Nucleophilic Displacement of Aromatic Fluorine. Part IV. Quinolinoquinolines and Benzochromenoquinolines (1)

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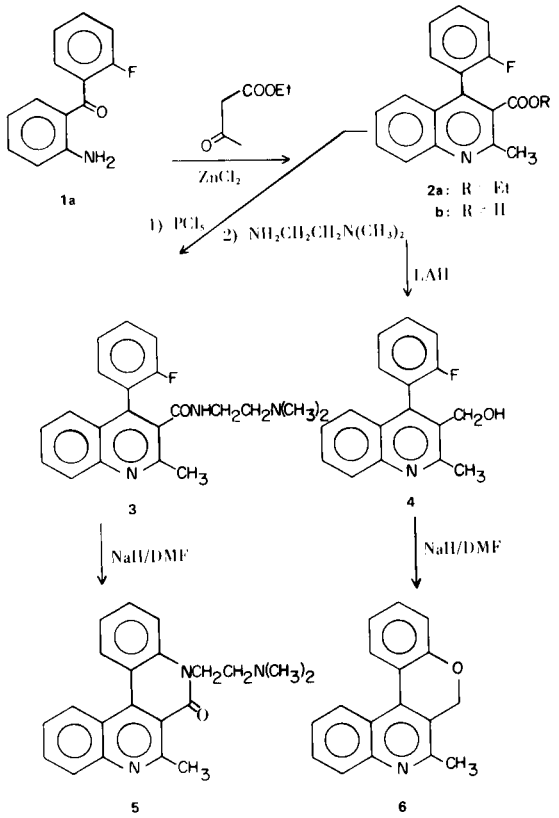
The title compounds were obtained by facile intramolecular nucleophilic displacement of aromatic fluorine from 4-(2-fluorophenyl)quinolines bearing substituents such as a carboxamide, carboxaldehyde, carboxaldoxime or a hydroxymethyl group in the 3-position.

We have applied the facile intramolecular nucleophilic displacement of aromatic fluorine to the synthesis of various polycyclic compounds reported in previous papers (1). We found this reaction to be particularly useful for the preparation of the title compounds starting from 4-(2-fluorophenyl)quinolines suitably substituted in the 3-position. The quinolines required for the ring closure were readily available from the benzophenones **1a** and **1b** by Friedlander synthesis (2). While E. A. Fehnel (2b) has described the acid catalized reaction of 2-aminobenzophenone with a variety of dicarbonyl compounds, we used zinc chloride in refluxing benzene or toluene for the condensation of **1a** or **1b** with ethyl acetoacetate, acetylacetone and tetramethoxypropane respectively and obtained comparable yields.

Scheme I

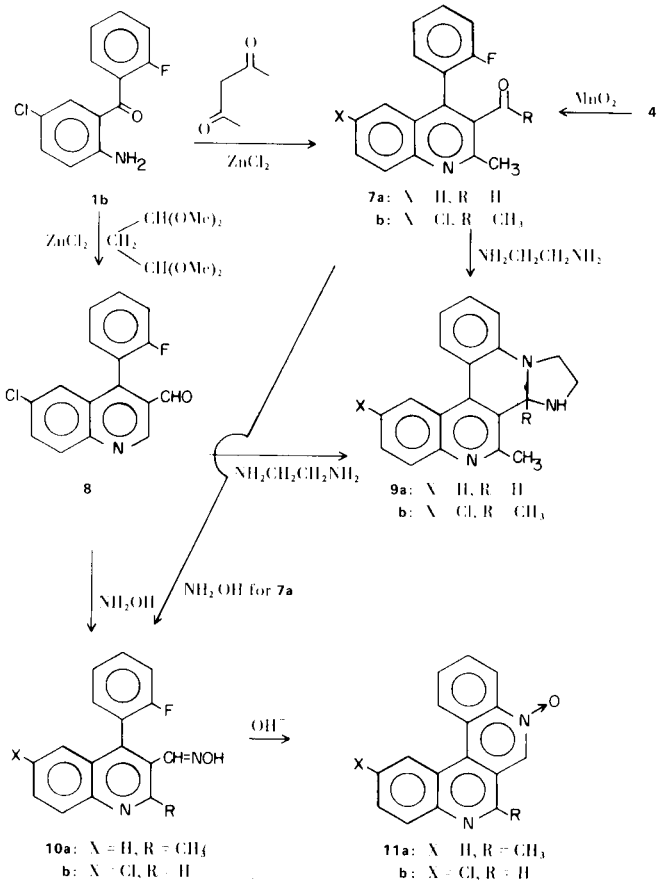


Hydrolysis of the ester **2a** (Scheme I) yielded the corresponding acid **2b** which was converted to the basic amide **3** by subsequently reacting the acid with phosphorus pentachloride and unsymmetrical *N,N*-dimethylethylenediamine. To effect ring closure to **5**, a solution of the amide **3** in dimethylformamide was treated with sodium hydride with warming on the steam bath for a short period of time. Under similar conditions, the alcohol **4**, which was obtained by reduction of **2a** with lithium aluminum hydride, cyclized to the benzopyranoquinoline **6**.

