

about 100 ml. and cooling caused the separation of some unreacted *o*-nitrocinnamic acid. Further concentration yielded some additional *o*-nitrocinnamic acid (total recovery, 1.3 g.). Continued concentration then yielded the crystalline adduct XIV, which was collected by filtration, washed with 95% ethanol and recrystallized from acetone to give 8.9 g. (55% based on *o*-nitrocinnamic acid, corrected for recovered material). The product was purified readily by sublimation at 170° (0.3 mm.), m.p. 187–188°.

*Anal.* Calcd. for  $C_{18}H_{13}NO_4$ : C, 63.15; H, 5.30; N, 5.67. Found: C, 63.42; H, 5.43; N, 5.64.

**6a,7,10,10a-Tetrahydro-6(5)-phenanthridinone (XV).**—A mixture of 5 g. of 2-(*o*-nitrophenyl)- $\Delta^4$ -tetrahydrobenzoic acid, 17.5 g. of sodium hydrosulfite and 100 ml. of 10% sodium hydroxide solution was heated under reflux for 70 minutes and then acidified with glacial acetic acid. The colorless product (2.3 g.) was collected and sublimed at 205° (0.08 mm.), m.p. 231–236°. The above filtrate was evaporated to dryness and the residue extracted with ether in a Soxhlet apparatus for eight hours. Evaporation of the ether yielded an additional 0.15 g. of product; total yield, 2.5 g. (62%). The product was purified by sublimation, m.p. 235.5–237.5°.

*Anal.* Calcd. for  $C_{13}H_{13}NO$ : C, 78.36; H, 6.58; N, 7.03. Found: C, 78.57; H, 6.47; N, 7.02.

**6a,7,8,9,10,10a-Hexahydro-6(5)-phenanthridinone (XVI).**—A solution of 2.47 g. of 2-(*o*-nitrophenyl)- $\Delta^4$ -tetrahydrobenzoic acid in 100 ml. of purified dioxane was shaken with four atmospheres of hydrogen in the presence of Raney nickel at room temperature for 13.5 hours. Removal of the catalyst by filtration and dilution of the filtrate with 200 ml. of water caused the separation of 1.64 g. of product, m.p. 226–227°. Concentration of the filtrate to about 100 ml. yielded an additional 0.11 g. of crude product. Sublimation of the combined material at 210° (0.5 mm.) then yielded 1.69 g. (84%) of white crystals, m.p. 226–228°.

*Anal.* Calcd. for  $C_{18}H_{15}NO$ : C, 77.57; H, 7.51; N, 6.96. Found: C, 77.75; H, 7.43; N, 7.09.

Reduction of 6a,7,10,10a-tetrahydro-6(5)-phenanthridinone (XV) under similar conditions yielded XVI in 90% yield.

**6(5)-Phenanthridinone (XVII).**—An intimate mixture of 1.44 g. of 6a,7,8,9,10,10a-hexahydro-6(5)-phenanthridinone and 3.0 g. of sulfur was heated for one hour at 170–180°, for another hour at 225–230°, and finally at 250° for 30 minutes. After cooling, the solid mass was powdered and extracted with 100 ml. of boiling carbon disulfide. The insoluble residue was purified by sublimation at 230° (0.5 mm.) to give 0.71 g. (51%) of pure 6(5)-phenanthridinone, m.p. 290–293°, identical in all respects with an authentic sample.

PRINCETON, NEW JERSEY

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

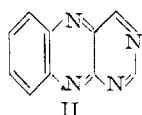
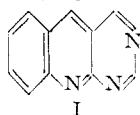
## The Synthesis of Pyrimido[4,5-*b*]quinolines<sup>1-3</sup>

By E. C. TAYLOR, JR.,<sup>4</sup> AND NORMAN W. KALENDA

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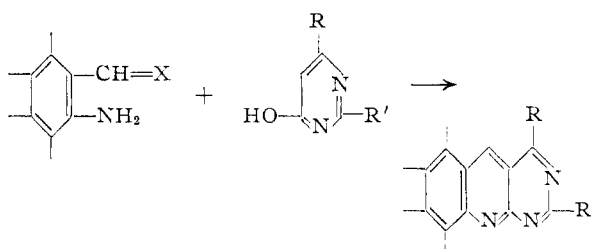
A number of pyrimido[4,5-*b*]quinolines (I) of interest because of structural similarity to the flavins have been prepared by four independent routes which are described in detail. Method 1 involves the cyclization of 2-aminoquinoline-3-carboxamide with reagents such as formamide, acetic anhydride, phenyl isocyanate, phenyl isothiocyanate and diethyl carbonate to give a variety of 4-hydroxypyrimido[4,5-*b*]quinolines. Method 2 involves the cyclization of 2-amino-3-cyanoquinoline with reagents such as ammonia, urea and formamide to give derivatives of 4-aminopyrimido[4,5-*b*]quinoline. Method 3 involves preliminary reduction of 2-amino-3-cyanoquinoline to 2-amino-3-aminomethylquinoline, followed by cyclization with a variety of reagents to a series of 3,4-dihydropyrimido[4,5-*b*]quinolines. Method 4 involves the synthesis and subsequent nucleophilic displacement reactions of 2,4-dichloropyrimido[4,5-*b*]quinoline.

Relatively little has been reported on the synthesis and properties of pyrimido[4,5-*b*]quinolines, although this system (I) is of interest because of its structural similarity to the pyrimido[4,5-*b*]quinoxaline ring system (II) of the naturally-occurring flavins. Most of the known pyrimido[4,5-*b*]quinolines were prepared by the condensation of barbi-



turic acid with *o*-aminobenzaldehydes<sup>5-8</sup> and with *o*-aminobenzilidinetoluidines,<sup>9</sup> and the reaction has been extended to include the condensation of

*o*-aminobenzaldehyde with a number of pyrimidine derivatives related to barbituric acid.<sup>8</sup> An alternative route to these compounds involved the condensation of barbituric acid with isatin and N-



methylisatin to give 3,3-di-(5-barbituryl)-oxindole and its N-methyl derivative, followed by cyclization of these intermediates with acid to give 2,4-dihydroxypyrimido[4,5-*b*]quinoline-5-carboxylic acid and the 10-methyl derivative, respectively. Standard transformations operating on the 5-carboxylic acid group provided a number of additional derivatives.<sup>10</sup>

In all these synthetic procedures, the pyrimidine ring of the product was constructed from a pre-

(1) Supported in part by a grant (NSF-G1095) from the National Science Foundation.

(2) Taken in part from the doctoral dissertation of N.W.K., University of Illinois, 1955.

(3) Presented before the Division of Medicinal Chemistry of the 128th National ACS Meeting, September, 1955, in Minneapolis, Minnesota.

(4) Frick Chemical Laboratory, Princeton University.

(5) M. Conrad and H. Reinbach, *Ber.*, **34**, 1339 (1901).

(6) J. Tröger and C. Cohaus, *J. prakt. Chem.*, **117**, 97 (1927).

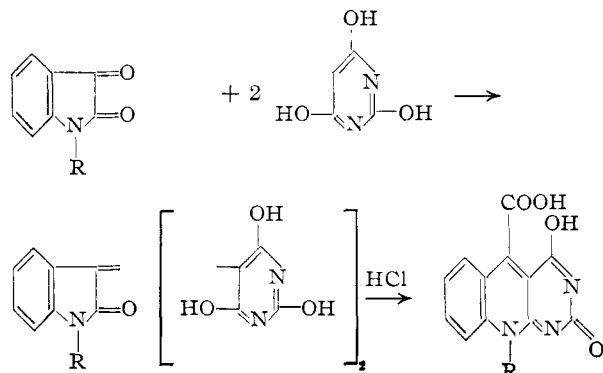
(7) J. Tröger and St. Gerö, *ibid.*, **113**, 293 (1926).

(8) F. E. King and T. J. King, *J. Chem. Soc.*, 726 (1947).

