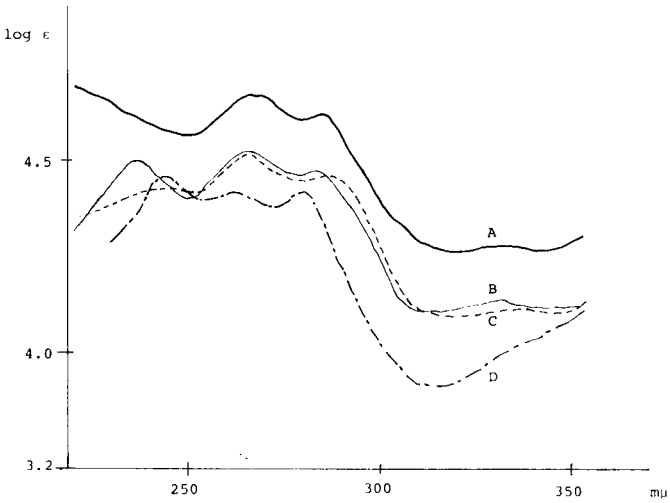


Figure 2. Uv spectra in methanol of compounds, (3b)(A); (4a)(B); (4b)(C); (6b)(D).

Compound **3a**, likewise, reacted with ethanolic or thioethanolic potassium hydroxide to give the corresponding 4-amino-3-carboxy-7-ethoxy-1-ethyl- (**5c**) and 4-amino-3-carboxy-1-ethyl-7-ethylmercapto-6-hydroxyquinolinium betaine (**5b**) in 95 and 20% yields, respectively, which led to 7-ethoxy-1-ethyl- (**1c**) and 1-ethyl-7-ethylmercapto-1,4-dihydro-6-hydroxy-4-oxo-3-quinolinecarboxylic aid (**1d**) by alkaline hydrolysis, respectively. The position of the ethoxy and ethylmercapto groups in **5c** and **5d** was assigned by analogy. Reaction of **3a** with ethanolic potassium hydroxide at room temperature afforded **5a** in 58% yield, which was converted to a phenolic compound **5c** by treatment with potassium hydroxide in refluxing ethanol.

Furthermore, the reactions of 4-anilino-3-carbethoxy-1-ethyl-6,7-methylenedioxyquinolinium iodide (**3b**), obtained from 3-carbethoxy-4-chloro-1-ethyl-6,7-methylene dioxyquinolinium iodide (**2**) (9) and aniline, with alcoholic or thioethanolic potassium hydroxide were carried out to afford 7-substituted compounds **6b-d** in 53, 87 and 78% yields, respectively. The structural assignments for **6b-d** are based on elemental analysis, nuclear magnetic resonance and ultraviolet spectra and their conversion to the corresponding 4-oxo-3-quinolinecarboxylic acid (**1b-d**). The ultraviolet spectrum of 1-ethyl-1,4-dihydro-6-hydroxy-7-methoxy-4-phenylimino-3-quinolinecarboxylic acid (**6b**) closely resembles that of ethyl 1-ethyl-1,4-dihydro-6,7-methylenedioxy-4-phenylimino-3-quinolinecarboxylate (**4b**), whereas **3b** does not exhibit the maximum absorption in the region between 220 and 250 nm. This fact indicates that the imino form **6b** may predominate over the tautomeric betaine form **5e**, as shown in Figure 2.

With the object of the formation of the C-N bond at the C-7 position, the reactions of **3b** with piperidine under several conditions were attempted. Refluxing in piperidine gave only **4b** in 31% yield, together with intractable tar. Heating **3b** in piperidine and potassium hydroxide gave **4a** in 42% yield, the structure of which was assigned 1-ethyl-1,4-dihydro-6,7-methylenedioxy-4-phenylimino-3-quinolinecarboxylic acid on the basis of the nuclear magnetic resonance and ultraviolet spectra, as shown in Figure 2. Treatment of **4b** with piperidine in the presence of sodium hydride afforded **4a** and 1-ethyl-1,4-dihydro-6,7-dihydroxy-4-phenylimino-3-quinolinecarboxylic acid (**6e**), which was resistant to aklaline hydrolysis, in 26 and 43% yields, respectively. Compound **4a** was identical with a sample described above, and the structure of **6e** was determined on the basis of elementary analysis and nuclear resonance spectrum showing the absence of methylenedioxy protons.

In order to determine the mechanistic pathway of the reaction of **3b** with nucleophiles, the reaction of **3b** with ethanolic potassium hydroxide under several conditions was attempted. The reaction of **3b** with one equivalent of potassium hydroxide at room temperature afforded **4b** in 90% yield and the use of three equivalents of potassium hydroxide gave **4b** and **4a** in 66 and 17% yields, respectively.

In agreement with the aforementioned observation with **5a**, treatment of **4a** with ethanolic potassium hydroxide yielded 7-ethoxy-1-ethyl-1,4-dihydro-6-hydroxy-4-phenylimino-3-quinolinecarboxylic acid (**6c**) in almost quantitative yield. In this reaction, the silver mirror test of the reaction solution gave a positive result, implying the formation of formaldehyde. From these observations, it appears that **4a** is an intermediate in the formation of **6b-d** from **3b**.

Mechanistically this reaction may be rationalized as shown in Chart 3. The ion **a** would be formed by an electronic shift caused by the formal positive charge on the nitrogen atom in **5a** and by protonation of the imino group in **4a**. In the key intermediate **a**, a nucleophilic attack at the C-7 position and subsequent aromatization would cause the cleavage of 1,3-dioxolo ring, thus forming the ion **c**. Elimination of formaldehyde from the ion **c** would give the 7-substituted compounds **5b-d** or **6b-d**.