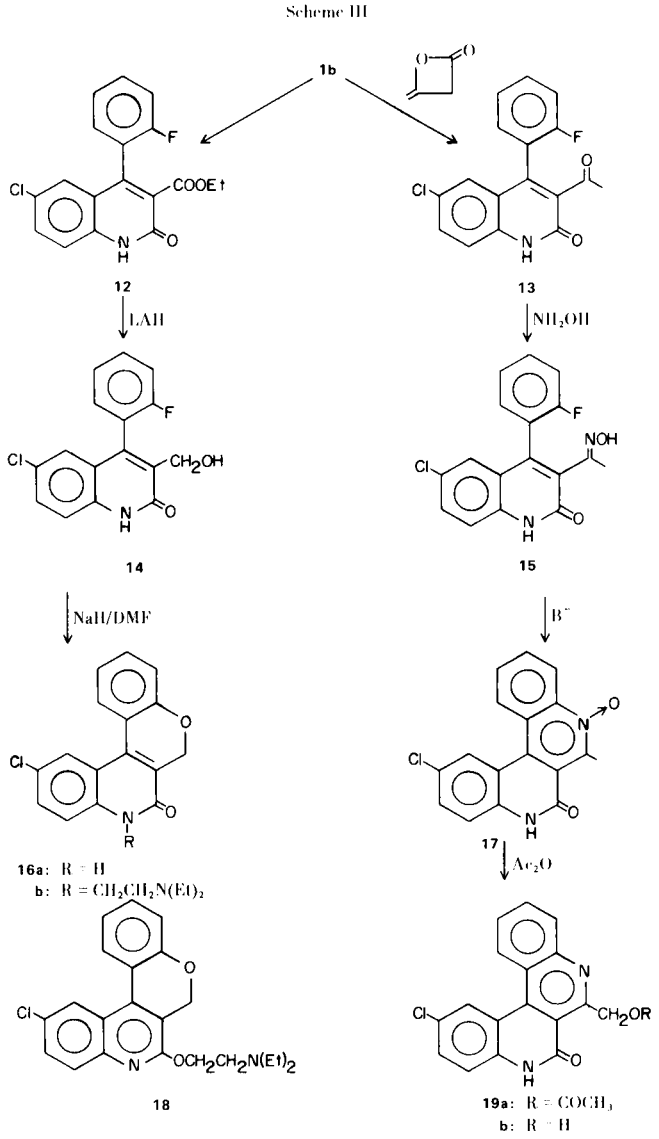
The reduction with lithium aluminum hydride produced beside the desired alcohol **4** a considerable amount of an unidentified dihydroquinoline which was converted to alcohol **4** by short treatment with activated manganese dioxide.

The quinoline-3-carboxaldehyde **7a** (Scheme II) was accessible by a much slower oxidation of alcohol **4** with activated manganese dioxide, while the aldehyde **8** was prepared by condensation of the benzophenone **1b** with tetramethoxypropane. Both aldehydes were converted to the corresponding oximes **10**, which smoothly yielded the quinolinoquinoline oxides **11** upon treatment with alkali hydroxide in refluxing ethanol. Reaction of **8** with ethylene diamine led to the imidazoline **9a** which was much more resistant to air oxidation than similar imidazolines in the indoloquinoline series (**1a**). The sterically more crowded compound **9b** was formed more slowly and in lower yield by refluxing the 3-acetylquinoline **9b** with ethylene diamine.

Scheme II



Scheme III



The preparation of the carbostyryl **12** (Scheme III) from the benzophenone **1b** was previously reported (3). The 3-acetylcarbostyryl **13** was obtained in high yield by reaction of **1b** with diketene in pyridine. Reduction of the ester **12** with lithium aluminum hydride led to the alcohol **14** without affecting the 2-carbonyl group, the enolic form of which apparently is stable to reduction under the conditions applied. The alcohol **14** again could be cyclized to the benzochromenoquinoline **16a**. Alkylation of this highly insoluble compound with 2-diethylaminoethyl chloride and sodium hydride in dimethylformamide yielded mainly the *N*-alkylated compound **16b** along with the *O*-alkylated product **18**. Ring closure of the oxime **15** with ethanolic potassium hydroxide proceeded readily to the *N*-oxide **17**. This *N*-oxide was used for functionalization of the methyl group. Thus treatment of **17** with acetic anhydride afforded the acetate **19a** which was hydrolized to the corresponding alcohol **19b**.