(9) W. Borsche, M. Wagner-Roemmich and J. Barthenheier, *Ann.*, **550**, 160 (1942).

(10) F. E. King, T. J. King and G. B. Thompson, *J. Chem. Soc.*, 552 (1948).

formed pyrimidine reactant, and the substitution achieved in the pyrimidine ring of the product was thus dependent upon an appropriate choice of starting material. Since the type of pyrimidine which can serve as reactant is severely limited, these routes lack flexibility and versatility. King and King,<sup>8</sup> for example, have shown that *o*-aminobenzaldehyde will not condense with pyrimidines in which triketo isomerism is excluded.



Four new synthetic routes which offer more flexibility and which allow the preparation of many derivatives unavailable by the previously described methods have now been developed. Route 1 involves the cyclization of 2-aminoquinoline-3-carboxamide (III) with reagents such as formamide, acetic anhydride, phenyl isocyanate, phenyl isothiocyanate and diethyl carbonate to give a variety of 4-hydroxypyrimido(4,5-*b*)quinolines. Method 2 involves the cyclization of 2-amino-3-cyanoquinoline (XVIII) to give derivatives of 4-aminopyrimido(4,5-*b*)quinoline. Method 3 involves preliminary reduction of 2-amino-3-cyanoquinoline to 2-amino-3-aminomethylquinoline (XXIII) followed by cyclization with a variety of reagents to a series of 3,4-dihydropyrimido(4,5-*b*)quinolines. Method 4 involves the synthesis and subsequent nucleophilic displacement reactions of 2,4-dichloropyrimido(4,5-*b*)quinoline (XXXIII). In the first three of these methods, the pyrimidine ring of the final product is formed during the final cyclization reaction. These methods are thus independent of a preformed reactant and appear to offer a convenient and versatile route to a variety of hitherto unavailable derivatives of pyrimido(4,5-*b*)quinoline. The present paper presents the details of these cyclization procedures and describes a number of new derivatives of this ring system.

**Method 1. Cyclizations with 2-Aminoquinoline-3-carboxamide (III).**—The cyclization of an *o*-aminoamide with suitable one-carbon intermediates has been widely used for the preparation of numerous heterocyclic systems containing a fused pyrimidine ring.<sup>11</sup> We have now found that a

variety of pyrimido(4,5-*b*)quinolines may be formed by adaptations and extensions of these cyclization procedures, utilizing 2-aminoquinoline-3-carboxamide (III)<sup>12</sup> as the requisite intermediate. Thus, 4-hydroxypyrimido(4,5-*b*)quinoline (IV) was prepared by the cyclization of III with formamide at 160–170° for 2 hr. An alternative synthesis of IV with ethyl orthoformate and acetic anhydride yielded, in addition, a lower melting solid with the empirical formula C<sub>17</sub>H<sub>17</sub>N<sub>3</sub>O<sub>4</sub>. This latter compound was the major product of the reaction of III with a large excess of ethyl orthoformate and acetic anhydride. Examination of the infrared spectrum of the compound showed the absence of any bands in the N–H stretching region, the presence of two carbonyl bands at 1693 and 1711 cm.<sup>–1</sup> and the presence of two prominent bands at 1070 and 1235 cm.<sup>–1</sup>, which may be assigned to a carbon–oxygen single bond. The compound would thus appear to be 1,3-diacetyl-2-ethoxy-1,2,3,4-tetrahydropyrimido(4,5-*b*)quinoline-4-one (V), and its mode of formation from III may be pictured as resulting from initial reaction of III with ethyl orthoformate to give an intermediate ethyl N-substituted formimidate Va,<sup>13</sup> which then undergoes ring closure to Vb, and this is followed by acetylation to yield V. It is curious that the cyclization of related β-aminocarboxamides with ethyl orthoformate and acetic anhydride apparently fails to yield products analogous to V.<sup>14,15</sup> Cyclization of III with acetic anhydride in the presence of sulfuric acid, followed by treatment of the product with dilute alkali and subsequent reacidification, gave 2-methyl-4-hydroxypyrimido(4,5-*b*)quinoline (VI) in good yield.

In an attempt to prepare a monobenzoyl derivative of III which could be cyclized to 2-phenyl-4-hydroxypyrimido(4,5-*b*)quinoline (VIII), III was treated with an equivalent amount of benzoyl chloride in pyridine solution. A water-soluble product was formed which reverted to III when treated with dilute alkali. Excess benzoyl chloride in pyridine solution converted III into a dibenzoyl derivative, which by analogy with the dibenzoyl derivative obtained from 2-aminopyridine under similar conditions,<sup>14</sup> is probably 1-benzoyl-2(1*H*)benzimidazoquinoline-3-carboxamide (VII). The water-soluble product above is therefore probably the 1-benzoyl derivative of III. Attempts to cyclize VII with cold sodium hydroxide or cold sodium ethoxide were unsuccessful.

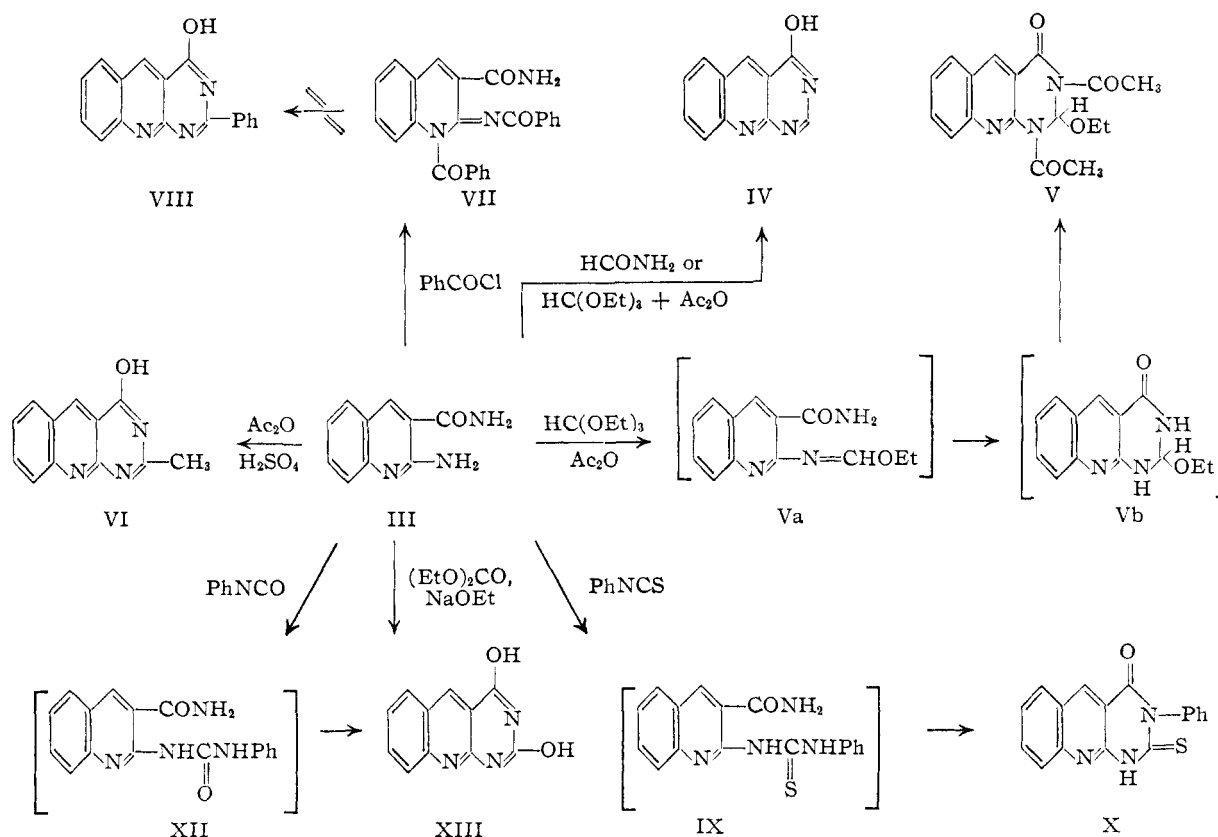
The reaction of III with phenyl isothiocyanate in pyridine solution gave 3-phenylpyrimido(4,5-*b*)quinoline-2(1*H*)-thione-4(3*H*)-one (X) in good yield. No 2-(3-phenylthioureido)-quinoline-3-carboxamide (IX) was isolated from the reaction, although it probably was formed and underwent cyclization with loss of ammonia to give X. However, the reaction of III with phenyl isocyanate under similar conditions did not give 3-phenyl-