As an extension of this reaction, the reaction of a variety of ethyl 1-ethyl-1,4-dihydro-4-phenylimino-3-quinolinecarboxylates (**16a-e**) with ethanolic potassium hydroxide was attempted. Compounds **16a-e** as starting materials were prepared from 4-chloro-1-ethylquinolinium iodides (**14a-e**) by the method described above, as shown in Chart 4. Namely, treatment of **14a-e** with aniline in ethanol afforded 4-anilino-3-carbethoxy-1-ethylquinolinium iodides (**15a-e**), which were converted to **16a-e** by treatment with ethanolic potassium hydroxide at room temperature. Compounds **14a-c** were prepared from anilines (**11a-c**) *via* three steps including *N*-ethylation, condensation with diethyl ethoxymethylenemalonate and cyclization with phosphorus oxychloride by the method reported in a previous paper (9). 3-Carbethoxy-4,7-dichloro-1-ethylquinolinium idoide (**14d**) and 3-carbethoxy-4-chloro-1-ethyl-7-methylmercaptoquinolinium iodide (**14e**) were also prepared by the known method (9) which involves treat-

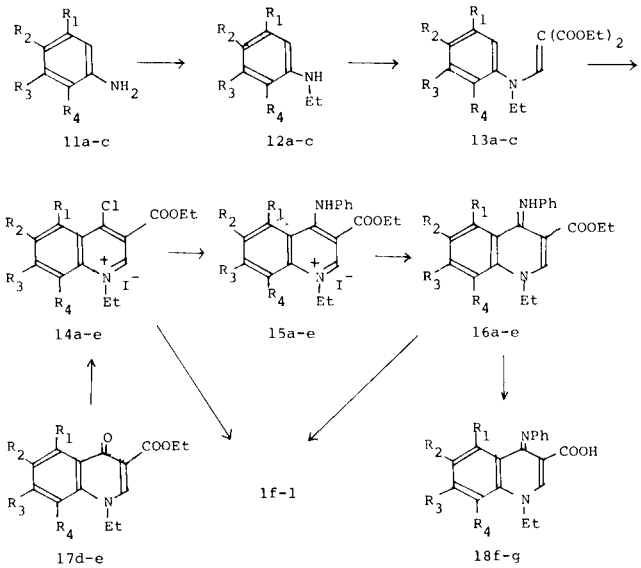


Chart 4

ment of ethyl 1-ethyl-1,4-dihydro-6,7-methylenedioxy-4-oxo-3-quinolinecarboxylate with phosphorus oxychloride to give the corresponding 4-chloroquinolinium halide.

The reaction of **16a** with ethanolic potassium hydroxide gave 7-ethoxy-1-ethyl-1,4-dihydro-6-methoxy-4-phenylimino-3-quinolinecarboxylic acid (**18f**), 7-ethoxy-1-ethyl-1,4-dihydro-6-methoxy-4-oxo-3-quinolinecarboxylic acid (**1l**) and 1-ethyl-6,7-dimethoxy-4-oxo-3-quinolinecarboxylic acid (**1f**) in 6, 17 and 11% yields, respectively. The reaction of **16a** with thioethanolic potassium hydroxide afforded 1-ethyl-7-ethylmercapto-1,4-dihydro-6-methoxy-4-phenylimino-3-quinolinecarboxylic acid (**18g**) in 16% yield, with the recovery of starting material. The positions of the ethoxy and ethylmercapto groups in **18f** and **1k** were assigned by analogy, since the product of the reaction of **3a** with methanolic potassium hydroxide has been

Table I

Nmr Data for 1-Ethyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic Acids

Compound No.	CH_3	CH_2	H_2	H_5	H_6	H_7	H_8
1a	1.78 (t, J = 7)	4.83 (q, J = 7) 6.42 (s)	9.22 (s)	7.95 (s)			7.55 (s)
1b	1.83 (t, J = 7) 4.32 (s)	4.58 (q, J = 7)	8.92 (s)	8.12 (s)			7.53 (s)
1c	1.67 (t, J = 7) 1.78 (t, J = 7)	4.53 (q, J = 7) 4.87 (q, J = 7)	9.20 (s)	8.10 (s)			7.48 (s)
1d	1.57 (t, J = 7) 1.83 (t, J = 7)	3.25 (q, J = 7) 4.92 (q, J = 7)	9.23 (s)	8.03 (s)			7.92 (s)
1e	1.82 (t, J = 7) 4.30 (s)	4.89 (q, J = 7)	9.18 (s)	8.05 (s)			7.73 (s)
1f	1.83 (t, J = 7) 4.27 (s) 4.32 (s)	4.95 (q, J = 7)	9.33 (s)	8.08 (s)			7.57 (s)
1g	1.73 (t, J = 7) 4.13 (s) 4.23 (s)	5.23 (q, J = 7)	9.10 (s)	7.72 (s)		7.45 (s)	
1h	1.77 (t, J = 7) 4.25 (s) 4.35 (s)	4.80 (q, J = 7)	9.33 (s)		7.10 (b)		7.10 (bs)
1i	1.82 (t, J = 7)	4.93 (q, J = 7)	9.30 (s)	8.58 (d, J = 9)	8.02 (dd, J = 9, J = 1)		8.28 (d, J = 1)
1j	1.78 (t, J = 7) 2.73 (s)	4.87 (q, J = 7)	9.23 (s)	8.58 (d, J = 9)	7.86 (dd, J = 9, J = 1)		7.80 (d, J = 1)
1k	1.67 (t, J = 7) 1.80 (t, J = 7) 4.23 (s)	4.52 (q, J = 7) 4.88 (q, J = 7)	9.23 (s)	8.00 (s)			7.47 (s)
1l	1.58 (t, J = 7) 1.82 (t, J = 7) 4.25 (s)	3.23 (q, J = 7) 4.93 (q, J = 7)	9.28 (s)	7.92 (s)			7.80 (s)

