doublets, 1 H, J = 3.0, 1.5 Hz, bridgehead α to N), 5.83–6.67 (m, 3 H), and 6.32 (s, 3 H, OCH_3); ir (CCl_4) 1710 (C=O) and 1596 cm^{-1} (C=C). The analytical sample was further purified by glc (10 ft × 0.25 in. 5% SE-30 at 125°, retention time 60 min).

Anal. Calcd for $C_7H_9NO_2$: C, 60.42; H, 6.52. Found: C, 60.24; H, 6.54.

Registry No.—**1**, 33707-36-7; **2**, 33707-37-8; **4**, 33707-38-9; **5**, 33666-44-3; **8**, 33707-39-0.

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2,4-Diaminopyrimidines from Dicyandiamide. IV. Condensation with Bicyclic Aromatic Ketones[1,2]

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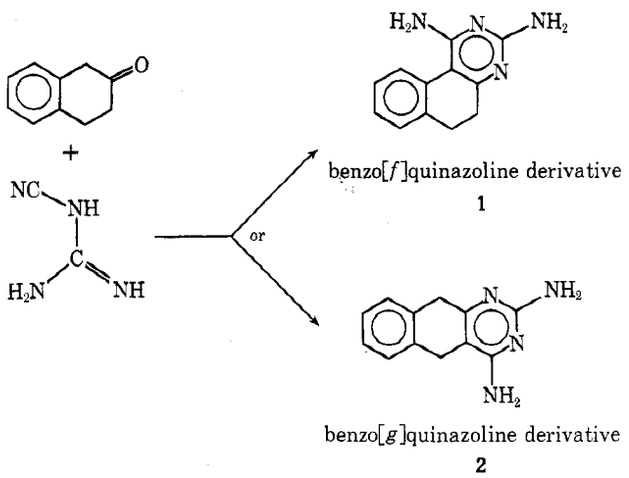
The synthesis of several tricyclic diaminopyrimidine derivatives by condensation of dicyandiamide with bicyclic aromatic ketones is reported. An interesting skeletal rearrangement was observed when 2,4-diaminobenzo[*g*]quinazoline (**5a**) was isolated as the major product of palladium–charcoal dehydrogenation (under disproportionation conditions) of 1,3-diamino-5,6-dihydrobenzo[*f*]quinazoline (**1**), the 2-tetralone/dicyandiamide condensation product. Representatives of the 2,4-diaminobenzo[*h*]quinazoline, the 2,4-diaminothieno[2,3-*h*]-quinazoline, and the 2,4-diamino-5*H*-indeno[1,2-*d*]pyrimidine ring systems are described.

In a program of synthesis of pyrimidine derivatives as potential folic acid antagonists and antitumor agents,[3] a number of 2,4-diaminopyrimidine ring systems have been synthesized in our laboratory by the direct, one-step condensation of dicyandiamide with ketones having an available α-methylene group.[2–5] We reported the isolation of a single product from the condensation of 2-tetralone with dicyandiamide.[2,4] Although cyclization can theoretically involve the methylene group on either side of the carbonyl group of 2-tetralone, leading to **1** or **2**, we have established the structure of the reaction product as 1,3-diamino-5,6-dihydrobenzo[*f*]quinazoline (**1**).[6,7] A number of substituted 1,3-diamino-5,6-dihydrobenzo[*f*]quinazolines were subsequently prepared by this route.[8,9] Application of this versatile pyrimidine ring-forming reaction to bicyclic aromatic ketones is now described; in connection with the present work, an interesting thermal rearrangement was observed and confirmed by alternative synthesis.

A disproportionation reaction of compound **1** was conducted in the presence of tetralin and 10% palladium–charcoal catalyst in 2-(2-ethoxyethoxy)ethanol at 198–202° for 38 hr. The major product was 2,4-diaminobenzo[*g*]quinazoline (**5a**), the structure of which was proved by comparison with an authentic



sample prepared by an unambiguous synthesis.[10–14] Isolation of **5a** suggested that the product of condensation of 2-tetralone and dicyandiamide might have been 2,4-diamino-5,10-dihydrobenzo[*g*]quinazoline. It is now obvious that **5a** resulted by rearrangement under disproportionation conditions. This, to our knowledge, is the only example of a thermal rearrangement of a benzo[*f*]quinazoline to a benzo[*g*]quinazoline. The minor product from this reaction (**10**) retained the benzo[*f*]quinazoline ring structure of the parent compound.[15]

An authentic sample of 2,4-diaminobenzo[*g*]quinazoline was prepared according to the procedures of Curd, Landquist, and Rose[10] and Legrand[11–14] with certain modifications. 2,4-Dihydroxybenzo[*g*]quinazoline (**3a**) was obtained by reaction of 2-amino-3-

(1) This investigation was supported in part by research grant C6516 and research career development award K3-CA-22,151 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

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(5) E. J. Modest, S. Chatterjee, and H. K. Protopapa, *J. Org. Chem.*, **30**, 1837 (1965). This is part III of the series.

(6) A. Rosowsky, E. P. Burrows, S. K. Sengupta, and E. J. Modest, Abstracts of Papers, First International Congress of Heterocyclic Chemistry, Albuquerque, N. M., June 15, 1967, Abstract No. 104.

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(8) A. Rosowsky and E. J. Modest, *Ann. N. Y. Acad. Sci.*, **186**, 258 (1971).

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(10) F. H. S. Curd, J. K. Landquist, and F. L. Rose, *J. Chem. Soc.*, 1759 (1948).

(11) A. Etienne and M. Legrand, *C. R. Acad. Sci.*, **229**, 220 (1949).

(12) A. Etienne and M. Legrand, *ibid.*, **231**, 232 (1950).

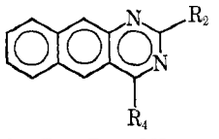
(13) M. Legrand, *ibid.*, **231**, 1318 (1950).

(14) M. Legrand, private communication.