(11) See, for example, (a) W. Abt, *J. prakt. Chem.*, **39**, 140 (1889); (b) A. H. Gowenlock, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 517 (1948); (c) A. Albert, D. J. Brown and G. Cheeseman, *ibid.*, 474 (1951); (d) E. C. Taylor, Jr., J. A. Carbon and D. R. Hoff, *THIS JOURNAL*, **75**, 1904 (1953); (e) J. Sarasin and E. Wegmann, *Helv. Chim. Acta*, **7**, 713 (1924); (f) A. H. Cook and E. Smith, *J. Chem. Soc.*, 2329 (1949); (g) F. G. Mann and J. W. G. Porter, *ibid.*, 761 (1945); (h) E. C. Taylor, Jr., R. B. Garland and C. F. Howell, *THIS JOURNAL*, **78**, 211 (1956).

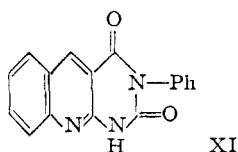
(12) For the synthesis and proof of structure of this compound, previously reported to be a dihydroindole, see E. C. Taylor, Jr., and N. W. Kalenda, *J. Org. Chem.*, **18**, 1755 (1953).

(13) R. M. Roberts and R. H. DeWolfe, *THIS JOURNAL*, **76**, 2411 (1954).

(14) S. J. Angyal, W. O. Morris and W. K. Warburton, *Aust. J. Sci. Research*, **A5**, 368 (1952).

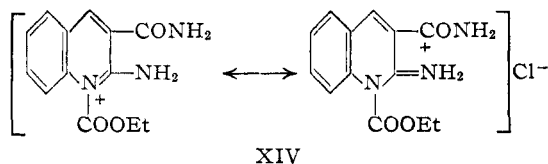


pyrimido(4,5-*b*)quinoline-2,4(1*H*,3*H*)-dione (XI) as expected



but rather 2,4-dihydroxypyrimido(4,5-*b*)quinoline (XIII). Evidently 2-(3-phenylureido)-quinoline-3-carboxamide (XII) which was formed initially underwent subsequent ring closure with loss of aniline rather than ammonia. This mode of cyclization was unexpected, since it has been shown that 2-amino-5,6-diphenylpyrazine-3-carboxamide yields 3,6,7-triphenylpteridine-2,4-(1*H*,3*H*)-dione upon treatment with phenyl isocyanate and pyridine under similar conditions.<sup>11b</sup>

2,4-Dihydroxypyrimido(4,5-*b*)quinoline (XIII) was prepared independently by the reaction of III with diethyl carbonate in sodium ethoxide solution. An attempt to prepare XIII by the reaction of III with ethyl chloroformate led instead to a yellow solid, m.p. 288–289°, which regenerated III upon treatment with cold, dilute alkali. This solid is probably XIV, since the alternative 2-carbethoxyaminoquinoline-3-carboxamide structure would



not be expected to be so labile to cold dilute alkali.

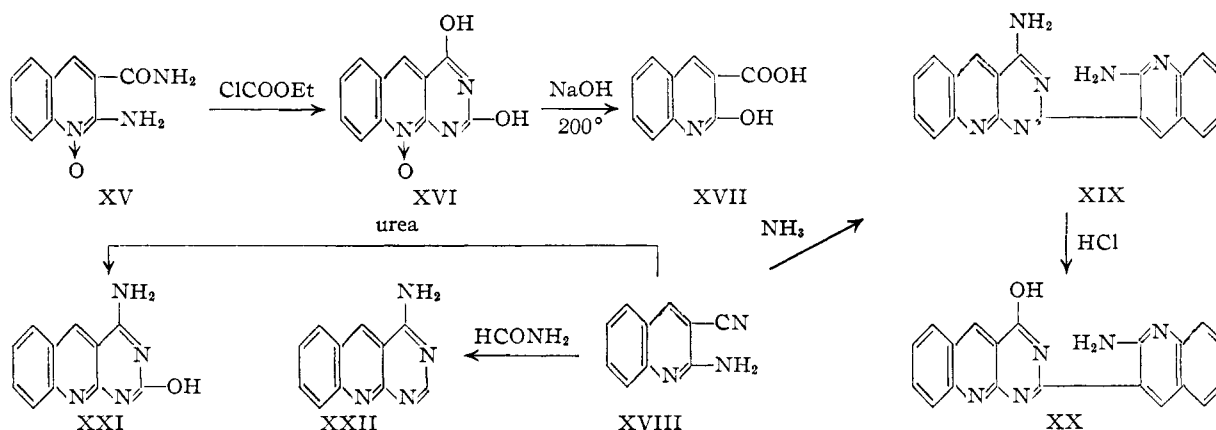
In this connection, it is interesting that 2-aminoquinoline-3-carboxamide-1-oxide (XV)<sup>12</sup> reacted with ethyl chloroformate under similar conditions to give 2,4-dihydroxypyrimido(4,5-*b*)quinoline-10-oxide (XVI). Hydrolysis of XVI with 5 *N* sodium hydroxide at 200° gave 2-hydroxyquinoline-3-carboxylic acid (XVII). Evidently the high temperature under which the hydrolysis was effected caused deoxygenation of the *N*-oxide function. Similar high temperature deoxygenations with *N*-oxides of pyridine and quinoline have been reported.<sup>15</sup> Attempts to prepare XVI by fusion with urea or by treatment with diethyl carbonate and sodium ethoxide were unsuccessful.

**Method 2. Cyclizations with 2-Amino-3-cyanoquinoline (XVIII).**—The formation of a fused pyrimidine ring by reaction of an appropriate reagent with an *o*-aminonitrile has seen recent application in the synthesis of pteridines<sup>16</sup> and pyrazolo(3,4-*b*)pyrimidines.<sup>17</sup> Since 2-amino-3-cyanoquinoline (XVIII) is now readily available,<sup>12</sup> we attempted a number of cyclizations with it in the hope of developing another general synthetic route to the pyrimido(4,5-*b*)quinolines. Unfortunately, the nitrile group of XVIII is not as reactive as in previously employed *o*-aminocyan intermediates, and these efforts met with only moderate success. Thus, no definable product could be isolated from the reaction of XVIII with dicyandi-

(15) M. Katada, *J. Pharm. Soc. Japan*, **67**, 53 (1947); *C.A.*, **45**, 9536f (1951).

(16) E. C. Taylor, Jr., and W. W. Paudler, *Chem. and Ind.*, 1061 (1955).