Chemical shifts are reported in δ units (ppm) in trifluoroacetic acid with TMS as internal standard. Coupling constants (J) are reported in Hz. Signals are designated as follows: s, singlet; bs, broad singlet; dd, doublet of doublet; t, triplet; q, quartet.

assigned to the 6-hydroxy-7-methoxy structure **5b**. Compounds **18f-g** were converted to the corresponding 4-oxo-3-quinolinecarboxylic acid (**1k-l**) by alkaline hydrolysis. On the other hand, treatment of **16b-e** with ethanolic potassium hydroxide gave **1g-j**, which were identical with samples prepared by alkaline hydrolysis of **14b-e**.

From the mechanistic view that the C_4' C_5 and C_7 position would be highly active towards nucleophiles in this reaction, the fact that the nucleophilic displacement reaction at the C_7 position was not observed in the reaction of **16b** with ethanolic potassium hydroxide, is reasonable. With compounds **16c-e**, the nucleophilic attack at the C_4 position predominates over that at the C_5 or C_7 position to give 4-oxo compounds **1h-j**, which are expected to be resitant to the further displacement reaction at the C_5 or C_7 position due to the fact that the reaction of **1a** with ethanolic potassium hydroxide resulted in recovery of starting material **1a**.

EXPERIMENTAL

All melting points were determined in capillary tubes (Thomas-Hoover melting point aparatus) and are uncorrected. The ir spectra were determined for Nujol mulls on a JASCO IRA-1 spectrophotometer and mass spectra on a Shimazu LKB-9000 mass spectrometer operating at 70 eV. The uv spectra were taken in methanol with a Hitachi 323 spectrophotometer, the nmr spectra with a Varian T-60 spectrometer and compared with TMS as internal standard. In thin layer chromatography, silica gel on plastic sheet (Spotfilm fluorescent, Tokyo Kasei Kogyo Co. Ltd.) was used throughout this work unless otherwise stated.

4-Aminino-3-carbethoxy-1-ethyl-6,7-methylenedioxyquinolinium Iodide (**3b**).

A mixture of 10 g. of **2**, 2.23 g. of aniline, and 30 ml. of ethanol was refluxed for 3.5 hours. The solvent was evaporated *in vacuo* and the resulting yellow solid was washed with water, collected by filtration , and dried. Recrystalization from ethanol gave 7.91 g. (70%) of **3b** as yellow prisms, m.p. 208-209° dec; nmr (deuteriochloroform): δ 1.48 (CH_3' t), 1.68 (CH_3' t), 4.47 (CH_2' q), 5.00 (CH_2'q), 6.22 (CH_2' s), 7.05 and 7.55 (ring protons), 7.20-7.55 (phenyl protons, m), 9.57 (C-2 proton, s).

Anal. Calcd. $C_{21}H_{21}IN_2O_4$: C, 51.23; H, 4.30; N, 5.69. Found: C, 51.22; H, 4.30; N, 5.46.

1-Ethyl-1,4-dihydro-6,7-methylenedioxy-4-phenylimino-3-quinolinecarboxylic Acid (**4a**).

A mixture of 1.45 g. of **3b** 0.99 g. of 85% potassium hydroxide, and 30 ml. of piperidine was refluxed for 10 hours. After evaporation of the solvent *in vacuo* the resulting solid was dissolved in water and the solution was acidified to *p*H 4 by the addition of 6*N* hydrochloric acid. The deposited solid was collected by filtration, washed with water and recrystallized from ethanol, yielding 0.42 g. (42%) of **4a** as yellow needles, m.p. 261-262° dec; nmr (trifluoroacetic acid): δ 1.73 (CH_3' t), 4.67 (CH_2' q), 6.20 (CH_2' s), 7.10-7.73 (ring protons, m), 9.07 (C-2 proton, s).

Anal. Calcd. for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.80; N, 8.33. Found: C, 67.33; H, 4.92; N, 8.15.

Ethyl 1-Ethyl-1,4-dihydro-6,7-methylenedioxy-4-phenylimino-3-quinolinecarboxylate (**4b**).

A mixture of 14.76 g. of **3b**, 2.16 g. of 85% potassium hydroxide, and 300 ml. of ethanol was stirred at room temperature for 4 hours. After removal of the solvent *in vacuo* the solid was washed with water, filtered, dried, and recrystalized from ethanol, affording 9.5 g. (90%) of **4b** as yellow needles, m.p. 177-178°; nmr (trifluoroacetic acid): δ 1.52 (CH_3' t), 1.7 CH_3' t), 4.6 (CH_2' q), 4.67 (CH_2' q), 6.2 (CH_2' s), 7.03-7.73 (ring protons, m), 9.0 (C-2 proton, s).

Anal. Calcd. for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.00; H, 5.32; N, 7.53.

4-Amino-3-carboxy-1-ethyl-6,7-methylenedioxyquinolinium Betaine (**5a**).

A mixture of 1.45 g. of **3a**, 0.33 g. of 85% potassium hydroxide, and 30 ml. of ethanol was stirred at room temperature for 2 hours. After evaporation of the solvent *in vacuo* the resulting solid was washed with water, filtered, and dried. Recrystallization from acetic acid gave 0.53 g. (58%) of **5a** as white powder, m.p. 324° dec, identical with an authentic sample (ir and nmr spectrum) (4).

4-Amino-3-carboxy-1-ethyl-6-hydroxy-7-methoxyquinolinium Betaine (**5b**).