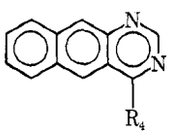
(15) Compound **10** was identified as 3-amino-1-[2-(2-ethoxyethoxy)-ethoxy]benzo[*f*]quinazoline (see Experimental Section). Mass spectrometric analysis of **10**, together with the fragmentation pattern of the ether side chain, is described separately: S. K. Sengupta, H. K. Protopapa, E. J. Modest, and B. C. Das, *Org. Mass Spectrom.*, (submitted for publication).

naphthoic acid and urea.[10,16] Chlorination of **3a** with phosphorus oxychloride in refluxing bromobenzene afforded 2,4-dichlorobenzo[*g*]quinazoline (**4a**); conventional chlorination in refluxing phosphorus oxychloride was less satisfactory. The method of Legrand[13,14] for amination of **4a** to **5a** in ethanolic ammonia required increased temperature, pressure, and reaction time for complete reaction.

In view of the isolation of **5a** from the disproportionation reaction, several additional derivatives of the seldom reported benzo[*g*]quinazoline ring system were synthesized for possible comparative purposes in connection with the solid-phase dehydrogenation described below. Condensation of formamide with 2-amino-3-naphthoic acid *via* Niementowski's reaction[17] afforded 4-hydroxybenzo[*g*]quinazoline (**3b**), which was converted into 4-chlorobenzo[*g*]quinazoline (**4b**). Amination of **4b** gave **5b**.[13,18] This amination was more facile than that of 2,4-dichlorobenzo[*g*]quinazoline (**4a**).



3a, $R_2 = R_4 = OH$
4a, $R_2 = R_4 = Cl$
5a, $R_2 = R_4 = NH_2$
6, $R_2 = NH_2$; $R_4 = OH$



3b, $R_4 = OH$
4b, $R_4 = Cl$
5b, $R_4 = NH_2$

2-Amino-4-hydroxybenzo[*g*]quinazoline (**6**) was synthesized in low yield by high-temperature condensation of 2-amino-3-naphthoic acid and guanidine in boiling phenol. The same material (**6**) was obtained in good yield when **5a** was subjected to selective acid hydrolysis of the 4-amino group. The preferential hydrolysis of the 4- and 6-amino groups as compared with the 2-amino groups in pyrimidine ring systems is well known.[19]

When the dehydrogenation of **1** was carried out with 10% palladium–charcoal catalyst at 270–320° without solvent, a reaction product was obtained which was shown to be a mixture of three components by paper chromatography. One component, the starting material (**1**), was removed by sublimation. Sublimation of the residue at a higher temperature yielded a mixture of the other two components. Fractional crystallization from absolute ethanol yielded the second component in pure form, identified as 3-aminobenzo[*f*]quinazoline (**7**) by comparison with an authentic sample.[20,21] Obviously deamination had occurred during or following dehydrogenation of **1** with the formation of 3-aminobenzo[*f*]quinazoline (**7**) as one product of the reaction. Dehydrogenation had been accompanied by evolution of considerable gaseous ammonia. Primary aromatic amino groups can be hydrogenolyzed in the presence of various catalysts.[22]

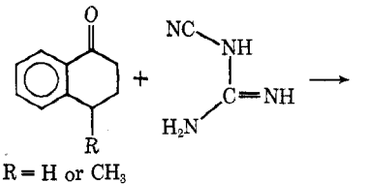
(16) M. T. Bogert and G. Scatchard, *J. Amer. Chem. Soc.*, **41**, 2052 (1919).
(17) S. v. Niementowski, *J. Prakt. Chem.*, [2] **51**, 564 (1895).
(18) A. R. Osborn, K. Schofield, and L. N. Short, *J. Chem. Soc.*, 4191 (1956).
(19) (a) E. C. Taylor and C. K. Cain, *J. Amer. Chem. Soc.*, **71**, 2282 (1949); (b) R. B. Trattner, G. B. Elion, G. H. Hitchings, and D. M. Sharefkin, *J. Org. Chem.*, **29**, 2674 (1964).
(20) A. Rosowsky, N. Papathanasopoulos, M. E. Nadel, S. K. Sengupta, and E. J. Modest, Abstracts of Papers, 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 28, 1966, I-1.
(21) A. Rosowsky and E. J. Modest, *J. Org. Chem.*, **31**, 2607 (1966).
(22) Nathan Kornblum in "Organic Reactions," Vol. II, Wiley, New York, N. Y., 1947, p 262.

Neither fractional crystallization nor cellulose column chromatography afforded a pure sample of the third component. Therefore, the original dehydrogenation mixture was subjected to ion exchange chromatography with a cation exchange resin, and the column was eluted with different strengths of aqueous hydrochloric acid. Hydrochloric acid (2 *N*) extracted monoamine **7**, identified as the free base. The 4 *N* hydrochloric acid eluate was free from **7**. Work-up afforded a single, pure compound with infrared absorption at 5.85 μ; it was shown to be an amido compound by elemental analysis. The material, isomeric with **6**, was identified as 1-hydroxy-3-aminobenzo[*f*]quinazoline (**8**) by comparison with an authentic sample.[20,21] This must have come from 1,3-diaminobenzo[*f*]quinazoline (*via* solvent-free dehydrogenation of **1**) by acid hydrolysis during the prolonged process of elution from the column. The preferential acid hydrolysis of the 1-amino group of 1,3-diaminobenzo[*f*]quinazoline has already been recorded,[21] as well as the formation of 1,3-diaminobenzo[*f*]quinazoline by mild, selenium dioxide–acetic acid dehydrogenation of **1**.[6,7]

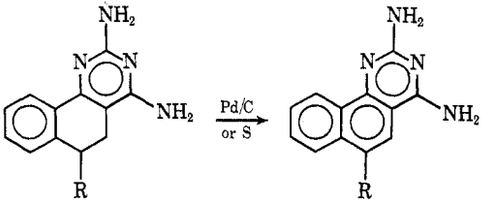
Mild nitrosation of **1** yielded 1-hydroxy-3-amino-5,6-dihydrobenzo[*f*]quinazoline (**9**) by preferential reaction of the 1-amino group. Dehydrogenation of **9** gave **8**. Nitrosation of **1** under forcing conditions gave small amounts of 1,3-dihydroxybenzo[*f*]quinazoline.