EXPERIMENTAL

Melting points were determined in a capillary melting point apparatus or on a Reichert hot stage microscope. The uv spectra were measured in 2-propanol on a Cary Model 14 spectrophotometer. Nmr spectra were recorded on a Varian A-60 or Varian T-60 instrument with TMS as internal standard. Ir spectra were determined on a Beckman IR-9 spectrometer and mass spectra on a CEC-100 B instrument. Silica gel Merck (70-325 mesh) was used for chromatography and anhydrous sodium sulfate for drying purposes.

Ethyl 4-(2-Fluorophenyl)-2-methylquinoline-3-carboxylate, **2a**.

A mixture of 45.4 g. (0.2 mole) of 2-(2-fluorobenzoyl)aniline, **1a**, (4) 45.4 g. of ethyl acetoacetate, 4.5 g. of zinc chloride and 500 ml. of benzene was refluxed for 24 hours with separation of water. The benzene solution was washed with water, dried and evaporated. Crystallization from ethanol and recrystallization from the same solvent yielded 54.1 g. (83%) of colorless product with m.p. 123-125°. The analytical sample was again recrystallized from ethanol, m.p. 126-128°; uv: λ max 208 mμ (ε = 40,700), 236 (43,450), sh 263 (5,100), sh 271 (5,600), 282 (5,780), infl 305 (3,920), 320 (3,280); ir (chloroform): 1730 cm^{-1} (COOEt); nmr (deuteriochloroform): δ 1.0 ppm (t, 3, J = 7 Hz, CH_3), 2.85 (s, 3,

CH_3) 4.13 (q, 2, J = 7 Hz, OCH_2) 7-8.3 (m, 8, aromatic H).

Anal. Calcd. for $C_{19}H_{16}FNO_2$: C, 73.8; H, 5.2; N, 4.5. Found: C, 73.5; H, 5.3; N, 4.4.

4-(2-Fluorophenyl)-2-methylquinoline-3-carboxylic Acid, **2b**.

A mixture of 31 g. (0.1 mole) of **2a**, 15 g. of potassium hydroxide, 200 ml. of ethanol and 20 ml. of water was refluxed for 4 hours. After acidification with glacial acetic acid, the reaction mixture was concentrated under reduced pressure and the product was precipitated by addition of water. It was collected and recrystallized from methanol/2-propanol to yield 24 g. (85%) of colorless crystals with m.p. 263-265°.

Anal. Calcd. for $C_{17}H_{12}FNO_2$: C, 72.6; H, 4.3; N, 5.0. Found: C, 72.4; H, 4.2; N, 4.8.

N-(2-Dimethylaminoethyl)-4-(2-fluorophenyl)-2-methylquinoline-3-carboxamide, **3**.

Phosphorus pentachloride, 10.5 g. (0.0505 mole) was added to a suspension of 14 g. (0.05 mole) of **2b** in 150 ml. of methylene chloride cooled to -20°. After stirring for 30 minutes at this temperature, this mixture was added to a stirred solution of 12.5 g. of 2-dimethylaminoethylamine in 250 ml. of methylene chloride layered with 250 ml. of 10% aqueous sodium carbonate and 50 g. of ice. The two-phase mixture was stirred for 30 minutes and following the addition of 100 ml. of carbonate solution for another 15 minutes. The methylene chloride layer was separated, dried and filtered. Another portion of 12.5 ml. of 2-dimethylaminoethylamine was added to the solution and this mixture was heated to reflux for 20 minutes, diluted with methylene chloride and washed with water. The methylene chloride solution was dried and evaporated. Crystallization from ether and recrystallization from methylene chloride/hexane yielded 12 g. (70%) of colorless needles with m.p. 185-187°; uv: λ max 236 mμ (ε = 40,200), 281 (5,820), 293 (5,520), 306 (4,710), 320 (4,500); ir (chloroform): 3400 cm^{-1} (NH) 1660, 1520 (CONH).

Anal. Calcd. for $C_{21}H_{22}FN_3O$: C, 71.8; H, 6.3; N, 12.0. Found: C, 71.5; H, 6.1; N, 12.0.

4-(2-Fluorophenyl)-3-hydroxymethyl-2-methylquinoline, **4**.