A mixture of 6 g. of **3a**, 7.5 g. of 85% potassium hydroxide, and 150 ml. of methanol was refluxed for 50 hours. After evaporation of the solvent *in vacuo* the resulting solid was dissolved in water and the solution acidified to *p*H 4 by the addition of 6*N* hydrochloric acid. The deposited solid was collected by filtration, washed with water, and poured into boiling hot dimethylformamide (*ca.* 100 ml.). The insoluble solid was collected by filtration, yielding 2.65 g. (70%) of crude **5b**. Recrystallization from acetic acid gave 1.51 g. (40%) of **5b** as colorless needles, m.p. 319-321° dec; nmr (trifluoroacetic acid): δ 1.73 (CH_3' t), 4.25 (CH_3' s), 4.7 (CH_2' q), 7.85 (ring protons, each s), 9.1 (C-2 proton, s).

Anal. Calcd. for $C_{13}H_{14}N_2O_4$: C, 59.38; H, 5.38; N, 10.68. Found: C, 59.38; H, 5.75; N, 10.43.

The dimethylformamide filtrate was allowed to stand at room temperature overnight. The precipitate was collected by filtration, yielding 0.13 g. (3.5%) of **1a** as colorless needles, m.p. 315-316° dec, identical with an authentic sample (9).

4-Amino-3-carboxy-7-ethoxy-1-ethyl-6-hydroxyquinolinium Betaine (**5c**).

A mixture of 1.2 g. of **3a**, 1.5 g. of 85% potassium hydroxide, and 40 ml. of ethanol was refluxed for 44 hours. Evaporation of the solvent *in vacuo* gave a yellow solid, which was dissolved in water. The resulting solution was adjusted to *p*H 6-7 by the addition of 6*N* hydrochloric acid. The yellow solid deposited was collected by filtration, washed with water and dried. Recrystallization from acetic acid yielded 0.76 g. (95%) of **5c** as colorless needles, m.p. 333° dec; nmr (trifluoroacetic acid): δ 1.67 (CH_3' t), 1.77 (CH_3' t), 4.52 (CH_2' t), 4.72 (CH_2' q), 7.43 and 7.87 (ring protons, each s). 9.08 (C-2 proton, s).

Anal. Calcd. for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.70; H, 5.89; N, 10.00.

Compound **5c** was similarly prepared from **5a** in 89% yield.

4-Amino-3-carboxy-1-ethyl-7-ethylmercapto-6-hydroxyquinolinium Betaine (**5d**).

A mixture of 6 g. of **3a**, 9.5 g. of 85% potassium hydroxide, 9 g. of ethyl mercaptan, and 30 ml. of ethanol was refluxed for 19 hours. After evaporation of the solvent and the excess reagent *in vacuo* the resulting solid was dissolved in hot water. Acidification of the solution by the addition of acetic acid afforded 1.3 g. (31%) of a pale yellow solid, which was again dissolved in 1% aqueous sodium carbonate. Treatment of the solution with charcoal and subsequent acidification with acetic acid gave 0.82 g. (19.5%) of **5d** as pale yellow powder, m.p. 344° dec; nmr (trifluoroacetic acid): δ 1.48 (CH_3' t), 1.75 (CH_3' t), 3.17 (CH_2' q), 4.72 (CH_2' q), 7.83 and 7.97 (ring protons, each s), 9.1 (C-2 proton, s).

Anal. Calcd. for $C_{14}H_{16}N_2O_3S$: C, 57.53; H, 5.52; N, 9.59; S, 10.95. Found: C, 57.53; H, 5.54; N, 9.54; S, 10.68.

1-Ethyl-1,4-dihydro-6-hydroxy-7-methoxy-4-phenylimino-3-quinolinecarboxylic Acid (**6b**).

A mixture of 1.93 g. of **3b**, 2 g. of 85% potassium hydroxide and 30 ml. of methanol was refluxed for 6 hours. Evaporation of the solvent *in vacuo* left a yellow solid, which was dissolved in water. The insoluble solid was collected by filtration, and recrystallized from methanol, yielding 0.15 g. (11%) of **3b** as yellow needles, m.p. 208-209° dec, identical with a sample described above. Acidification of the aqueous filtrate by the addition of

acetic acid precipitated 1.05 g. (76.6%) of **6b**, which was recrystallized from methanol to afford 0.73 g. (53.3%) of yellow prisms, m.p. 268° dec; nmr (trifluoroacetic acid): δ 1.8 (CH_3' t), 4.2 (CH_3' s), 4.73 (CH_2' q), 7.17-7.73 (ring protons, m), 9.17 (C-2 proton, s).

Anal. Calcd. for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.50; H, 5.31; N, 8.26.

7-Ethoxy-1-ethyl-1,4-dihydro-6-hydroxy-4-phenylimino-3-quinolinecarboxylic Acid (**6c**).

A mixture of 4.92 g. of **3b**, 2.16 g. of 85% potassium hydroxide and 50 ml. of ethanol was refluxed for 6 hours. After evaporation of the solvent *in vacuo* the resulting yellow solid was dissolved in hot water and the solution adjusted to *p*H 3-4 by the addition of concentrated hydrochloric acid, yielding 3.47 g. (98.6%) of **6c**. Recrystallization from acetic acid afforded 2.67 g. (76%) of a first crop as yellow prisms, m.p. 287° dec, and 0.37 g. (11%) of a second crop as yellow prisms, 285° dec; nmr (trifluoroacetic acid): δ 1.63 (CH_3' t), 1.78 (CH_3' t), 4.48 (CH_2' q), 4.75 (CH_2' q), 7.23-7.77 (ring protons, m), 9.15 (C-2 proton, s).