In summary of the palladium–charcoal reactions on **1**, dehydrogenation under disproportionation conditions with tetralin in 2-(2-ethoxyethoxy)ethanol gave the rearranged product **5a** in major yield, whereas dehydrogenation without solvent afforded the unrearranged **7** and **8**, derivable from **1** by dehydrogenation and by deamination and hydrolysis, respectively, of the 1-amino group. Since each reaction was repeated several times and since the purity of **1** was rigorously substantiated (see Experimental Section), it is clear that the disproportionation reaction involves extensive ring rearrangement, for which we cannot at present offer a mechanistic explanation. See Scheme I.

Studies were also carried out with 1-tetralone and related bicyclic ketones. Reaction of 1-tetralone with dicyandiamide afforded 2,4-diamino-5,6-dihydrobenzo[*h*]quinazoline (**11a**) in about 58% yield. Similarly, 2,4-diamino-5,6-dihydro-6-methylbenzo[*h*]quinazoline (**11b**) was prepared from 4-methyl-1-tetralone in 63% yield. In contrast to **1** (the 2-tetralone condensation product), **11a** was readily dehydrogenated to the fully



R = H or CH_3



11a, R = H
b, R = CH_3

Pd/C or S

12, R = H (from **11a**)

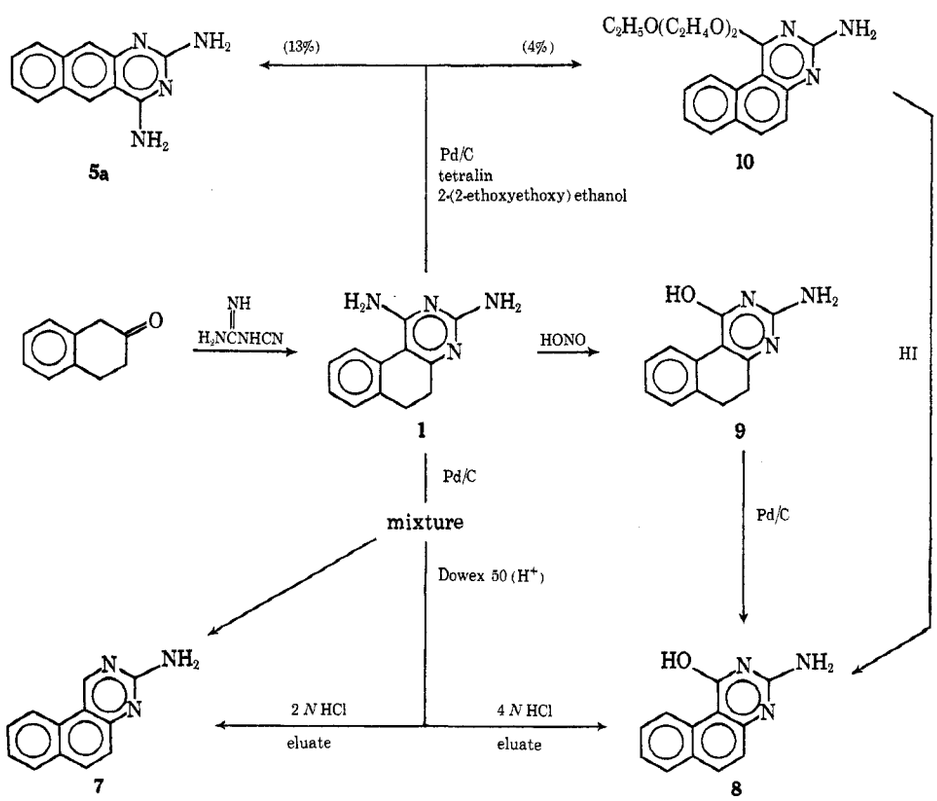
TABLE I

NMR[a] AND ULTRAVIOLET SPECTRA

Compd	δ, ppm: Methylene	δ, ppm: Aromatic	(Solvent)	λmax, nm (ε × 10⁻³): EtOH	λmax, nm (ε × 10⁻³): pH 1	λmax, nm (ε × 10⁻³): DMF
1	3.03 (singlet)	7.63 (four peaks)	(TFA)	276 (18.7) **294** (16.9)	**271** (17.1) 282 (13.1)[b]	282 (14.9) **305** (16.9)
	2.85 (multiplet)	7.63 (multiplet)	(DMF-d_7)		289 (12.1)[b]	
9	3.01 (singlet)	7.40 (four peaks)	(TFA)	235 (10.0) 264 (19.3)	262 (18.6) **305** (9.1)	267 (8.3) 297 (8.4)
	2.75 (multiplet)	7.92 (quartet)	(DMF-d_7)	284 (7.1) 296 (7.9)		**328** (15.5)
		7.15 (triplet)	(DMF-d_7)	**325** (12.2)		
11a	3.05 (octet)	7.75 (multiplet)	(TFA)	240 (25.5) 280 (3.2)[b] 292 (3.3)	226 (17.0) 239 (16.9) 286 (5.9)[b]	281 (3.3) 292 (2.9) **332** (7.1)
	2.85 (multiplet)	7.63 (multiplet)	(DMF-d_7)	**328** (8.35)	298 (8.6) 320 (12.7)[b] **327** (13.4) 340 (9.0)[b]	
13	3.23 (octet)	7.35 (singlet)	(TFA)	243 (17.2) 264 (14.1) 269 (13.3) **299** (7.6) 330 (2.6)[b]	240 (25.5) **333** (13.1) 347 (8.9)[b]	
15	4.10 (singlet)	8.05 (three peaks)	(TFA)	238 (25.5) 284 (4.5) 291 (6.1) **318** (10.4)	226 (17.8) 238 (16.5) **316** (18.6) 329 (12.9)	283 (3.2) 291 (3.8) **322** (6.13)

[a] Nmr peak values are center of multiple peaks wherever applicable. [b] Shoulder.