(17) R. K. Robins, *THIS JOURNAL*, **78**, 784 (1956).



amide in acid or alkaline solution,<sup>18</sup> with *S*-methylisothiourea hydroiodide or with phenyl isothiocyanate and pyridine. However, the reaction of XVIII with liquid ammonia in a sealed steel bomb gave a product which is assigned the structure 2-[3-(2-aminoquinolinyl)]-4-aminopyrimido(4,5-*b*)-quinoline (XIX) on the basis of analysis and mode of formation.<sup>19</sup> XIX was readily hydrolyzed with dilute hydrochloric acid to 2-[3-(2-aminoquinolinyl)]-4-hydroxypyrimido(4,5-*b*)-quinoline (XX). Fusion of XVIII with urea gave 2-hydroxy-4-aminopyrimido(4,5-*b*)-quinoline (XXI), while heating with formamide gave 4-aminopyrimido(4,5-*b*)-quinoline (XXII). The closure of a pyrimidine ring by reaction of formamide with an *o*-aminonitrile has been reported to be unsuccessful in the pyrazine series,<sup>11c</sup> although it is successful in the pyrazole series.<sup>17</sup>

**Method 3. Cyclizations with 2-Amino-3-aminomethylquinoline.**—Reduction of 2-amino-3-cyanoquinoline with Raney nickel and hydrogen at 80° and 1200 p.s.i. for 6 hr. gave 2-amino-3-aminomethylquinoline (XXIII) in high yield. XXIII proved to be a useful intermediate for the synthesis of a number of 3,4-dihydropyrimido(4,5-*b*)-quinolines.<sup>20</sup> Thus, heating a mixture of the formate salt of 2-amino-3-aminomethylquinoline (XXIII) and xylene under reflux and removing the water formed during the reaction as an azeotrope with xylene resulted in the formation of 3,4-dihydropyrimido(4,5-*b*)-quinoline (XXIV). It was found to be more convenient not to isolate the salt but to prepare it in the reaction vessel and to remove the excess formic acid along with the water as an azeotrope with xylene.

(18) The reaction of XVIII with three molar equivalents of dicyandiamide in ethanolic sodium ethoxide solution gave a product, m.p. 309–310°, for which analytical data indicated an empirical formula of (C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O)<sub>2</sub>. The infrared spectrum of this compound showed the presence of several bands (3290, 3400, 3500 cm.<sup>-1</sup>) in the N–H stretching region and the absence of the characteristic nitrile band. No structure could be devised for the compound on the basis of available information.

(19) It has been established recently that 2-amino-3-cyanopyridine undergoes a base-catalyzed dimerization under similar conditions to give 2-[3-(2-aminopyridyl)]-4-aminopyrimido(4,5-*b*)pyridine (analogous to XIX) and that the latter is readily hydrolyzed to the corresponding 4-hydroxy derivative (analogous to XX). This work is being published in detail separately and provides support, by analogy, for the structures assigned here to XIX and XX.

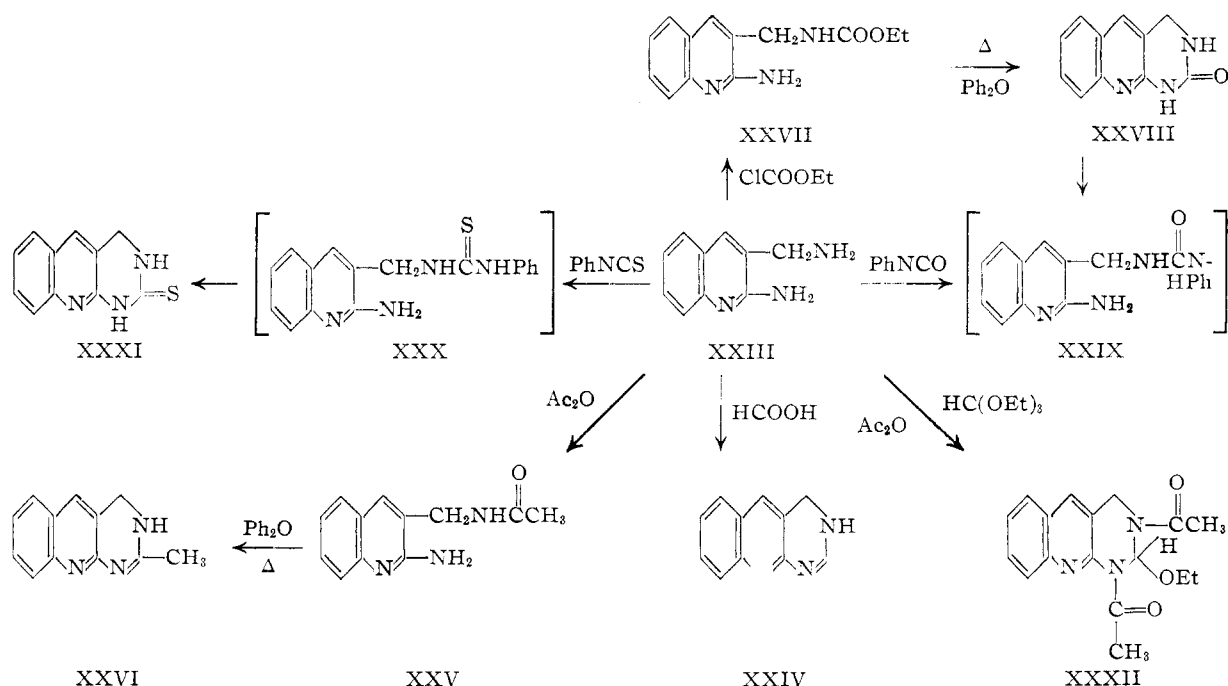
(20) For examples of ring closures of similarly constructed cyclic intermediates to give fused dihydropyrimidines, see P. J. Vanderhorst and C. S. Hamilton, *THIS JOURNAL*, **75**, 656 (1953).

Two acylated derivatives of 2-amino-3-aminomethylquinoline (XXIII), 2-amino-3-acetamidomethylquinoline (XXV) and 2-amino-3-carbethoxyaminomethylquinoline (XXVII), were prepared by conventional methods and cyclized in refluxing diphenyl ether to give 2-methyl-3,4-dihydropyrimido(4,5-*b*)-quinoline (XXVI) and 3,4-dihydropyrimido(4,5-*b*)-quinoline-2(1*H*)-one (XXVIII), respectively. Attempts to cyclize 2-amino-3-acetamidomethylquinoline (XXV) by treating with cold phosphorus oxychloride or by heating under reflux in xylene were unsuccessful. Heating XXV under reflux with phosphorus oxychloride alone or with added phosphorus pentachloride gave mixtures which could not be separated.

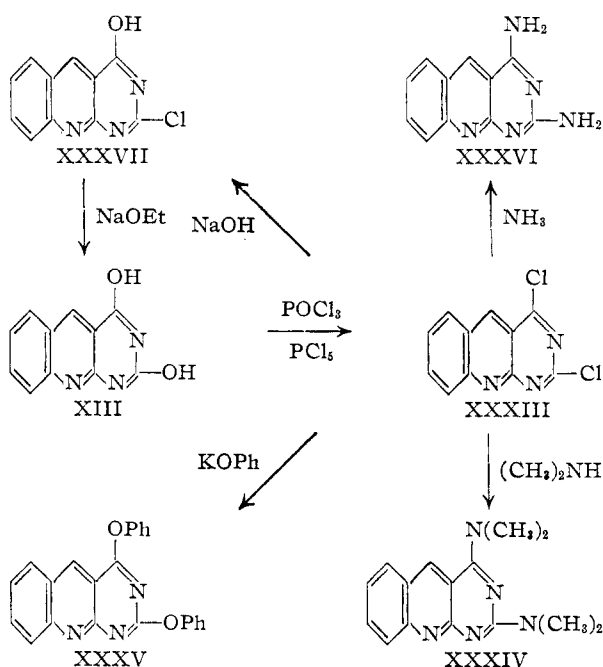
3,4-Dihydropyrimido(4,5-*b*)-quinoline-2(1*H*)-one (XXVIII) was also formed by treatment of 2-amino-3-aminomethylquinoline (XXIII) with a mixture of phenyl isocyanate and pyridine. The intermediate in this reaction was undoubtedly 2-amino-3-(3-phenylureidomethyl)-quinoline (XXIX), which underwent ring closure with elimination of aniline to give XXVIII. Treatment of XXIII with phenyl isothiocyanate in pyridine under similar conditions gave 3,4-dihydropyrimido(4,5-*b*)-quinoline-2(1*H*)-thione (XXXI), which undoubtedly arose by elimination of aniline from the intermediate thioureido derivative XXX.