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.40; H, 5.98; N, 7.87.

1-Ethyl-7-ethylmercapto-1,4-dihydro-6-hydroxy-4-phenylimino-3-quinolinecarboxylic Acid (**6d**).

A mixture of 4.92 g. of **3b**, 2.16 g. of 85% potassium hydroxide, 15 ml. of ethyl mercaptan, and 50 ml. of ethanol was refluxed for 10 hours. After the reaction, the mixture was treated in the same procedure as described above. There was obtained 3.62 g. (52.2%) of crude **6d**. Recrystallization from acetic acid afforded 2.87 g. (78%) of **6d** as colorless prisms, m.p. 294° dec; nmr (trifluoroacetic acid): δ 1.47 (CH_3' t), 1.77 (CH_3' t), 3.15 (CH_2' q), 4.72 (CH_2' q), 7.0-7.93 (ring protons, m), 9.15 (C-2 proton, s).

Anal. Calcd. fo$C_{20}H_{20}N_2O_3S$: C, 65.22; H, 5.43; N, 7.61. Found: C, 64.97; H, 5.62; N, 7.41.

1-Ethyl-1,4-dihydro-6,7-dihydroxy-4-phenylimino-3-quinolinecarboxylic Acid (**6e**).

A mixture of 1.82 g. of **4b**, 0.44 g. of sodium hydride (55% in mineral oil), and 30 ml. of piperidine was stirred at 100° for 6 hours. After evaporation of the solvent *in vacuo* the residue was mixed with water and chloroform. The chloroform solution was separated, washed with water, and dried over sodium sulfate. Evaporation of the solvent to dryness and recrystallization from ethanol gave 0.44 g. (26%) of **4a** as yellow needles, m.p. 261-263° dec, identical with a sample described above. The aqueous layer after separation of the chloroform solution was acidified to *p*H 3-4 by the addition of 6*N* hydrochloric acid. The yellow solid which precipitated was collected by filtration and washed with water and with ethanol. Recrystallization from aqueous acetic acid afforded 0.7 g. (43%) of **6e** as yellow prisms, m.p. 302-303° dec, nmr (trifluoroacetic acid): δ 1.75 (CH_3' t), 4.67 (CH_2' q), 7.17-7.72 (ring protons, m), 9.13 (C-2 proton, s).

Anal. Calcd. for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.38; H, 4.99; N, 8.37.

Reaction of **3b** with Piperidine.

A mixture of 2.64 g. of **3b** and 30 ml. of piperidine was refluxed for 5 hours. After evaporation of the solvent *in vacuo* the residue was extracted with chloroform. The chloroform solution was washed with water, dried over sodium sulfate, and decolorized with charcoal. Removal of the chloroform *in vacuo* yielded a yellow oil, which was triturated with ethanol. A yellow solid which had formed was collected by filtration, giving 0.56 g. (30.8%) of **4b** as yellow needles, m.p. 174-175°, identical with a sample described above. Evaporation of the ethanol filtrate afforded 1.46 g. of intractable tar.

Hydrolysis of 4-Aminoquinolinium Betaines (**5b-d**).

A mixture of 10 mmoles of **5b-d** and a 15-fold volume of 10% aqueous sodium hydroxide was refluxed for 5 hours. After the reaction was completed, the solution was acidified to *p*H 3-4 by the addition of concentrated hydrochloric acid while hot. The deposited solid was collected by filtration, washed with water and dried, yielding the 4-oxo-3-quinolinecarboxylic acid described below.

1-Ethyl-1,4-dihydro-6-hydroxy-7-methoxy-4-oxo-3-quinolinecarboxylic Acid (**1b**).

This compound had m.p. 309° dec, colorless rods (acetic acid), yield 3.09 g. (85%).

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.30; H, 4.96; N, 5.26.

7-Ethoxy-1-ethyl-1,4-dihydro-6-hydroxy-4-oxo-3-quinolinecarboxylic Acid (**1c**).

This compound had m.p. 311-312° dec, colorless needles (dimethylformamide), yield 3.22 g. (86%).

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.40; H, 5.58; N, 5.08.

1-Ethyl-7-ethylmercapto-1,4-dihydro-6-hydroxy-4-oxo-3-quinolinecarboxylic Acid (**1d**).

This compound had m.p. 315-316° dec, colorless needles (dimethylformamide), yield 3.37 g. (87%).

Anal. Calcd. for $C_{14}H_{15}NO_4S$: C, 57.34; H, 5.17; N, 4.78. Found: C, 57.05; H, 5.18; N, 4.78.

Compounds **1b-d** were similarly prepared by hydrolyzing **6b-d** with 10% aqueous sodium hydroxide.

Diethyl 3-Benzyloxy-4-methoxyanilinomethylenemalonate (**8**).

A mixture of 22.0 g. of 3-benzyloxy-4-methoxyaniline (**7**) and 25.4 g. of diethyl ethoxymethylenemalonate was stirred at 120-130° for 2 hours, during which period the liberated ethanol was removed. After cooling, a white solid which had formed was recrystallized from i-propyl ether, yielding 35 g. (87.7%) of **8** as colorless needles, m.p. 67-68°.

Anal. Calcd. for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51. Found: C, 66.29; H, 6.28; N, 3.53.

Ethyl 7-Benzyloxy-4-hydroxy-6-methoxy-3-quinolinecarboxylate (**9**).

To 100 ml. of a boiling Dowtherm A was added 5 g. of **8**. The mixture was maintained at the same temperature with stirring for 15 minutes. After cooling, the deposited solid was collected by filtration, washed with ethanol, and dried. Recrystallization from dimethylformamide gave 3.92 g. (89%) of **9** as yellow needles, m.p. 279-280°.