SCHEME I

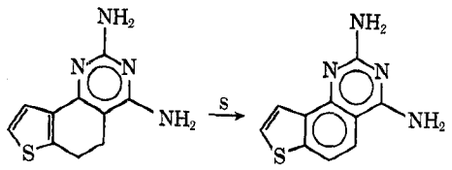


aromatic derivative 2,4-diaminobenzo[*h*]quinazoline (**12**) with 10% palladium–charcoal or sulfur.

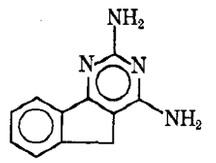
A thiophene analog of 1-tetralone, 4-keto-4,5,6,7-tetrahydrothionaphthene, reacted with dicyandiamide with formation of the expected 2,4-diaminopyrimidine derivative **13** in good yield; **13** underwent smooth dehydrogenation with sulfur to **14** in 70% yield. Compounds **13** and **14** represent the 2,4-diaminothieno-[2,3-*h*]quinazoline ring system, which, to the best of our knowledge, has not been reported in the literature.

Condensation of 1-indanone with dicyandiamide gave 2,4-diamino-5*H*-indeno[1,2-*d*]pyrimidine (**15**) (78% yield).

Compounds **11a** and **15**, which may be considered



13 14



15

tricyclic analogs of 2,4-diamino-6-phenylpyrimidine, have multiple ultraviolet absorption peaks in ethanol, whereas 2,4-diamino-6-phenylpyrimidine itself shows only two absorption maxima in ethanol, at 240 and 305 nm.[23] In contrast, the ultraviolet absorption spectrum of **1** in ethanol is very similar to that of the analogous 2,4-diamino-5-phenylpyrimidine,[23] having only two maxima. A reasonable explanation for these observations is that steric interaction between the 1-amino group and the proton at C-10 of **1** may effect enough loss of planarity to interrupt conjugation of the aromatic rings and to produce a loss of fine structure in the ultraviolet spectrum.[24] Replacement of the 1-amino group in **1** by a 1-oxo (or hydroxy) function in **9** restores planarity (multiple absorption maxima) (Table I).

The nmr spectrum of **1** in trifluoroacetic acid shows a singlet methylene peak (Table I), but the spectrum of **11a** shows a methylene octet in that solvent. Methylene multiplets are observed for both compounds in dimethylformamide-d_7, although the characteristic splitting pattern of the methylene protons of **1** differs from that of **11a**. Thus, the nmr data support the conclusion from the ultraviolet data that **11a** is a relatively planar, conjugated molecule in contrast to **1**.

Experimental Section[27]

1,3-Diamino-5,6-dihydrobenzo[*g*]quinazoline (**1**).—A mixture of 3.4 g (0.040 mol) of dicyandiamide and 3.6 g (0.025 mol) of 2-tetralone was heated for 1 hr (partial solution) at 150–170° (internal temperature) and then at 180–185° for another 45 min (complete solution). The heating was continued for 1 hr at 190°, at which point water started evolving and a yellow solid started separating from the reaction mixture. The resulting solid was washed with acetone and crystallized directly from dimethylformamide as a colorless, microcrystalline solid, yield 2.6 g (50%), mp 268–270°. Several further crystallizations from dimethylformamide afforded analytically pure material, yield 2 g (38%), mp 263–264°, R_{Ad} 1.41 (solvent A), 1.69 (solvent B), 1.63 (solvent C).

Anal. Calcd for $C_{12}H_{12}N_4$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.93; H, 5.93; N, 26.49.

Formation of 5a by Disproportionation of 1.—This procedure was the best of a number of experiments and was run three times. The purity of the starting material, 1,3-diamino-5,6-dihydrobenzo[*f*]quinazoline (**1**), was carefully established by comparison (paper chromatography, ultraviolet and nmr spectra, mixture melting point) with an authentic sample of the isomeric 2,4-diamino-5,10-dihydrobenzo[*g*]quinazoline, synthesized from methyl 2-tetralone-3-carboxylate.[28] Insofar as possible, all of the following operations, including the crystallizations, were carried out under a nitrogen atmosphere. A mixture of pure **1** (1.0 g, 0.0047 mol) and 10% palladium–charcoal (0.5 g) in tetralin (20 ml) and 2-(2-ethoxyethoxy)ethanol (45 ml) was refluxed for 38 hr in a flask equipped with magnetic stirring and an immersion thermometer. The internal temperature was maintained at 198–202°. The progress of the reaction was followed spectrophotometrically by the appearance of $\lambda_{max}^{pH\ 1}$ 248, 307, 321, and 374 nm. The reaction mixture was filtered while hot and the palladium–charcoal residue was washed with a hot 2:1 mixture of benzene and 2-(2-ethoxyethoxy)ethanol (300 ml). The combined reaction filtrate and washings (yellow fluorescent solution) were reduced to one-third volume. The remaining solvent was removed initially by vacuum distillation at 84–86° (internal temperature) and finally by prolonged evaporative distillation at 75–140° (0.5–0.7 mm). The colorless distillate (1.4 g) deposited some unchanged starting material (1, 0.25 g) upon prolonged refrigeration. Sublimation of the distillation residue at 180–190° (0.5–0.7 mm) for 24 hr yielded two distinct bands of sublimate: a more volatile, nearly colorless fraction (A), and a less volatile, yellow crystalline fraction (B). Sublimate B was dissolved in a 1:1 mixture of hot benzene and absolute ethanol (25 ml) and filtered free of a small insoluble residue. The volume of the yellow fluorescent filtrate was reduced to 2–3 ml. Overnight refrigeration afforded yellow needles (**5a**), yield 99.1 mg (13.2% based on recovered starting material), mp 284–285°. Two further crystallizations of this solid from absolute ethanol afforded analytically pure, yellow needles, yield 50.9 mg (6.8%), mp 284–285°, dried for analysis for 23 hr at 30–50° *in vacuo*.

Anal. Calcd for $C_{12}H_{10}N_4$: C, 68.55; H, 4.80; N, 26.65. Found: C, 68.49; H, 4.94; N, 26.44.