A solution of 15.5 g. (0.05 mole) of **2a** in 100 ml. of tetrahydrofuran was added dropwise to a suspension of 3 g. (0.075 mole) of lithium aluminum hydride in 150 ml. of dry ether kept at 5-10°. After addition the mixture was stirred for 30 minutes in an ice bath and then 30 minutes without cooling. The hydride was hydrolized by careful addition of 15 ml. of water. The inorganic material was filtered off and washed well with methylene chloride, The filtrate was dried and evaporated. The residue was dissolved in 250 ml. of methylene chloride and treated with 50 g. of activated manganese dioxide for 5 minutes. The manganese dioxide was removed by filtration. The filtrate was evaporated and the residue was crystallized from ether to yield 11.4 g. (85%) of product with 170-173°. For analysis it was recrystallized from methanol, m.p. 175-177°; nmr (deuteriochloroform): δ 2.6 ppm (s, 1, OH) 2.86 (s, 3, CH_3) 4.6 (s, 2, $-CH_2O$) 7-8.2 (m, 8, aromatic H).

Anal. Calcd. for $C_{17}H_{14}FNO$: C, 76.4; H, 5.3; N, 5.2. Found: C, 76.5; H, 5.3; N, 5.1.

7,8-Dihydro-8-(2-dimethylaminoethyl)-6-methyldibenzo[*c*,*f*][2,7]-naphthyridin-7-one, **5**.

Sodium hydride suspension (50% in mineral oil), 1.5 g. (0.031 mole) was added to a solution of 7 g. (0.02 mole) of **3** in 100 ml. of dimethylformamide. The mixture was stirred and heated on the steam bath for 10 minutes and then poured into 800 ml. of ice water layered with 20 ml. of ether. The mixture was stirred for 15 minutes and the crystals were collected, washed with water and dissolved in methylene chloride. The solution was dried and evaporated partially. The product was crystallized by addition of hexane and was recrystallized from methylene chloride/hexane to yield 5.1 g. (77%) with m.p. 112-115°; uv: λ max 223 mμ (ε = 25,000) sh 245 (29,500) 260 (39,800) 314 (4,480) 326 (4,450) infl 350 (5,500) 368 (8,700) 382 (7,810); ir (chloroform): 1650 cm^{-1} (CO); nmr (deuteriochloroform): δ 2.4 ppm (s, 6, $N(CH_3)_2$) 2.7 (t, 2, NCH_2) 3.22 (s, 3, CH_3) 4.48 (t, 2, NCH_2) 7.1-8.75 (m, 8, aromatic H).

Anal. Calcd. for $C_{21}H_{21}N_3O$: C, 76.1; H, 6.4; N, 12.7. Found: C, 76.1; H, 6.6; N, 12.5.

7-Methyl-6*H*-[1]benzopyrano[3,4-*c*]quinoline, **6**.

Sodium hydride suspension (50% in mineral oil), 1.3 g. (0.027 mole) was added to a solution of 5.4 g. (0.02 mole) of **4** in 50 ml. of dimethylformamide. The mixture was heated and stirred on the steam bath for 10 minutes and was then poured on ice water. The solidified precipitate was collected, washed with water and dissolved in methylene chloride. The solution was dried and evaporated. Crystallization of the residue from ethanol yielded 4.8 g. (75%) of product with m.p. 131-133°. For analysis it was recrystallized from ethanol, m.p. 132-134°; uv: λ sh 214 mμ (ε = 38,700), max 242 (27,750), 251 (26,100), 329 (11,150), infl 350 (7,600); nmr (deuteriochloroform): δ 2.65 ppm (s, 3, CH_3) 5.1 (s, 2, CH_2-O) 7-8.5 (m, 8, aromatic H).

Anal. Calcd. for $C_{17}H_{13}NO$: C, 82.6; H, 5.3; N, 5.7. Found: C, 82.5; H, 5.5; N, 5.7.

4-(2-Fluorophenyl)-2-methylquinoline-3-carboxaldehyde, **7a**.

Activated manganese dioxide, 50 g., was added to s solution of 5.4 g. of **4** in 200 ml. of methylene chloride in two portions at a 3 hour interval. After stirring over night, another portion of manganese dioxide, 25 g. was added and stirring was continued for another 3 hours. The manganese dioxide has separated by filtration over Celite and washed well with methylene chloride. The filtrate was evaporated and the residue was crystallized from methylene chloride/hexane to yield 4.4 g. (83%) of product with m.p. 108-111°. The analytical sample was recrystallized from the same solvents, m.p. 111-112°; uv: λ max 249 mμ (ε = 42,600), 291 (8,800), 328 (2,045), infl 345 (1,700); ir (chloroform): 1700 cm^{-1} (CO).