Anal. Calcd. for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.72; H, 5.35; N, 4.00.

Ethyl 7-Benzyloxy-1-ethyl-1,4-dihydro-6-methoxy-4-oxo-3-quinolinecarboxylate (**10**).

A mixture of 0.405 g. of **9**, 0.26 g. of potassium carbonate 0.72 g. of ethyl iodide, and 15 ml. of dimethylformamide was stirred at room temperature for 32 hours. The reaction was followed by tlc using a mixture of chloroform-methanol (10:1) as solvent. After removal of the excess ethyl iodide and the solvent *in vacuo*, the residue was mixed with water and extracted with chloroform. The chloroform layer was separated, washed with water, dried over sodium sulfate, and evaporated *in vacuo*, yielding 0.4 g. of a yellow solid. Recrystallization from ethanol afforded 0.35 g. (80%) of **10** as colorless needles, m.p. 155-156°.

Anal. Calcd. for $C_{22}H_{23}NO_5$: C, 69.27; H, 6.08; N, 3.67. Found: C, 69.15; H, 6.30; N, 3.55.

1-Ethyl-1,4-dihydro-7-hydroxy-6-methoxy-4-oxo-3-quinolinecarboxylic Acid (**1e**).

A solution of 0.19 g. of **10** and 5 ml. of concentrated hydrochloric acid was refluxed for 12 hours. After evaporation of the solvent *in vacuo* the resulting solid was washed with water, collected by filtration and recrystallized from acetic acid, yielding 0.08 g. (61.5%) of **1e** as colorless prisms, m.p. 265-266°, the ir and mass spectra of which were identical with those of **1e** reported by DiCarlo (7).

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.39; H, 5.02; N, 5.18.

General Preparation of *N*-Ethylanilines (**12b-c**).

N-Ethylanilines (**12b-c**) were prepared according to the method previously reported (9).

N-Ethyl-2,4-dimethoxyailine (**12b**).

This compound had b.p. 115-116°/5 mm, yield 87%.

Anal. Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.34; H, 8.61; N, 7.54.

N-Ethyl-3,5-dimethoxyaniline (**12c**).

This compound had b.p. 133-135°/3 mm, yield 79%.

Anal. Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.46; H, 8.26; N, 7.55.

General Preparation of Diethyl *N*-Ethylanilinomethylenemalonate (**13b-c**).

Diethyl *N*-ethylanilinomethylenemalonate (**13b-c**) were prepared according to the method previously reported (9).

Diethyl *N*-Ethyl-2,4-dimethoxyanilinomethylenemalonate (**13b**).

This compound was isolated as a yellow oil.

Anal. Calcd. for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.17; H, 7.13; N, 3.69.

Diethyl *N*-Ethyl-3,5-dimethoxyanilinomethylenemalonate (**13c**).

This compound was isolated as a yellow oil.

Anal. Calcd. for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.23; H, 7.17; N, 3.69.

General Preparation of 3-Carbethoxy-4-chloro-1-ethylquinolinium Iodides (**14 a-c**).

A mixture of 10 g. of a diethyl *N*-ethylanilinomethylenemalonate and 50 ml. of phosphorus oxychloride was refluxed for 4 hours. Excess phosphorus oxychloride was distilled under reduced pressure and the residue was dissolved in cold water. The resulting aqueous solution was filtered, and excess sodium iodide (*ca.* 10 g.) was added to the filtrate. The crystals that separated out were collected by filtration, washed with cold water and dried.

3-Carbethoxy-4-chloro-1-ethyl-6,7-dimethoxyquinolinium iodide (**14a**).

This compound had m.p. 300° dec, yellow prisms (ethanol), yield 8.87 g. (69%).

Anal. Calcd. $C_{16}H_{19}ClINO_4$: C, 42.48; H, 4.20; N, 3.10. Found: C, 42.45; H, 4.10; N, 3.30.

3-Carbethoxy-4-chloro-1-ethyl-6,8-dimethoxyquinolinium Iodide (**14b**).

lThis compound had m.p. 149-150° dec, red needles (ethanol), yield 6.3 g. (49%).

Anal. Calcd. for $C_{16}H_{19}ClINO_4$: C, 42.48; H, 4.20; N, 3.10. Found: C, 42.32; H, 4.26; N, 3.44.

3-Carbethoxy-4-chloro-1-ethyl-5,7-dimethoxyquinolinium Iodide (**14c**).

This compound had m.p. 141-142° dec, yellow prisms (acetone), yield 7.46 g. (58%).

Anal. Calcd. for $C_{16}H_{19}ClNO_4$: C, 42.48; H, 4.20; N, 3.10. Found: C, 42.09; H, 4.41; N, 3.26.

General Preparation of **14d-e**.

A mixture of 15 g. of an ester (**17d-e**) (10-11), and 60 ml. of phosphorus oxychloride was stirred and heated at 80-90° for 3 hours. Worked up in the same manner as stated above, compounds **14d-e** thus obtained were recrystallized from acetone.

3-Carbethoxy-4,7-dichloro-1-ethylquinolinium Iodide (**14d**).

This compound had m.p. 157-158° dec, prisms. yield 6.8 g. (30%).

Anal. Calcd. for $C_{14}H_{14}Cl_2INO_2$: C, 3.46; H, 3.20; N, 3.29. Found: C, 39.17; H, 3.25; N, 2.99.

3-Carbethoxy-4-chloro-1-ethyl-7-methylmercaptoquinolinium Iodide (**14e**).

This compound had m.p. 176-177° dec, red needles, yield 11.5 g. (51%).