A mixture melting point of this material with an authentic sample of **5a** prepared by a synthetic route was undepressed (mp 284–286°) and the two samples had identical ultraviolet and infared absorption spectra and R_{Ad} values: R_{Ad} 1.29 (solvent A), 1.17 (solvent B), 1.23 (solvent C).

Fractional crystallization of sublimate A from absolute ethanol afforded 49 mg (4.2%) of colorless solid, recrystallization of which from ethanol gave analytically pure **10** as colorless needles, mp 116–118°, molecular formula $C_{18}H_{21}N_3O_3$ (M^+ 327 amu). Ether cleavage of **10** with hydriodic acid generated **8**. These data, together with the mass spectrometric fragmentation behavior of the side chain, confirmed the identity of **10** in sublimate A.[15]

2,4-Dihydroxybenzo[*g*]quinazoline (**3a**).—A mixture of 2-amino-3-naphthoic acid (12 g, 0.064 mol), urea (24 g, 0.4 mol), and solid phenol (60 g) was fused at 180–190° (bath temperature) for 15 min and then heated under stirring and gentle reflux (air condenser) for 90 min, after which the resulting melt was cooled to *ca.* 70° and absolute ethanol (60 ml) was added cautiously with stirring. The solid residue was collected and dried, yield 12 g (90%), mp 345–350°, and crystallized (Darco[29]) from glacial acetic acid as a colorless solid, yield 10.15 g (77%), mp >360°

(23) (a) P. B. Russell, *J. Chem. Soc.*, 2951 (1954); (b) B. Roth and J. Z. Strelitz, *J. Org. Chem.*, **34**, 821 (1969).

(24) By analogy, the ethanolic spectrum of the sterically hindered 9,10-dihydro-4,5-dimethylphenanthrene has only one maximum, at 260 nm, similar to the spectrum of biphenyl, but unlike the spectrum of the relatively planar 9,10-dihydrophenanthrene, which has three maxima up to 330 nm.[25,26]

(25) (a) G. H. Beavan, D. M. Hall, M. S. Lesslie, and E. E. Turner, *J. Chem. Soc.*, 854 (1952); (b) K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon, and G. H. Wahl, Jr., *J. Amer. Chem. Soc.*, **86**, 1710 (1964).

(26) H. Suzuki, *Bull. Chem. Soc. Jap.*, **35**, 1715 (1962).

(27) The infrared spectra were recorded on a Perkin-Elmer Model 137B recording spectrophotometer in potassium bromide or potassium chloride disks. Uv spectra were measured with Cary Model 11 and Model 15 spectrophotometers at pH 1 (ethanolic 0.1 *N* hydrochloric acid), ethanol, and dimethylformamide. The nmr spectra were determined on a Varian Associates Model A-60 recording spectrophotometer in trifluoroacetic acid and heptadeuteriodimethylformamide. Tetramethylsilane (TMS) was used as the internal standard and all signals are given in parts per million (δ) relative to TMS at δ 0. Ascending paper chromatography was done on Whatman No. 1 paper in the following solvent systems: A, *n*-butyl alcohol–acetic acid–water (4:1:1); B, *n*-butyl alcohol saturated with water; C, isopropyl alcohol–ammonium hydroxide–water (70:5:25). Adenine was used as an internal standard in all chromatograms; spot locations are expressed as R_{Ad} values with adenine at 1.00. All melting points were measured in Pyrex capillary tubes in a modified Wagner–Meyer apparatus [E. C. Wagner and J. F. Meyer, *Ind. Eng. Chem., Anal. Ed.*, **10**, 584 (1938)] at a heating rate of 2°/min and are corrected wherever possible. Microanalyses were performed by the Scandinavian Microanalytical Laboratories, Herlev, Denmark, and Galbraith Laboratories, Knoxville, Tenn.

(28) A. Rosowsky, P. C. Huang, and E. J. Modest, Abstracts of Papers, Second Northeast Regional Meeting of the American Chemical Society, Providence, R. I., Oct 20, 1970, p 83.

(29) Darco G-60 activated carbon, Atlas Chemical Industries, Inc., Wilmington, Del.

(lit.[10,16] mp 358–359° and 360°). For analysis the material was recrystallized several times from glacial acetic acid.

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 67.65; H, 3.71; N, 13.18.

2,4-Dichlorobenzo[*g*]quinazoline (4a).—A mixture of **3a** (3.0 g, 0.014 mol), bromobenzene (150 ml, bp 151–152°), and phosphorus oxychloride (30 ml) was refluxed for 3 hr. Another 30-ml portion of phosphorus oxychloride was added and reflux was continued for another 12 hr. After removal of volatile solvents under reduced pressure, the residue was poured onto ice and brought to pH 10 with 1 *N* sodium carbonate. The aqueous phase was then stirred for 15 min with the addition of chloroform (150 ml) and thoroughly extracted with additional chloroform. The combined chloroform extracts were washed with water and dried. Removal of solvent gave a yellow residue (3 g, 90%), mp 200–204°. This material was sublimed at 160–165° (0.5 mm) and a lemon-yellow sublimate, yield 2.4 g (66%), mp 203–204°, was obtained and crystallized from dry benzene as yellow needles, yield 2.23 g (70%), mp 205–206° (lit.[13] mp 205°). For analysis this material was crystallized twice from benzene and dried at 60° (0.5 mm) for 10 hr. (The material had a tendency to sublime even at low temperatures.)

Anal. Calcd for $C_{12}H_6N_2Cl_2$: C, 57.86; H, 2.43; Cl, 28.47; N, 11.25. Found: C, 57.99; H, 2.57; Cl, 28.11; N, 11.05.