Anal. Calcd. for $C_{17}H_{12}FNO$: C, 77.0; H, 4.5; N, 5.3. Found: C, 77.0; H, 4.2; N, 5.2.

3-Acetyl-6-chloro-4-(2-fluorophenyl)-2-methylquinoline, **7b**.

A mixture of 50 g. (0.2 mole) of 4-chloro-2-(2-fluorobenzoyl)-aniline, **1b**, (4) 40 g. (0.4 mole) of acetylacetone, 10 g. of zinc chloride and 1 l. of toluene was heated to reflux with separation of water for 6 hours. The reaction mixture was washed with water, dried and evaporated. Crystallization from hexane yielded 42 g. (67%) of product with m.p. 113-116°. For analysis it was recrystallized twice from aqueous ethanol, m.p. 121-123°; uv: λ max 238 mμ (ε = 42,000), 271 (5,950), 316 (3,250), 329 (3,780); ir (chloroform): 1705 cm^{-1} (CO).

Anal. Calcd. for $C_{18}H_{13}ClFNO$: C, 68.9; H, 4.2; N, 4.5. Found: C, 68.6; H, 4.4; N, 4.5.

6-Chloro-4-(2-fluorophenyl)quinoline-3-carboxaldehyde, **8**.

A mixture of 24.9 g. (0.1 mole) of **1b**, 24.6 g. (0.15 mole) of 1,1,3,3-tetramethoxypropane, 20 g. of zinc chloride and 500 ml. of toluene was heated to reflux for 1½ hours. The cold reaction mixture was washed with water, dried and evaporated. The red

oil was chromatographed over 600 g. of silica gel using 10% (v/v) of ethyl acetate in methylene chloride. Crystallization of tlc-homogenous material from hexane yielded 10.7 g. (37.5%) of light yellow crystals with m.p. 124-126°; uv: λ max 250 mμ (ε = 50,400), 287 (8,800), infl 325 (1,700), 332 (1,780), 345 (1,750); ir (chloroform): 1695 cm^{-1} (CO).

Anal. Calcd. for $C_{16}H_9ClFNO$: C, 67.3; H, 3.2; N, 4.9. Found: C, 67.2; H, 3.2; N, 4.9.

9-Methyl-6,7,8,8a-tetrahydroimidazo[1′,2′-1,2]quino[3,4-*c*]quinoline, **9a**.

A mixture of 2.65 g. (0.01 mole) of **7a**, 10 ml. of ethylenediamine and 40 ml. of toluene was heated to reflux with separation of water for 1 hour. The reaction mixture was diluted with methylene chloride and washed with aqueous sodium bicarbonate solution, dried and evaporated. The residue was crystallized from methylene chloride/hexane to leave 1.8 g. (63%) of product with m.p. 174-177°. Recrystallization from the same solvents afforded yellow crystals with m.p. 174-178°; uv: λ max 217 mμ (ε = 38,400), 248 (32,500), 311 (6,450), infl 330 (4,450), 390 (3,750); nmr (deuteriochloroform): δ 2.15 ppm (broad s, 1, NH) 2.9 (s, 3, CH_3) 3.3 (broad m, 4, CH_2) 5.15 (s, 1, $-CH<^{N}_{N}$) 6.7-8.6 (m, 8, aromatic H) Ms m/e 287, M^+.

Anal. Calcd. for $C_{19}H_{17}N_3$: C, 79.4; H, 6.0; N, 14.6. Found: C, 79.4; H, 5.9; N, 14.7.

13-Chloro-8a,9-dimethyl-6,7,8,8a-tetrahydroimidazo[1′,2′-1,2]-quino[3,4-*c*]quinoline, **9b**.

A solution of 3.13 g. (0.01 mole) of **7b** in 10 ml. of ethylene diamine was heated to reflux for 3 days. The reaction mixture was poured into water and extracted with methylene chloride. The extracts were washed with water, dried and evaporated. The residue was chromatographed over 50 g. of silica gel using 20% ethanol in ethyl acetate. The clean fractions were combined and evaporated. Crystallization from ethanol yielded 0.4 g. (12%) of yellow crystals with m.p. 168-170°; uv: λ max 230 mμ (ε = 48,000), sh 245 (29,500), 295 (7,950) sh 309 (7,050), 336 (3,400), 412 (4,800); nmr (deuteriochloroform): δ 1.27 ppm (s, 1, CH_3) 2.32 (broad s, 1, NH) 3.0 (s, 3, CH_3) 3.47 (broad m, 4, CH_2) 6.65-8.5 (m, 7, aromatic H).