The reaction of 2-amino-3-aminomethylquinoline (XXIII) with a mixture of ethyl orthoformate and acetic anhydride gave a white solid with the empirical formula C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>. An examination of the infrared spectrum of the compound showed the absence of any band in the N–H stretching region, the presence of a single carbonyl band at 1683 cm.<sup>-1</sup> and a prominent band at 1070 cm.<sup>-1</sup>, which might be attributed to a carbon–oxygen single bond. The compound would thus seem to be similar in properties to V and is assigned the structure 1,3-diacetyl-2-ethoxy-1,2,3,4-tetrahydropyrimido(4,5-*b*)-quinoline (XXXII).

**Method 4. Nucleophilic Displacement Reactions of 2,4-Dichloropyrimido(4,5-*b*)-quinoline (XX-XIII).**—The methods elaborated above for the preparation of derivatives of the pyrimido(4,5-*b*)-quinoline system all involve the fusion of a pyrimidine ring to a suitable quinoline intermediate. A fourth synthetic method for the preparation of 2,4-disubstituted derivatives has been examined which involves the reaction of 2,4-dichloropyr-



imido(4,5-*b*)quinoline (XXXIII) with various nucleophilic reagents. Since the introduction of substituent groups into heterocyclic nuclei by displacement reactions of halogen intermediates is a widely-known and much exploited reaction type,<sup>21-25</sup> only a few typical reactions were carried out with XXXIII in order to establish the order of reac-



tivity of the halogens and to illustrate the general utility of the method.

2,4-Dichloropyrimido(4,5-*b*)quinoline (XXXIII) was prepared by the action of phosphorus oxychloride and phosphorus pentachloride on the corresponding 2,4-dihydroxy derivative XIII. Treatment of XXXIII with aqueous dimethylamine gave 2,4-bis-(dimethylamino)-pyrimido(4,5-*b*)quinoline (XXXIV), while treatment with potassium phenoxide in excess phenol gave the corresponding 2,4-diphenoxy derivative XXXV. From the reaction of XXXIII with liquid ammonia at 150° in a sealed bomb, there was isolated a yellow, high-melting solid which is believed to be 2,4-diaminopyrimido(4,5-*b*)quinoline (XXXVI), although we were unable to purify the compound for analysis.

With cold 1 *N* sodium hydroxide, one chlorine atom of XXXIII was replaced to give what is believed to be 2-chloro-4-hydroxypyrimido(4,5-*b*)quinoline (XXXVII). This structural assignment is supported by the similarity of the ultraviolet absorption spectrum of XXXVII with that of 4-hydroxy- (IV) and 2-methyl-4-hydroxypyrimido(4,5-*b*)quinoline (VI) and is thus in agreement with previous observations made of the enhanced reactivity of the 4-chloro group in the structurally related 2,4-dichloropyrido(2,3-*d*)pyrimidine<sup>26</sup> and 2,4-dichloroquinazoline.<sup>27-29</sup>

An attempt to prepare 2-ethoxy-4-hydroxypyrimido(4,5-*b*)quinoline by the reaction of 2-chloro-4-hydroxypyrimido(4,5-*b*)quinoline (XXXVII) with ethanolic sodium ethoxide yielded only 2,4-dihydroxypyrimido(4,5-*b*)quinoline (XIII). A similar attempt to prepare 2-ethoxy-4-hydroxy-

(21) E. Fischer, "Untersuchungen in der Puringruppe," Springer, Berlin, 1907.

(22) T. B. Johnson and D. A. Hahn, *Chem. Revs.*, **13**, 193 (1933).

(23) T. B. Johnson in "Organic Chemistry, An Advanced Treatise," ed. by H. Gilman, Vol. 2, John Wiley and Sons, New York, N. Y., 1938, p. 948, 1st ed.

(24) R. H. Wiley, *ibid.*, Vol. 4, 1953, p. 723.

(25) A. Bendich in "The Nucleic Acids," ed. by E. Chargaff and J. N. Davidson, Vol. 1, Academic Press, New York, N. Y., 1955, p. 81.

(26) R. K. Robins and G. H. Hitchings, *THIS JOURNAL*, **77**, 2256 (1955).

(27) N. A. Lange, W. E. Roush and H. J. Asbeck, *ibid.*, **52**, 3696 (1930).

(28) N. A. Lange and F. E. Sheibley, *ibid.*, **53**, 3867 (1931).

(29) F. H. S. Curd, J. K. Landquist and F. L. Rose, *J. Chem. Soc.*, 775 (1947).

quinazoline from 2-chloro-4-hydroxyquinazoline under similar conditions was reported to be unsuccessful.<sup>28</sup>

A number of additional displacement reactions involving XXXIII were carried out with apparently anomalous results. A forthcoming communication will be concerned with these latter reactions.

### Experimental<sup>30</sup>

**4-Hydroxypyrimido(4,5-*b*)quinoline (IV).** (a).—A mixture of 2.0 g. of 2-aminoquinoline-3-carboxamide and 30 ml. of formamide was heated for 2 hr. in an oil-bath maintained at 160–170°. Cooling caused the separation of a yellow solid (2.02 g., 96%), m.p. 355.5–356.5° dec. The product was purified by recrystallization from ethanol with no change in melting point.

(b).—A mixture of 3.0 g. of 2-aminoquinoline-3-carboxamide, 50 ml. of ethyl orthoformate and 50 ml. of acetic anhydride was heated under reflux for 3.5 hr. The mixture was then filtered and the dark brown solid which was collected was extracted several times with hot high boiling petroleum ether. The combined extracts were set aside (see below) and the remaining solid sublimed at 200° (0.5 mm.) to give 0.61 g. of a pale yellow solid, m.p. 350–352° dec. Recrystallization from ethanol raised the melting point to 353.5–354.5° dec.

*Anal.* Calcd. for  $C_{11}H_7N_3O$ : C, 67.0; H, 3.6; N, 21.3. Found: C, 67.1; H, 3.3; N, 21.0.

The products obtained by methods (a) and (b) were shown to be identical by comparison of infrared spectra in Nujol mull (a single carbonyl peak was present at 1700  $cm^{-1}$ ). The compound exhibited maximum absorption in the ultraviolet in 0.1 *N* sodium hydroxide solution at 246, 283, 316, 330, 363 (shoulder) and 376  $m\mu$  ( $\log \epsilon = 4.51, 3.85, 3.56, 3.61, 3.76$  and  $3.79$ ).

**1,3-Diacetyl-2-ethoxy-1,2,3,4-tetrahydropyrimido(4,5-*b*)quinoline-4-one (V).** (a).—Cooling of the high boiling petroleum ether extracts obtained from the preparation of 4-hydroxypyrimido(4,5-*b*)quinoline (see above) gave a light brown solid which was sublimed at 180° (0.5 mm.) to give 0.52 g. of light yellow crystals, m.p. 208–210°.

(b).—A mixture of 1.01 g. of 2-aminoquinoline-3-carboxamide, 30 ml. of acetic anhydride and 30 ml. of ethyl orthoformate was heated under reflux for 3.5 hr. and then cooled. Removal of the excess acetic anhydride and ethyl orthoformate under reduced pressure gave a viscous, dark brown material which was repeatedly recrystallized from aqueous dimethylformamide to give white needles, m.p. 211–212°.

*Anal.* Calcd. for  $C_{17}H_{17}N_3O_4$ : C, 62.4; H, 5.2; N, 12.8. Found: C, 62.5; H, 5.0; N, 12.9.

The products obtained by methods (a) and (b) above were shown to be identical by comparison of infrared spectra.

**2-Methyl-4-hydroxypyrimido(4,5-*b*)quinoline (VI).**—A mixture of 1.03 g. of 2-aminoquinoline-3-carboxamide, 7.5 ml. of acetic anhydride and 0.3 ml. of concentrated sulfuric acid was heated in a water-bath for 5 minutes. The cooled solution was then diluted with 10 ml. of water and made basic to pH 11 with 5 *N* sodium hydroxide. The yellow solid which separated was collected by filtration and suspended in 20 ml. of water. Addition of glacial acetic acid resulted in solution followed by separation of a white solid, m.p. 306–309° dec., which was purified either by recrystallization from water to give long, white silky needles or by vacuum sublimation (200° (0.5 mm.)) to give a white crystalline solid, m.p. 318–321° dec. The compound was slightly soluble in ethanol and acetone but soluble in hot chloroform, from which it separated on cooling. The infrared spectrum (Nujol mull) showed a single carbonyl band at 1697  $cm^{-1}$  and no apparent N–H bands (observed by Nujol bands). The ultraviolet spectrum in 0.1 *N* sodium hydroxide solution showed absorption maxima at 245, 280, 313, 327 and 375  $m\mu$  ( $\log \epsilon = 4.79, 4.11, 3.77, 3.80$  and  $4.00$ ).