2,4-Diaminobenzo[*g*]quinazoline (5a) from 4a.—A mixture of **4a** (300 mg, 0.0012 mol) and dry ethanol (60 ml) saturated with gaseous ammonia at 0° was heated at 170–180° for 70 hr in a stainless steel reactor. A nitrogen atmosphere was maintained during all subsequent operations, including the crystallizations. The greenish-yellow reaction mixture was taken to dryness on a steam bath with the aid of a jet of nitrogen. After extraction with 5% aqueous sodium hydroxide solution (20 ml) on a steam bath for 15 min, the greenish-yellow solid was collected, washed, dried (200 mg, 80%), and crystallized from absolute ethanol by concentration of the solution with a jet of nitrogen as yellow-green needles, yield 175 mg (70%), mp 280–282°, negative Beilstein test. Several crystallizations from absolute ethanol afforded yellow-green needles: yield 65 mg (25%); mp 284–286° (lit.[13,14] mp 285°, 287°); R_{Ad} 1.33 (solvent A), 1.14 (solvent B), 1.23 (solvent C).

Anal. Calcd for $C_{12}H_{10}N_4$: C, 68.55; H, 4.80; N, 26.65. Found: C, 68.34; H, 4.96; N, 26.59.

2-Amino-4-hydroxybenzo[*g*]quinazoline (6). A. From 2-Amino-3-naphthoic Acid.—A mixture of guanidine carbonate (24 g, 0.13 mol) and solid phenol (40 g) was fused at 180–190° (bath temperature) for 15 min and then 2-amino-3-naphthoic acid (24 g, 0.064 mol) was added. The mixture was heated under gentle reflux (air condenser) with stirring for 5 hr. After trituration of the reaction mixture with ethanol (60 ml), the resulting solid material was extracted with refluxing glacial acetic acid (350 ml). Crystallization of the insoluble residue from 8 *N* hydrochloric acid yielded **6** HCl (4 g, 25%), no melting point below 320°. The hydrochloride (500 mg) was stirred with 10 ml of concentrated ammonium hydroxide for 1 hr at room temperature and the resultant yellow solid material (**6**) (300 mg) was crystallized from dimethylformamide: yield 100 mg; mp >330°; R_{Ad} 1.46 (solvent A), 1.45 (solvent B), 1.18 (solvent C).

Anal. Calcd for $C_{12}H_8N_2O$: C, 68.24; H, 4.30; N, 19.89. Found: C, 68.05; H, 4.89; N, 19.87.

B. By Acid Hydrolysis of 5a.—A solution of 2,4-diaminobenzo[*g*]quinazoline (**5a**, 100 mg, 0.48 mmol) in 6 *N* hydrochloric acid (25 ml) was heated under reflux for 1 hr. The yellow reaction mixture started depositing white needles after 0.5 hr and the color of the solution was gradually discharged. The crystals were collected and dried, yield 100 mg (90%), no melting point below 350°. This material was stirred with concentrated ammonium hydroxide (10 ml) for 5 min, collected, washed with warm water, and dried as a bright yellow solid, yield 90 mg (80%), no melting point below 350°, identical with **6** prepared by procedure A.

4-Hydroxybenzo[*g*]quinazoline (3b).—A mixture of 2-amino-3-naphthoic acid (5 g, 0.027 mol) and formamide (2.5 g, 0.056 mol) was fused at 150–155° (internal temperature) in a beaker for 10 min with constant hand stirring to prevent formation of any lumps in the melt. Another portion of formamide (2.0 g, 0.44 mol) was added and the heating at 150–155° was continued for 4 hr with occasional stirring to keep the mass in a thin, pasty form. The reaction mixture was stirred with cold water (50 ml) and the slurry was filtered. Several crystallizations of the residue (4.6 g, 83%) from glacial acetic acid, the first with Darco, afforded colorless needles, mp 279–280° (lit.[11] mp 278°).

Anal. Calcd for $C_{12}H_8N_2O$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.21; H, 4.42; N, 14.15.

4-Chlorobenzo[*g*]quinazoline (4b).—A fine suspension of **3b** (4 g, 2.04 mmol) in 200 ml of chlorobenzene was refluxed for 34 hr with 25 ml of freshly distilled phosphorus oxychloride. The red solution was cooled, filtered through a sintered glass funnel, and poured into an aqueous suspension (400 ml) of sodium carbonate (30 g) and calcium hydroxide (30 g) containing crushed ice. After 30 min of stirring, the chlorobenzene layer was separated and the aqueous alkaline layer (pH 8) was extracted three times with chloroform. The combined organic extracts were washed with water (10 ml) and dried. The solvents were removed and the residue, yield 2.8 g (68%), mp 176–178°, was sublimed at 180–190° (0.5–0.7 mm), yield 1.9 g (45%) of yellow sublimate, mp 177–179° (lit.[11] mp 179°). Several crystallizations from benzene yielded analytically pure yellow needles, mp 178–179°, in 40% overall recovery, R_{Ad} 1.86 (solvent A), 1.70 (solvent C).

Anal. Calcd for $C_{12}H_7N_2Cl$: C, 67.14; H, 3.29; Cl, 16.52; N, 13.05. Found: C, 67.55; H, 3.36; Cl, 16.56; N, 12.97.

4-Aminobenzo[*g*]quinazoline (5b).—Amination of **4b** (400 mg, 1.9 mmol) by a procedure similar to that employed in the amination of **4a** (except that a nitrogen atmosphere was not necessary) afforded 300 mg of crude **5b**, mp 324–331°, which was halogen-free. Sublimation at 140–180° (0.5 mm) gave a yellow sublimate, yield 180 mg (50%), mp 335–338°. Three crystallizations from absolute ethanol yielded yellow needles, 120 mg (34% overall yield), mp 337–338° (lit. mp 363°,[11,12] *ca.* 365° dec[18]).

Anal. Calcd for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.62; H, 4.64; N, 21.61.

Isolation of 3-Aminobenzo[*f*]quinazoline (7) and 1-Hydroxy-3-aminobenzo[*f*]quinazoline Hydrochloride (8 HCl) on Dehydrogenation of 1.—An intimate mixture of **1** (800 mg) and 10% palladium–charcoal (70 mg) was placed in a Heymann's apparatus and heated in a metal bath at 270–300° under a slow stream of nitrogen. The evolved gases were found to contain ammonia throughout the reaction period of 1 hr. The yellow sublimate that had deposited on the cold finger was collected and the residue containing the catalyst was extracted with dimethylformamide. The total solid material obtained (430 mg, 53%) was sublimed at 120–150° (0.5 mm) and the sublimate, on crystallization from absolute ethanol, yielded 1 (100 mg), mp 260–262°, $\lambda_{max}^{pH\ 1}$ 272 nm. The residue in the sublimation tube on further sublimation at 170–180° (0.5 mm) furnished a yellow solid (180 mg, 23%), mp 201–205°.