Anal. Calcd. for $C_{20}H_{18}ClN_3$: C, 71.5; H, 5.4; N, 12.5. Found: C, 71.5; H, 5.4; N, 12.4.

4-(2-Fluorophenyl)-2-methylquinoline-3-carboxaldoxime, **10a**.

A mixture of 10.6 g. (0.04 mole) of **7a**, 7 g. (0.1 mole) of hydroxylamine hydrochloride, 8.2 g. (0.1 mole) of sodium acetate and 250 ml. of ethanol was heated to reflux for 1 hour. The ethanol was evaporated under reduced pressure and the residue was partitioned between ether and water. The precipitated crystals were collected and recrystallized from ethanol to yield 6.2 g. (55%) of product with m.p. 212-214°.

Anal. Calcd. for $C_{17}H_{13}FN_2O$: C, 72.8; H, 4.7; N, 10.0. Found: C, 73.0; H, 4.8; N, 10.0.

6-Chloro-4-(2-fluorophenyl)quinoline-3-carboxaldoxime, **10b**.

A mixture of 8.57 g. (0.03 mole) of **8**, 4.2 g. (0.06 mole) of hydroxylamine hydrochloride, 4.8 g. (0.059 mole) of sodium acetate and 400 ml. of ethanol was stirred and heated to reflux for 1 hour. The ethanol was evaporated under reduced pressure and the residue was partitioned between water and 100 ml. of methylene chloride. The crystalline insoluble material was collected to yield 7.5 g. (83%) of colorless crystals with m.p. 242-245°. The analytical sample was recrystallized from tetrahydrofuran/ethanol, m.p. 248-250°.

Anal. Calcd. for $C_{16}H_{10}ClFN_2O$: C, 63.9; H, 3.4; N, 9.3. Found: C, 64.0; H, 3.4; N, 9.3.

6-Methyldibenzo[*c*,*f*][2,7]naphthyridine 8-oxide, **11a**.

A mixture of 5.6 g. (0.02 mole) of **10a**, 125 ml. of ethanol and 3 ml. (0.02 mole) of 40% aqueous sodium hydroxide was heated to reflux for 5 minutes. The product was precipitated by addition of water, was collected, washed with water and recrystallized from ethanol/methylene chloride to yield 3.7 g. (71%) of yellowish crystals with m.p. 235-238°; uv: λ max 239 mμ (ε, 22,800), 259 (22,000), infl 283 (26,500), 292 (30,000), sh 307 (15,500), 320 (15,700), sh 354 (14,250), 364 (15,000).

Anal. Calcd. for $C_{17}H_{12}N_2O$: C, 78.6; H, 4.6; N, 10.8. Found: C, 78.6; H, 4.4; N, 10.9.

2-Chlorodibenzo[*c*,*f*][2,7]naphthyridine 8-oxide, **11b**.

A mixture of 12 g. (0.04 mole) of **10b**, 25 ml. of 3*N* sodium hydroxide solution and 250 ml. of ethanol was heated to reflux for 10 minutes. The crystalline yellow product was collected, washed with water and ethanol and recrystallized from ethanol/methylene chloride to yield 9.1 g. (81%) with m.p. 284-286°; uv: λ max 212 mμ (ε = 23,800), 238 (25,500), 259 (20,200), 291 (27,600), 319 (19,200), 346 (13,400), 360 (15,000), sh 395 (2,500).

Anal. Calcd. for $C_{16}H_9ClN_2O$: C, 68.5; H, 3.2; N, 10.0. Found: C, 68.4; H, 3.1; N, 10.0.

3-Acetyl-6-chloro-4-(2-fluorophenyl)-2(1*H*)quinolone, **13**.

Diketene, 10 ml., was added to a solution of 25 g. (0.1 mole) of **1b** in pyridine. After the strongly exothermic reaction had subsided, the solvent was evaporated and the residue was crystallized by addition of benzene. The crystals were collected and washed with ethanol and ether to leave 29.7 g. (94%) of product which was recrystallized from benzene/methanol for analysis, m.p. 254-256° dec.

Anal. Calcd. for $C_{17}H_{11}ClFNO_2$: C, 64.7; H, 3.5; N, 4.4. Found: C, 64.6; H, 3.6; N, 4.7.

6-Chloro-4-(2-fluorophenyl)-3-hydroxymethylquinolin-2(1*H*)one, **14**.