*Anal.* Calcd. for  $C_{12}H_9N_3O$ : C, 68.2; H, 4.3; N, 19.9. Found: C, 68.3; H, 4.3; N, 19.8.

(30) All melting points are corrected. The microanalyses were performed by Mrs. Lucy Chang, Mrs. Esther Fett and Mr. Joseph Nemeth of the University of Illinois and by Dr. Joseph F. Alicino of Metuchen, New Jersey.

**1-Benzoyl-2(1*H*)-benzimidazoquinoline-3-carboxamide (VII).**—A mixture of 1.00 g. (0.005 mole) of 2-aminoquinoline-3-carboxamide and 15 ml. of pyridine was shaken and cooled while 2.5 ml. (3.0 g., 0.0214 mole) of benzoyl chloride was added. The resulting mixture was allowed to stand for several hours and was then treated with 2 *N* sulfuric acid to precipitate 1.33 g. (63%) of an orange granular solid, m.p. 191–208°. Repeated recrystallization of this solid from aqueous dimethylformamide yielded long, white needles, m.p. 215–216°. The infrared spectrum (Nujol mull) of the compound showed a single carbonyl band at 1730  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{24}H_{17}N_3O_3$ : C, 72.9; H, 4.3; N, 10.6. Found: C, 72.8; H, 4.2; N, 10.7.

Treatment of 2-aminoquinoline-3-carboxamide (1.02 g., 0.0055 mole) in 15 ml. of pyridine with an equivalent amount of benzoyl chloride (0.73 g., 0.0052 mole) and allowing the mixture to stand overnight yielded 0.94 g. of a white precipitate, m.p. 298.5–299.5°. The material was water soluble and treatment of an aqueous solution of it with dilute sodium hydroxide regenerated 2-aminoquinoline-3-carboxamide.

**3-Phenylpyrimido(4,5-*b*)quinoline-2(1*H*)-thione-4(3*H*)-one (X).**—A mixture of 1.01 g. of 2-aminoquinoline-3-carboxamide, 1.0 ml. of phenyl isothiocyanate and 30 ml. of dry pyridine was heated under reflux for 3 hr. and then poured into an excess of ethyl alcohol. A pale yellow solid (0.58 g., 35%) was collected, m.p. 321–324°. The infrared spectrum (Nujol mull) of the compound showed an N–H stretching band at 3150  $cm^{-1}$ , a carbonyl band at 1700  $cm^{-1}$ , a thiocarbonyl band at 1531  $cm^{-1}$  and what is probably a monosubstituted benzene band at 693  $cm^{-1}$ . The compound was difficultly soluble in petroleum ether and water, slightly soluble in benzene and hot carbon tetrachloride and soluble in dimethylformamide, dioxane, chloroform and hot ethanol.

*Anal.* Calcd. for  $C_{17}H_{11}N_3OS$ : C, 66.9; H, 3.6; N, 13.8. Found: C, 67.2; H, 3.3; N, 13.5.

**2,4-Dihydroxypyrimido(4,5-*b*)quinoline (XIII).** (a).—A mixture of 1.00 g. of 2-aminoquinoline-3-carboxamide, 1.0 ml. of phenyl isocyanate and 20 ml. of dry pyridine was heated under reflux for 1 hr. During the reaction a heavy precipitate formed in the reaction mixture. Cooling and filtering yielded 1.08 g. (95%) of a white, granular solid which was purified by recrystallization from aqueous dimethylformamide or by vacuum sublimation (250° (0.5 mm.)), m.p. > 320°.

(b).—A mixture of 2 ml. of diethyl carbonate and 1.01 g. of 2-aminoquinoline-3-carboxamide was added to a solution of 0.28 g. of sodium in 40 ml. of absolute ethanol. The resulting mixture was heated under reflux for 1 hr. and cooled to give a yellow solid which was collected by filtration, suspended in a small amount of 1 *N* hydrochloric acid and refiltered to give 0.70 g. (61%) of a light brown solid, m.p. > 320°. Repeated recrystallization from aqueous dimethylformamide gave the product in the form of a light yellow, granular solid.

*Anal.* Calcd. for  $C_{11}H_7N_3O_2$ : C, 62.0; H, 3.3; N, 19.7. Found: C, 61.9; H, 3.2; N, 19.5.

The products obtained by methods (a) and (b) were shown to be identical by comparison of infrared spectra, which showed two low intensity N–H stretching bands at 3050 and 3150  $cm^{-1}$  and two carbonyl bands at 1705 and 1725  $cm^{-1}$ .

**Treatment of 2-Aminoquinoline-3-carboxamide (III) with Ethyl Chloroformate.**—A mixture of 1.02 g. of 2-aminoquinoline-3-carboxamide and 20 ml. of ethyl chloroformate was heated under reflux for 22 hr., and the yellow solid which had formed was filtered from the cooled solution to give 0.80 g., m.p. 288–292°. Since treatment of the solid with cold 5 *N* sodium hydroxide regenerated 2-aminoquinoline-3-carboxamide, it is probable that the solid was XIV.

**2,4-Dihydroxypyrimido(4,5-*b*)quinoline-10-oxide (XVI).**—A mixture of 1.00 g. of 2-aminoquinoline-3-carboxamide-1-oxide<sup>12</sup> and 25 ml. of ethyl chloroformate was heated under reflux for 1.5 hr. During this period a heavy, yellow solid separated from the reaction mixture. Cooling and filtering yielded 0.72 g. (63%) of a yellow solid, m.p. > 350°, which was recrystallized from aqueous dimethylformamide to give the product in the form of long, pale yellow needles. The infrared spectrum (Nujol mull) showed two N–H stretching bands at 3140 and 3345  $cm^{-1}$  and two carbonyl bands at 1700 and 1807  $cm^{-1}$ . The compound was insoluble in

petroleum ether and carbon tetrachloride, difficultly soluble in chloroform and hot benzene and slightly soluble in dioxane, hot ethanol and hot water. It was soluble in hot cello-solve, from which it separated on cooling.

*Anal.* Calcd. for  $C_{11}H_7N_3O_2$ : C, 57.7; H, 3.1; N, 18.3. Found: C, 57.6; H, 3.2; N, 18.6.

**2-Hydroxyquinoline-3-carboxylic Acid (XVII).**—A mixture of 1.02 g. of 2,4-dihydroxypyrimido(4,5-*b*)quinoline-10-oxide and 50 ml. of 5 *N* sodium hydroxide in a sealed steel bomb was heated at 200° for 5 hr. The cooled solution was filtered and acidified with hydrochloric acid to give 0.74 g. (88%) of a slightly pink solid, m.p. 341.5–342.5° dec., which was purified by vacuum sublimation, m.p. 347–347.5° dec.

*Anal.* Calcd. for  $C_{10}H_7NO_3$ : C, 63.5; H, 3.7; N, 7.4. Found: C, 63.8; H, 3.6; N, 7.6.

**Reaction of 2-Amino-3-cyanoquinoline (XVIII) with Dicyandiamide.**—To a solution of 0.32 g. of sodium in 40 ml. of absolute ethanol was added 1.02 g. of 2-amino-3-cyanoquinoline<sup>12</sup> followed by 1.52 g. of dicyandiamide. The mixture was heated under reflux for 2 hr. The precipitate obtained from the cooled reaction mixture was stirred with a large volume of water and filtered to give 1.01 g. of a yellow crystalline solid, m.p. 309–310°. It could be recrystallized from water or sublimed *in vacuo* without change in the melting point.