The latter sublimate (170 mg) was dissolved in 150 ml of warm 0.5 *N* hydrochloric acid and chromatographed on a column of Dowex 50W-X8 (H^+) cation exchange resin, 100–120 mesh (column volume 6.5 ml in a 50-ml buret). Elution with 2 *N* hydrochloric acid (the progress of the elution being monitored by the absorbance of the characteristic 291-nm peak) gave 30 mg of white solid which on treatment with dilute (1:3) aqueous ammonia (30 ml) at room temperature furnished a yellow solid (15 mg). Crystallization from absolute ethanol gave yellow solid (12 mg), mp 263–264° dec, R_{Ad} 1.80 (solvent A), 1.81 (solvent B), 1.72 (solvent C). A mixture melting point of this sample with authentic **7** prepared in this laboratory was undepressed.[20,21]

Anal. Calcd for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.53. Found: C, 73.54; H, 4.61; N, 21.59.

Further elution with 4 *N* hydrochloric acid afforded colorless material (60 mg, λ_{max}^{KBr} 5.85 μ), which was redissolved in warm 4 *N* HCl, filtered, and refrigerated. Colorless needles of **8** HCl were collected, yield 35 mg, no melting point below 360°, R_{Ad} 1.78 (solvent B), 1.43 (solvent C). (The mother liquor afforded another 15 mg of product on evaporation.)

Anal. Calcd for $C_{12}H_9N_3O \cdot HCl$: C, 58.19; H, 4.07; Cl, 14.32; N, 16.96. Found: C, 58.58; H, 4.21; Cl, 13.87; N, 16.60.

The free base of **8** from this analytical sample was identical with free base from authentic $8 \cdot {}^1/_2CH_3COOH$ prepared previously.[21]

3-Amino-1-hydroxy-5,6-dihydrobenzo[f]quinazoline (9.)—Sodium nitrite (500 mg, 7.2 mmol) in water (2 ml) was added dropwise at 5–10° to a stirred solution of 1,3-diamino-5,6-dihydrobenzo[*f*]quinazoline (**1**, 500 mg, 2.35 mmol) in 4 *N* hydrochloric acid (80 ml). The reaction mixture was stirred for an addi-

tional 0.5 hr at 5–10° and then at room temperature for 16 hr. The white solid that separated was collected and combined with additional material obtained on concentration of the filtrate to *ca.* 10 ml. The combined solids were stirred with 4 *N* ammonium hydroxide for 30 min. A greyish-white solid was obtained: yield 300 mg (60%); no melting point below 330°; λ_{max}^{KBr} 6.0 and 6.1 μ. Several crystallizations from 25% acetic acid yielded 100 mg (20%) of off-white solid, no melting point below 340°, R_{Ad} 1.79 (solvent A), 1.77 (solvent B), 1.46 (solvent C).

Anal. Calcd for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.38; H, 5.25; N, 19.79.

1,3-Dihydroxy-5,6-dihydrobenzo[*f*]quinazoline.[30]—The preceding nitrosation of **1** was carried out under forcing conditions (with twice the ratio of nitrous acid and at 40–50° for 5 hr) and the reaction product was triturated with hot water and crystallized successively from 25% acetic acid and 95% ethanol (Darco). In addition to **9**, another compound was isolated as off-white crystals: yield 60 mg; mp 342–345°; λ_{max}^{EtOH} 303 nm (ϵ 9150), 253 (15,400); λ_{inf}^{EtOH} 294 nm; λ_{max}^{KBr} 5.78, 6.1 μ.

Anal. Calcd for $C_{12}H_{10}N_2O_2$: C, 67.27; H, 4.70; N, 13.08. Found: C, 67.12; H, 4.86; N, 13.15.

3-Amino-1-hydroxybenzo[*f*]quinazoline Hydrochlorides (8 HCl).—A mixture of 3-amino-1-hydroxy-5,6-dihydrobenzo[*f*]-quinazoline (**9**, 90 mg, 0.39 mmol) and 5% palladium–charcoal (30 mg) was heated slowly in a Heymann's apparatus (nitrogen flow) from 210 to 320° and then kept for 1.5 hr at 300–320°. The sublimate on the cold finger (20 mg, 22%) was purified twice by dissolution in 2 *N* hydrochloric acid and precipitation with ammonia. Crystallization from 9 *N* hydrochloric acid yielded white needles of **8** HCl: yield 10–11 mg (10%); no melting point below 360°; R_{Ad} 1.70 (solvent A), 1.78 (solvent B), 1.43 (solvent C). The material was identical with the sample of **8** HCl obtained by solid state dehydrogenation of **1**.

2,4-Diamino-5,6-dihydrobenzo[*h*]quinazoline (11a).—A mixture of 1-tetralone (1.46 g, 0.01 mol), dicyandiamide (1.26 g, 0.015 mol), and Triton B (0.1 ml, as catalyst) was heated for 5.5 hr at 195–201° (internal temperature). A clear solution resulted in 25 min and solid started to deposit shortly thereafter. The yellowish semisolid mixture was evaporated to dryness. Trituration with 4 ml of 3 *N* hydrochloric acid yielded solid, 2.31 g (55%). Crystallization from 1 *N* hydrochloric acid (Darco) gave colorless needles (46% recovery), which darken and shrink somewhat above 245° but do not melt below 310°. Recrystallization from 50% ethanol afforded analytically pure colorless needles, no melting point below 310°.

Anal. Calcd for $C_{12}H_{12}N_4 \cdot HCl \cdot H_2O$: C, 54.03; H, 5.67; Cl, 13.29; N, 21.01. Found: C, 53.90; H, 5.69; Cl, 13.41; N, 21.12.