Anal. Calcd. for $C_{15}H_{17}ClINO_2S$: C, 41.15; H, 3.92; N, 3.20. Found: C, 40.83; H, 3.88; N, 3.22.

General preparation of 4-Anilinoquinolinium Iodide (**15a-e**).

A mixture of 25 mmoles of a 4-chloroquinolinium iodide (**14a-e**), 50 mmoles of aniline, and 100 ml. of ethanol was refluxed for 2 hours. After evaporation of ethanol, the resulting yellow solid was recrystallized from ethanol, yielding **14a-e**.

4-Anilino-3-carbethoxy-1-ethyl-6,7-dimethoxyquinolinium Iodide (**15a**).

This compound had m.p. 201-202° dec, yellow prisms, yield 12 g. (95%).

Anal. Calcd. for $C_{22}H_{25}IN_2O_4$: C, 51.97; H, 4.91; N, 5.51. Found: C, 51.93; H, 4.93; N, 5.68.

4-Anlino-3-carbethoxy-1-ethyl-6,8-dimethoxyquinolinium Iodide (**15b**).

This compound had m.p. 186-187° dec. yellow prisms, yield 10.99 g. (87%).

Anal. Calcd. for $C_{22}H_{25}In_2O_4$: C, 51.97; H, 4.92; N, 5.51. Found: C, 51.85; H, 4.94; N, 5.71.

4-Anilino-3-carbethoxy-1-ethyl-5,7-dimethoxyquinolinium Iodide (**15c**).

This compound had m.p. 108-110°, yellow needles, yield 9.9 g. (78%).

Anal. Calcd. for $C_{22}H_{25}IN_2O_4$: C, 51.97; H, 4.92; N, 5.51. Found: C, 51.62; H, 4.97; N, 5.36.

4-Anilino-3-carbethoxy-7-chloro-1-ethylquinolinium Iodide (**15d**).

This compound had m.p. 210-211° dec, yellow prisms, yield 8.33 g. (69%).

Anal. Calcd. for $C_{20}H_{20}ClIN_2O_2$: C, 49.76; H, 4.18; N, 5.80. Found: C, 49.64; H, 4.17; N, 5.62.

4-Anilino-3-carbethoxy-1-ethyl-7-methylmercaptoquinolinium Iodide (**15e**).

This compound had m.p. 183-184° dec, yellow prisms, yield 8.53 g. (69%).

Anal. Calcd. for $C_{21}H_{23}N_2O_2SI$: C, 51.01; H, 4.69; N, 5.67. Found: C, 51.39; H, 4.75; N, 5.66.

General Preparation of **16a-e**.

A mixture of 20 mmoles of a 4-anilinoquinolinium iodide (**15a-e**), 20 mmoles of 85% aqueous potassium hydroxide, and 200 ml. of ethanol was stirred at room temperature for 3 hours. After evaporation of ethanol, the resulting solid was washed with water, filtered and recrystallized from ethanol, yielding **16a-e**.

Ethyl 1-Ethyl-1,4-dihydro-6,7-dimethoxy-4-phenylimino-3-quinolinecarboxylate (**16a**).

This compound had m.p. 178-179° dec, yellow needles, yield 6.5 g. (86%).

Anal. Calcd. for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.76; H, 6.38; N, 7.39.

Ethyl 1-Ethyl-1,4-dihydro-6,8-dimethoxy-4-phenylimino-3-quinolinecarboxylate (**16b**).

This compound had m.p. 147-148°, yellow prisms, yield 6.46 g. (85%).

Anal. Calcd. for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.35; H, 6.52; N, 7.30.

Ethyl 1-Ethyl-1,4-dihydro-5,7-dimethoxy-4-phenylimino-3-quinoline carboxylate (**16c**).

This compound had m.p. 191-192°, yellow prisms, yield 3.8 g. (50%).

Anal. Calcd. for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.41; H, 6.25; N, 7.31.

Ethyl 7-Chloro-1-ethyl-1,4-dihydro-4-phenylimino-3-quinolinecarboxylate (**16d**).

This compound had m.p. 114-115°, yellow prisms, yield 4.82. (68%).

Anal. Calcd. for $C_{20}H_{19}ClN_2O_2$: C, 67.72; H, 5.40; N, 7.90. Found: C, 67.53; H, 5.25; N, 7.81.

Ethyl 1-Ethyl-1,4-dihydro-7-methylmercapto-4-phenylimino-3-quinolinecarboxylate (**16e**).

This compound had m.p. 116-117°, yellow needles. yield 3.66 g. (50%).

Anal. Calcd. for $C_{21}H_{22}N_2O_2S$: C, 68.82; H, 6.05; N, 7.65. Found: C, 68.96; H, 5.75; N, 7.43.

Alkaline Hydrolysis of **14a-e**.

A mixture of 10 mmoles of **14a-e** and 30 ml. of 10% aqueous sodium hydroxide was heated under reflux for 1 hour. After cooling the resulting solution was acidified to *p*H 1-2 by the addition of 6*N* hydrochloric acid, yielding **1f-j**. The nmr data are summarized in Table I.

1-Ethyl-1,4-dihydro-6,7-dimethoxy-4-oxo-3-quinolinecarboxylic Acid (**1f**).

This compound had m.p. 224-225°, colorless needles (methanol), yield 2.0 g. (72%).

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.04; H, 5.45; N, 5.05. Found: C, 60.53; H, 5.18; N, 4.95.

1-Ethyl-1,4-dihydro-6,8-dimethoxy-4-oxo-3-quinolinecarboxylic Acid (**1g**).

This compound had m.p. 201-202°, pale yellow needles (aqueous dimethylformamide), yield 1.84 g. (66%).