*Anal.* Found: C, 56.9; H, 4.4; N, 38.4.

**2-[3-(2-Aminoquinolinyl)]-4-aminopyrimido(4,5-*b*)quinoline (XIX).**—A mixture of 3.02 g. of 2-amino-3-cyanoquinoline and 40 ml. of liquid ammonia was placed in a glass-lined steel bomb and heated at 190° for 9 hr. The bomb was allowed to cool overnight and the ammonia was bled off at 50°. A bright yellow solid was obtained which was washed well with water to give 2.71 g. (90%), m.p. > 350°.

*Anal.* Calcd. for  $C_{20}H_{14}N_6$ : C, 71.0; H, 4.2; N, 24.8. Found: C, 70.8; H, 4.0; N, 24.4.

**2-[3-(2-Aminoquinolinyl)]-4-hydroxypyrimido(4,5-*b*)quinoline (XX).**—A mixture of 0.68 g. of 2-[3-(2-aminoquinolinyl)]-4-aminopyrimido(4,5-*b*)quinoline and 30 ml. of concentrated hydrochloric acid was heated under reflux for 3.5 hr. and then cooled. The yellow solid was collected by filtration, suspended in dilute ammonium hydroxide and the mixture again filtered to give 0.56 g. (82%) of a brownish yellow solid, m.p. > 350°. The product was purified by sublimation at 250° (0.5 mm.).

*Anal.* Calcd. for  $C_{20}H_{13}N_5O$ : C, 70.8; H, 3.9; N, 20.6. Found: C, 71.1; H, 3.7; N, 20.9.

**2-Hydroxy-4-aminopyrimido(4,5-*b*)quinoline (XXI).**—An intimate mixture of 1.5 g. of 2-amino-3-cyanoquinoline and 4.0 g. of urea was heated in an oil-bath at 300–310° for 15 minutes. The material first liquefied and then quickly set to a hard, yellow solid. After cooling, the solid was powdered, extracted with cold water followed by boiling ethanol and the solid residue recrystallized from aqueous dimethylformamide to give 1.18 g. (63%) of yellow needles, m.p. 359° dec.

*Anal.* Calcd. for  $C_{11}H_8N_4O$ : C, 62.2; H, 3.8; N, 26.4. Found: C, 62.0; H, 3.8; N, 26.2.

**4-Aminopyrimido(4,5-*b*)quinoline (XXII).**—A mixture of 1.5 g. of 2-amino-3-cyanoquinoline and 5 ml. of formamide was heated under reflux for 30 minutes, cooled, diluted with 100 ml. of water and filtered. The solid which separated was collected by filtration, washed well with water and sublimed at 200° (0.1 mm.) to give 0.62 g. of a yellow solid, m.p. > 325° dec.

*Anal.* Calcd. for  $C_{11}H_8N_4$ : C, 67.3; H, 4.1; N, 28.6. Found: C, 67.2; H, 4.5; N, 28.5.

**2-Amino-3-aminomethylquinoline (XXIII).**—A mixture of 9.85 g. of 2-amino-3-cyanoquinoline, 10 g. of Raney nickel (wet with ethanol) and 250 ml. of ethanol saturated with ammonia was placed in a glass-lined bomb and hydrogenated at 80° and 1200 p.s.i. for 6 hr. The Raney nickel catalyst was filtered from the cooled reaction mixture and the filtrate was concentrated under reduced pressure. Dilution with a large volume of water followed by cooling caused the separation of 9.40 g. (93%) of white needles, m.p. 144–147°. The compound was purified by recrystallization from high boiling petroleum ether or by vacuum sublimation, m.p. 147–149°.

*Anal.* Calcd. for  $C_{10}H_{11}N_3$ : C, 69.3; H, 6.4; N, 24.3. Found: C, 69.6; H, 6.3; N, 24.2.

**3,4-Dihydropyrimido(4,5-*b*)quinoline (XXIV).**—In a 100-ml. round-bottom flask, 0.51 g. of 2-amino-3-aminomethylquinoline was stirred with 0.6 ml. of 90% formic acid until a homogeneous, viscous mass was obtained, and then 50 ml. of xylene was added. The flask was equipped with a Dean-Stark trap and a reflux condenser, and the mixture was heated under reflux for 4.5 hr. The reaction mixture (final volume ca. 20 ml.) was cooled to give 0.33 g. (61%) of a light brown material, m.p. 189–191°. The product was purified by vacuum sublimation to give a yellow solid, m.p. 204–207°.

*Anal.* Calcd. for  $C_{11}H_9N_3$ : C, 72.1; H, 4.9; N, 22.9. Found: C, 71.9; H, 4.8; N, 22.7.

**2-Amino-3-acetamidomethylquinoline (XXV).**—A mixture of 0.33 g. of 2-amino-3-aminomethylquinoline and 3 ml. of acetic anhydride was stirred for a few minutes, diluted with 5 ml. of water and allowed to stand for 1 hr. at room temperature. The mixture was then neutralized with 5 *N* sodium hydroxide, and the solid which separated was collected by filtration, washed well with water and air-dried to give 0.37 g. (90%) of a white solid, m.p. 164.5–167°. The product was purified by vacuum sublimation at 120° (0.5 mm.), m.p. 214–215°.

*Anal.* Calcd. for  $C_{12}H_{13}N_3O$ : C, 67.0; H, 6.0; N, 19.5. Found: C, 66.7; H, 6.0; N, 19.6.

**2-Methyl-3,4-dihydropyrimido(4,5-*b*)quinoline (XXVI).**—A mixture of 0.41 g. of 2-amino-3-acetamidomethylquinoline and 10 ml. of diphenyl ether was heated under reflux for 80 minutes and cooled to give 0.09 g. (26%) of a dark brown solid, m.p. 193–197°, which was purified by sublimation at 150° (0.5 mm.) to give a yellow solid, m.p. 199.5–201°.

*Anal.* Calcd. for  $C_{12}H_{11}N_3$ : C, 73.1; H, 5.6; N, 21.3. Found: C, 72.9; H, 5.8; N, 21.1.

**2-Amino-3-carbethoxyaminomethylquinoline (XXVII).**—A mixture of 0.49 g. of 2-amino-3-aminomethylquinoline and 5 ml. of ethyl chloroformate was well stirred for a few minutes and then allowed to stand for 1 hr. at room temperature. A pale yellow solid was collected, washed with ether and then dissolved in 5 ml. of water. The solution was treated with charcoal and the filtrate made basic to pH 8 with dilute ammonium hydroxide. The white solid which separated (0.57 g., 82%), m.p. 159–162°, was collected, washed with water and air-dried. Recrystallization from water gave long, white needles with the same melting point.

*Anal.* Calcd. for  $C_{13}H_{15}N_3O_2$ : C, 63.7; H, 6.2; N, 17.1. Found: C, 63.9; H, 6.0; N, 17.1.

**3,4-Dihydropyrimido(4,5-*b*)quinoline-2(1*H*)-one (XXVIII).** (a).—A mixture of 0.34 g. of 2-amino-3-carbethoxyaminomethylquinoline and 5 ml. of diphenyl ether was heated under reflux for 70 minutes while being stirred by means of a mechanical stirrer. Cooling caused the separation of 0.21 g. (76%) of shiny, dark brown plates, m.p. 346–350°. The material was purified by sublimation at 195° (0.05 mm.) to give a pale yellow solid, m.p. 349.5–351.5°.

(b).—A mixture of 0.52 g. of 2-amino-3-aminomethylquinoline, 0.4 ml. of phenyl isocyanate and 10 ml. of dry pyridine was heated under reflux for 1 hr. Most of the solvent was then removed by distillation under reduced pressure, and the residue was diluted with a large volume of water. The resulting precipitate was collected by filtration, washed with water, air-dried and then stirred with ether to remove any diphenylurea which might have been formed during the reaction. A slightly pink solid was obtained, m.p. 345–347°. The material was purified by recrystallization from aqueous dimethylformamide followed by vacuum sublimation at 195° (0.05 mm.) to give a pale yellow solid, m.p. 349.5–351.5°.