A solution of 3.5 g. (0.01 mole) of ethyl 6-chloro-4-(2-fluorophenyl)quinolin-2(1*H*)one-3-carboxylate, **12**, (3) in 50 ml. of tetrahydrofuran was added to a suspension of 1 g. (0.022 mole) of lithium aluminum hydride in 50 ml. of tetrahydrofuran. After stirring for 30 minutes at -20° to 0°, the hydride was hydrolized by addition of 5 ml. of water. The mixture was then partitioned between methylene chloride and 2*N* hydrochloric acid. The methylene chloride layer was washed with water, dried and evaporated. Crystallization of the residue from ethanol/chloroform yielded 2.5 g. (82%) of product with m.p. 282-286°; uv: λ max 210 mμ (ε = 37,000), infl 235 (40,500), 240 (42,500), infl 262 (7,800), 271 (6,850), sh 280 (5,850), infl 330 (4,900), 344 (6,430), infl 358 (4,800), ir (potassium bromide): 1650 cm^{-1} (CO); nmr (d-DMSO): δ 4.23 ppm (m, 2, AB-part of ABX-system, $-CH_2O$) ($J_{AX} = J_{BX}$ = 5.5 Hz, J_{AB} = 12 Hz), 4.76 (t, 1, J = 5.5 Hz, OH) 6.86 (s, with fine structure, 1, C_5-H), 7.1-7.9 (m, 6, aromatic H) 12.3 (broad s, 1, NH).

Anal. Calcd. for $C_{16}H_{11}ClFNO_2$: C, 63.3; H, 3.7; N, 4.6. Found: C, 63.4; H, 3.8; N, 4.4.

6-Chloro-4-(2-fluorophenyl)-3-[1-(hydroxyimino)ethyl]-2(1*H*)-quinolone, **15**.

A mixture of 3.15 g. (0.01 mole) of **13**, 1.4 g. (0.02 mole) of hydroxylamine hydrochloride, 1.65 g. (0.02 mole) of sodium acetate and 60 ml. of ethanol was heated to reflux for 1 hour. Half of the solvent was distilled off and the product was crystallized by

addition of water. It was collected, washed with water and recrystallized from ethanol/tetrahydrofuran to yield 2.5 g. (76%) of colorless prisms which transformed into needles at 255-260° and did not melt completely until 330°; nmr (DMSO): δ 1.72 ppm (s, *ca.* 0.5) and 1.9 (s, *ca.* 2.5) (-CH_3 of syn and antioxime) 6.8 (s with fine structure, 1, C_5-H) 7-7.7 (m, 6,-aromatic H) 10.9 (broad s, 1, OH) 12.3 (broad s, 1, NH).

Anal. Calcd. for $C_{17}H_{12}ClFN_2O_2$: C, 61.7; H, 3.7; N, 8.5. Found: C, 61.7; H, 4.0; N, 8.5.

2-Chloro-7*H*-chromeno[3,4-*c*]quinolin-6(5*H*)one **16a**.

Sodium hydride suspension (50% in mineral oil), 10 g., was washed with hexane and added to a solution of 20 g. (0.066 mole) of **14** in 350 ml. of dimethylformamide. This mixture was stirred and refluxed under an atmosphere of nitrogen for 5 minutes. The cool reaction mixture was diluted with water and the product was precipitated by acidifying with 1 *N* hydrochloric acid. It was collected, washed with water and recrystallized from dimethylformamide to yield 9.5 g. (50.5%) with m.p. > 350°. uv: λ infl 250 mμ (ε = 24,250), max 284 (6,000), 295 (7,200), 336 (9,600), infl 352 (8,800), infl 369 (4,600); ir (potassium bromide): 3150 cm^{-1} (NH) 1655 (CO); MS m/e 283 (M^+).

Anal. Calcd. for $C_{16}H_{10}ClNO_2$: C, 67.7; H, 3.5; N, 4.9. Found: C, 67.9; H, 3.5; N, 4.7.

2-Chloro-7-methyldibenzo[*c*,*f*][2,7]naphthridin-6(5*H*)one 8-oxide, **17**.

A mixture of 3.3 g. (0.01 mole) of **15**, 50 ml. of ethanol and 2.5 ml. of 40% aqueous sodium hydroxide was heated to reflux for 2 hours. The hot mixture was then acidified with 3 *N* hydrochloric acid and the precipitated product was collected and recrystallized form dimethylformamide to yield 2.3 g. (74%) of yellow needles with m.p. 315-320° dec.

Anal. Calcd. for $C_{17}H_{11}ClN_2O_2$: C, 65.7; H, 3.6; N, 9.0. Found: C, 65.6; H, 3.7; N, 8.9.