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C 60.60; H, 5.28; N, 4.91.

1-Ethyl-1,4-dihydro-5,7-dimethoxy-4-oxo-3-quinolinecarxylic Acid (**1h**).

This compound had m.p. 247-248°, colorless needles (ethanol), yield 2.04 g. (73%).

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.77; H, 5.38; N, 4.97.

7-Chloro-1-ethyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic Acid (**1i**).

This compound had m.p. 272-273° (lit. (10) m.p. 274°), colorless needles (aqueous dimethylformamide), yield 1.47 g. (70%).

1-Ethyl-1,4-dihydro-7-methylmercapto-4-oxo-3-quinolinecarboxylic Acid (**1j**).

This compound had m.p. 227-228° (lit. (11) m.p. 226-228°), pale yellow needles (aqueous dimethylformamide), yield 1.94 g. (74%).

7-Ethoxy-1-ethyl-1,4-dihydro-6-methoxy-4-phenylimino- (**18f**) and 7-Ethoxy-1-ethyl-1,4-dihydro-6-methoxy-4-oxo-3-quinolinecarboxylic Acid (**1k**).

A mixture of 3.8 g. of **16a**, 1.44 g. of 85% potassium hydroxide and 50 ml. of ethanol was heated under reflux for 6 hours. After evaporation of the solvent, the residue was dissolved in water and treated with charcoal. Acidification of the filtrate with concentrated hydrochloric acid separated a fawn syrup, which was extracted with chloroform. The extract was washed with water, dried over sodium sulfate and evaporated, yielding 2.7 g. of a fawn solid. Recrystallization from ethanol gave 0.81 g. of colorless needles, which was again recrystallized from aqueous dimethylformamide to afford 0.5 g. (17%) of **1k** as colorless prisms, m.p. 257-258°.

Anal. Calcd. for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.58; H, 5.51; N, 4.68.

The ethanolic filtrate was treated with charcoal and evaporated *in vacuo* to yield a fawn solid, which was dissolved in 10% aqueous sodium hydroxide. The *p*H of the resulting aqueous solution was adjusted to *p*H 6-7 by the addition of a 6*N* hydrochloric acid, yielding 0.87 g. of a yellow solid. Recrystallization from petroleum ether-ethanol gave 0.13 g. (6.3%) of **18f** as yellow prisms, m.p. 224-225°; nmr (trifluoroacetic acid): δ 1.55 (CH_3' t), 1.72 (CH_3' t), 3.42 (OCH_3' s), 4.38 (CH_2' q), 4.7 (CH_2' q), 7.2-7.3 (ring protons, m), 9.17 (C-2 proton, s).

Anal. Calcd. for $C_{21}H_{22}N_2O_4$: C, 68.83; H, 6.05; N, 7.65. Found: C, 68.43; H, 6.00; N, 7.24.

The aqueous filtrate after separation of **18f** was acidified to *p*H 1 by the addition of 6*N* hydrochloric acid to give 0.75 g. of a pale yellow solid. Recrystallization from methanol gave 0.31 g. (11%) of **1f** as colorless needles, m.p. 223-225°, identical with a sample described above.

1-Ethyl-7-ethylmercapto-1,4-dihydro-6-methoxy-4-phenylimino-3-quinolinecarboxylic Acid (**18g**).

A solution of 1.9 g. of **16a**, 0.72 g. of 85% potassium hydroxide, 10 ml. of ethyl mercaptan, and 60 ml. of ethanol was heated under reflux for 7 hours. After evaporation of the solvent, the residue was triturated with water. The insoluble solid was collected by filtration, washed with water and dried, yielding 1.19 g. (63%) of **16a**. The filtrate was acidified to *p*H 3-4 by the addition of 6*N* hydrochloric acid, affording a yellow solid. Recrystallization from petroleum ether-ethanol gave 0.29 g. (16%) of **18g** as yellow needles, m.p. 178-180° dec; nmr (trifluoroacetic acid): δ 1.48 (CH_3' t), 3.10 (CH_2' q), 3.37 (OCH_3' s), 4.70 (CH_2' q), 7.13 (ring proton, s), 7.20-7.77 (ring protons, m), 9.10 (C-2 proton, s).

Anal. Calcd. for $C_{21}H_{22}N_2O_3S$: C, 68.45; H, 6.02; N, 3.80. Found: C, 68.13; H, 5.75; N, 3.72.

Reaction of **16b** with Ethanolic Potassium Hydroxide.

A mixture of 1.9 g. of **16b**, 0.72 g. of 85% potassium hydroxide, and 25 ml. of ethanol was heated under reflux for 6 hours. After evaporation of the solvent, the residue was dissolved in water. The resulting aqueous solution was acidified to *p*H 3-4 by the addition of 6*N* hydrochloric acid, affording a white solid. Recrystallization from ethanol gave 0.43 g. (31%) of **1g** as colorless needles, m.p. 201-202°, undepressed on admixture with the sample described above. The aqueous filtrate was allowed to stand at room temperature for 2 days, precipitating 0.71 g. of yellow needles. Recrystallization from ether-ethanol gave 0.53 g. (33%) of **18b** as yellow needles, m.p. 228-229° dec, nmr (deuteriochloroform): δ 1.50 (CH_3' t), 4.90 (OCH_3' s), 5.70 (OCH_3' s), 6.43 (CH_2' q), 6.62 (ring proton, d), 6.83 (ring proton, d), 7.00-7.60 (phenyl protons, m), 8.97 (C-2 proton, s).

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.51; H, 5.61; N, 7.54.

Treatment of **16c-e** with ethanolic potassium hydroxide gave **1h-j** in 66, 57, and 60% yields, respectively, in the similar manner as described above.

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