*Anal.* Calcd. for  $C_{11}H_9N_3O$ : C, 66.3; H, 4.5; N, 21.1. Found: C, 66.6; H, 4.5; N, 21.1.

The products obtained by methods (a) and (b) above were shown to be identical by a mixture melting point determination and by comparison of infrared spectra.

**3,4-Dihydropyrimido(4,5-*b*)quinoline-2(1*H*)-thione (XXIX).**—A mixture of 0.50 g. of 2-amino-3-aminomethylquinoline, 0.4 ml. of phenyl isothiocyanate and 10 ml. of dry pyridine was heated under reflux for 5 hr. and then cooled. The solution was concentrated under reduced pressure and diluted with a large volume of water. The precipitate was collected, washed with water, dried and then stirred with ether to remove any diphenylthiourea which might have

formed during the reaction. A pale yellow solid (0.51 g., 82%), m.p. 280–282°, was collected. The product was purified by vacuum sublimation at 190° (0.10 mm.) (a small forerun subliming below 140° (0.10 mm.) was discarded) to give a yellow solid, m.p. 292.5–293.5°. The product was obtained in the form of pale yellow needles on recrystallization from water.

*Anal.* Calcd. for  $C_{11}H_9N_3S$ : C, 61.4; H, 4.2; N, 19.5. Found: C, 61.4; H, 4.1; N, 19.7.

**1,3-Diacetyl-2-ethoxy-1,2,3,4-tetrahydropyrimido(4,5-*b*)-quinoline (XXXII).**—A mixture of 0.79 g. of 2-amino-3-aminomethylquinoline, 15 ml. of ethyl orthoformate and 15 ml. of acetic anhydride was heated under reflux for 5 hr. The resulting solution was concentrated under reduced pressure, diluted with water and allowed to stand overnight. The light brown solid which had separated was collected, washed with water and air-dried to give 0.40 g., m.p. 138.5–141°. The material was purified by sublimation at 100° (0.05 mm.) to give a white, crystalline solid, m.p. 139–141°.

*Anal.* Calcd. for  $C_{17}H_{19}N_3O_3$ : C, 65.2; H, 6.1; N, 13.4. Found: C, 65.4; H, 6.2; N, 13.8.

**2,4-Dichloropyrimido(4,5-*b*)-quinoline (XXXIII).**—A mixture of 10 g. of 2,4-dihydroxypyrimido(4,5-*b*)-quinoline, 10 g. of phosphorus pentachloride and 80 ml. of phosphorus oxychloride was heated under reflux for 9 hr. to give a clear, deep brown solution. This was concentrated under reduced pressure to a sirup which was poured onto ice. After the ice-cold mixture had stood for several hours, it was extracted with several 250-ml. portions of chloroform, the chloroform extracts dried over anhydrous magnesium sulfate and evaporated to dryness to give 8.3 g. (71%) of a yellow solid, m.p. 222.5–224°. The product was purified by vacuum sublimation, m.p. 226.5–228.5°.

*Anal.* Calcd. for  $C_{11}H_8N_2Cl_2$ : C, 52.8; H, 2.0; N, 16.8. Found: C, 53.1; H, 1.9; N, 16.5.

**2,4-Bis-(dimethylamino)-pyrimido(4,5-*b*)-quinoline (XX-XIV).**—A mixture of 0.59 g. of 2,4-dichloropyrimido(4,5-*b*)-quinoline and 5 ml. of 25% aqueous dimethylamine was heated under reflux on a steam-bath for 2 hr. and then allowed to go to dryness. The residue was stirred with 25 ml. of water and the mixture then made basic with 10% sodium hydroxide to give 0.42 g. (67%) of a bright yellow solid, m.p. 187–190°. The product was purified by recrystallization from water or by vacuum sublimation, m.p. 194–195.5°.

*Anal.* Calcd. for  $C_{14}H_{17}N_5$ : C, 67.4; H, 6.4; N, 26.2. Found: C, 67.3; H, 6.4; N, 26.4.

**2,4-Diphenoxypyrimido(4,5-*b*)-quinoline (XXXV).**—Over a period of 10–15 minutes, 0.54 g. of 2,4-dichloropyrimido(4,5-*b*)-quinoline was added to a hot (80°) mixture of 0.5 g. of potassium hydroxide in 5 ml. of phenol. After the addi-

tion was complete, the mixture was placed in a water-bath, and the temperature of the bath was gradually raised to 90° over the course of 30 minutes. The mixture was then poured with stirring into 25 ml. of 2 *N* sodium hydroxide, and the resulting precipitate was collected by filtration, washed with a little 1 *N* sodium hydroxide followed by water and air-dried to give 0.54 g. (69%) of a tan solid (sintered 230°, m.p. 239.5–241.5°). The product was purified by repeated recrystallization from aqueous dimethylformamide or by vacuum sublimation, m.p. 265.5–267°.

*Anal.* Calcd. for  $C_{23}H_{18}N_2O_2$ : C, 75.6; H, 4.4; N, 11.5. Found: C, 75.6; H, 4.0; N, 11.7.

**2,4-Diaminopyrimido(4,5-*b*)-quinoline (XXXVI).**—A mixture of 2.0 g. of 2,4-dichloropyrimido(4,5-*b*)-quinoline and 45 ml. of liquid anhydrous ammonia was heated in a sealed steel autoclave at 150° for 8 hr. After cooling, the bomb was bled of excess ammonia and the solid residue washed with water to give a yellow solid, m.p. 344–347°. All efforts to purify the material were unsuccessful.

**2-Chloro-4-hydroxypyrimido(4,5-*b*)-quinoline (XXXVII).**—A mixture of 0.50 g. of 2,4-dichloropyrimido(4,5-*b*)-quinoline and 20 ml. of 1 *N* sodium hydroxide was stirred for 30 minutes at room temperature, decolorizing charcoal added and the resulting mixture filtered. Acidification of the filtrate to pH 5 with acetic acid caused the separation of 0.36 g. (78%) of a yellow, granular solid (sintered 240°, m.p. 312–314° dec.). The product was purified for analysis by solution in dilute sodium hydroxide followed by precipitation with acetic acid. The infrared spectrum (Nujol mull) showed an N–H stretching band at 3145  $cm^{-1}$  and a carbonyl band at 1675  $cm^{-1}$ . The ultraviolet spectrum in 0.1 *N* sodium hydroxide showed maximum absorption at 244, 278, 313, 330, 350 and 372  $m\mu$  ( $\log \epsilon = 4.56, 4.02, 3.59, 3.76, 3.78$  and  $3.88$ ).

*Anal.* Calcd. for  $C_{11}H_8N_2OCl$ : C, 57.0; H, 2.6; N, 18.1. Found: C, 57.3; H, 3.0; N, 17.7.

**Reaction of 2-Chloro-4-hydroxypyrimido(4,5-*b*)-quinoline (XXXVII) with Sodium Ethoxide.**—To a solution of 0.44 g. of sodium in 25 ml. of absolute ethanol was added 0.44 g. of 2-chloro-4-hydroxypyrimido(4,5-*b*)-quinoline and the mixture stirred at room temperature for 13 hours, heated under reflux for 30 minutes and finally filtered. After several hours standing, the filtrate deposited a solid which was collected by filtration and dissolved in 5 ml. of water. Acidification of the solution with acetic acid caused the separation of pale yellow needles, m.p. > 350°, which were purified by vacuum sublimation. The product was shown to be 2,4-dihydroxypyrimido(4,5-*b*)-quinoline by analysis and by direct comparison with an authentic sample.

*Anal.* Calcd. for  $C_{11}H_7N_3O_2$ : C, 62.0; H, 3.3; N, 19.7. Found: C, 61.9; H, 3.2; N, 19.5.

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