Basification of an aqueous solution of **11a** HCl with sodium hydroxide gave **11a** (58% yield). Crystallization from 50% ethanol (Darco) yielded analytically pure colorless plates mp 207–209°.

Anal. Calcd for $C_{12}H_{12}N_4$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.74; H, 5.75; N, 26.36.

2,4-Diaminobenzo[*h*]quinazoline (12). A.—An intimate mixture of 2,4-diamino-5,6-dihydrobenzo[*h*]quinazoline (**11a**, 1.0 g, 47 mmol) and sulfur (0.23 g, 71 g-atoms) was heated for 0.5 hr in an open test tube at 210–280° (bath temperature). The dark brown, glassy melt was pulverized and purified by high vacuum sublimation at 200–220° (0.005–0.001 mm) as a yellow crystalline sublimate, yield 0.25 g (25%), mp 262–275°. One more sublimation afforded analytically pure yellow prisms, mp 273–277°.

Anal. Calcd for $C_{12}H_{10}N_4$: C, 68.55; H, 4.80; N, 26.65. Found: C, 68.52; H, 4.64; N, 26.30.

B.—An intimate mixture of **11a** (0.5 g, 2.3 mmol) and 10% palladium–charcoal (800 mg) was introduced into a metal bath at 200°, slowly heated to 265°, and then maintained at 265–285° for 35 min. A dimethyl sulfoxide extract of the reaction mixture was filtered, concentrated on a steam bath, and triturated with a 1:1 mixture of ether–benzene. The residue (210 mg, 43%) was sublimed twice at 250–260° (0.5–0.7 mm). A yellow solid, yield 30 mg (6%), mp 275–277°, was obtained, identical with the sample of **12** prepared by method A.

2,4-Diamino-6-methyl-5,6-dihydrobenzo[*h*]quinazoline (11b).—A mixture of 4-methyl-1-tetralone (1.60 g, 0.01 mol), dicyandiamide (1.26 g, 0.015 mol), and Triton B (0.08 ml) was heated for 5 hr under nitrogen at 194–204° (internal temperature). A complete solution was not observed at any time. The syrupy reaction mixture was triturated with acetone, yield 0.7 g (31%) of crude tan solid. The mother liquor was evaporated and triturated with ether, yield 1.13 g (15%) of tan crystalline solid. Part of the crude solid, 1.1 g, was dissolved in 80 ml of 95% ethanol (Darco) and the volume of the yellow filtrate was reduced to 4–5 ml. After overnight refrigeration the solid was collected as yellowish rods (0.69 g, 63% recovery), mp 217–222°. Two more crystallizations from 95% ethanol afforded analytically pure, pale yellow plates, mp 223–227°.

Anal. Calcd for $C_{13}H_{14}N_4$: C, 69.00; H, 6.24; N, 24.76. Found: C, 68.77; H, 6.51; N, 24.48.

2,4-Diamino-5,6-dihydrothieno[2,3-*h*]quinazoline (13).—A mixture of 4-keto-4,5,6,7-tetrahydrothianaphthene (9.12 g, 0.06 mol) and dicyandiamide (7.56 g, 0.09 mol) was heated for 5 hr at 182–200° (internal temperature). The reaction mixture was triturated with acetone to obtain yellow crystals (5.41 g). The mother liquor, on evaporation and trituration with ether, yielded 7.7 g of yellow crystalline solid. Crystallization from 95% ethanol (Darco) afforded 6.97 g (63% yield) of off-white crystals. Recrystallization once more from 95% ethanol (recovery 59%) and finally from 50% aqueous ethanol gave the analytical sample, mp 240–246°.

Anal. Calcd for $C_{10}H_{10}N_4S$: C, 55.02; H, 4.62; N, 25.67; S, 14.69. Found: C, 54.97; H, 4.86; N, 25.56; S, 14.57.

2,4-Diaminothieno[2,3-*h*]quinazoline (14).—An intimate mixture of **13** (328 mg, 15 mmol) and sulfur (73 mg, 22.5 g-atoms) was heated for 0.5 hr at 231–278° (bath temperature). The brown crystalline solid was dissolved in 100 ml of 95% ethanol and filtered, and the volume was reduced to 15 ml. After overnight refrigeration, the yellow prismatic solid (230 mg, 71%) melted at 305–308° dec. Recrystallization from 95% ethanol afforded analytically pure yellow rods, mp 320–322° dec.

Anal. Calcd for $C_{10}H_8N_4S$: C, 55.53; H, 3.73; N, 25.91; S, 14.83. Found: C, 55.33; H, 3.72; N, 26.11; S, 14.87.

2,4-Diaminoindeno[1,2-*d*]pyrimidine (15).—Dicyandiamide (0.84 g, 0.01 mol) and 1-indanone (1.98 g, 0.015 mol) was heated for 6 hr at 173–187° (internal temperature). Trituration of the glassy solid with warm acetone afforded a tan powder (1.3 g, 66%) which was crystallized from methanol as yellow prisms (69% recovery), mp 274–277°. Crystallization from 14 ml of 0.1 *N* hydrochloric acid (78% recovery) and then from water gave analytically pure pale yellow needles of the monohydrochloride, which decompose at 355°.

Anal. Calcd for $C_{11}H_{10}N_4 \cdot HCl$: C, 56.29; H, 4.72; Cl, 15.11; N, 23.87. Found: C, 56.40; H, 4.60; Cl, 15.00; N, 23.50.

Registry No.—**1**, 16061-72-6; **3a**, 33986-99-1; **3b**, 33987-00-7; **4a**, 33987-01-8; **4b**, 33987-02-9; **5a**, 33987-03-0; **5b**, 33987-04-1; **6**, 33987-05-2; **7**, 7066-18-4; **8** HCl, 33987-07-4; **9**, 33987-08-5; **10**, 33987-09-6; **11a**, 33987-10-9; **11a** HCl, 33987-11-0; **11b**, 33987-12-1; **12**, 33987-13-2; **13**, 33987-14-3; **14**, 33987-15-4; **15** HCl, 33987-16-5; 1,3-dihydroxy-5,6-dihydrobenzo-[*f*]quinazoline, 33987-17-6.

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