2-Chloro-5-(2-diethylaminoethyl)-4,7-dihydro-6*H*-chromeno[3,4-*c*]-quinolin-6-one (**16b**) and 2-Chloro-6-(2-diethylaminoethoxy)-7*H*-chromeno[3,4-*c*]quinoline (**18**).

A suspension of 9.5 g. (0.033 mole) of **16a** in 500 ml. of dry dimethylformamide was heated to 120° when 2.74 g. (0.057 mole) of sodium hydride suspension (50% in mineral oil) was added. The mixture was stirred without heating for 5 minutes. A solution of 19.7 g. (0.06 mole) of 2-(diethylamino)ethylchloride in 25 ml. of benzene was added at 80°. After stirring for 30 minutes the reaction mixture was diluted with ice/water. The precipitated solids were collected and dissolved in benzene. The benzene solution was dried and evaporated. Crystallization from hexane and recrystallization from methanol yielded 3 g. (23.5%) of **16b** with m.p. 101-103°; uv (2-propanol): λ max 235 mμ (ε = 41,000), sh 253 (27,000), 289 (6,000), 298 (7,450), 340 (9,800), infl 353 (9,000), infl 370 (5,100); ir (chloroform): 1640 cm^{-1} (C=O); nmr (deuteriochloroform): δ 1.10 ppm (t, 6, J = 7 Hz, CH_3) 2.4-3.0 (m, 6, N-CH_2-) 4.47 (m, 2, N-CH_2) 5.10 (s, 2, OCH_2) 7-8.3 (m, 7, aromatic H).

Anal. Calcd. for $C_{22}H_{23}ClN_2O_2$: C, 69.0; H, 6.1; N, 7.3. Found: C, 68.5; H, 6.1; N, 7.2.

The original mother liquor was heated with ethanolic hydrogen chloride and the crystalline hydrochloride was reconverted to the free base by partitioning between aqueous sodium carbonate solution and benzene. The benzene solution was dried and evaporated. The residue was crystallized from methanol/water to yield 1.6 g. (12.5%) of **18** with m.p. 76-78°; uv (2-propanol): λ max 227 mμ (ε = 42,000), sh 242 (31,200), sh 273 (5,900), 285 (6,000), 297 (7,200), infl 323 (9,000) 334 (10,600), 348 (8,800); ir (chloroform): no carbonyl; nmr (deuteriochloroform): δ 1.10 ppm (t, 6, J = 7 Hz, -CH_3) 2.66 (q, 4, J = 7 Hz, -N-CH_2-CH_3) 2.92 (t, 2, J = 6 Hz, -CH_2-CH_2N) 4.58 (t, 2, J = 6 Hz, O-CH_2-CH_2) 5.11 (s, 2, OCH_2) 7-8.5 (m, 7, aromatic H).

Anal. Calcd. for $C_{22}H_{23}ClN_2O_2$: C, 69.0; H, 6.1; N, 7.3. Found: C, 68.9; H, 6.0; N, 7.3.

7-Acetoxymethyl-2-chlorodibenzo[*c*,*f*][2,7]naphthyridin-7(5*H*)-one, **19a**.

A mixture of 6.2 g. (0.02 mole) of **17** and 50 ml. of acetic anhydride was heated to reflux for 2 hours. The crystals were collected from the cooled reaction mixture and washed with ethanol and ether to leave 5.4 g. (75%) of tan product with m.p. 285-295° dec. For analysis it was recrystallized from dimethylformamide, m.p. 298-305°; nmr (DMSO): δ 2.33 ppm (s, 3, $COCH_3$) 6.14 (s, 2, -CH_2-O) 7.6-8.8 (m, 7, aromatic H) 12.2 (broad s, 1, NH).

Anal. Calcd. for $C_{19}H_{13}ClN_2O_3$: C, 64.7; H, 3.7; N, 7.9. Found: C, 64.5; H, 3.8; N, 8.0.

2-Chloro-7-hydroxymethyldibenzo[*c*,*f*][2,7]naphthyridin-6(5*H*)-one, **19b**.

A mixture of 7 g. (0.02 mole) of **19a**, 500 ml. of ehtanol and 50 ml. of 1 *N* sodium hydroxide solution was heated until solution was complete. The solution was acidified with acetic acid and the precipitated crystals were collected and recrystallized from dimethylformamide to yield 4.1 g. (66%) of yellowish fine needles with m.p. 305-310° dec.

Anal. Calcd. for $C_{17}H_{11}ClN_2O_2$: C, 65.7; H, 3.6; N, 9.0. Found: C, 65.7; H, 3.4; N, 9.0.

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