carbon during 1 hr at 25°. The solution was filtered and evaporated to a small volume. Addition of water afforded 1.7 g of a colorless solid (95%). Recrystallization from ethanol yielded **32** as colorless needles (1.5 g, 84%). One further recrystallization afforded an analytically pure sample: mp >320°; nmr (TFA) δ 1.3–2.3 (br, 11, C_6H_{11}), 7.18 (s, 1), 8.42 (s, 1), 9.20 (s, 1); mass spectrum *m/e* 258 (M^+).

Anal. Calcd for $C_{14}H_{18}N_4O$: C, 65.09; H, 7.02; N, 21.69. Found: C, 64.92; H, 6.86; N, 21.51.

3-Cyclohexylimidazo[4,5-*g*]quinazolin-8-one (33). A solution of **32** (0.85 g, 3.0 mmol) in 98% formic acid (50 ml) was heated at reflux for 1 hr. The reaction mixture was treated with decolorizing charcoal, diluted with water (50 ml), and concentrated *in vacuo* to a small volume. Dilute ammonia was added to afford **33** as a colorless powder (0.75 g, 85%). Two recrystallizations from ethanol yielded colorless prisms: mp 268–270°; nmr [$(CD_3)_2SO$] δ 1.2–2.2 (br, 11, C_6H_{11}), 7.90 (s, 1), 8.01 (s, 1), 8.40 (s, 1), 8.55 (s, 1); mass spectrum *m/e* 268 (M^+).

Anal. Calcd for $C_{15}H_{16}N_4O$: C, 67.15; H, 6.01; N, 20.28. Found: C, 67.19; H, 5.95; N, 20.57.

3-Cyclohexyl-8-mercaptoimidazo[4,5-*g*]quinazoline (34). A stirred slurry of **33** (0.75 g, 3 mmol) and purified phosphorus pentasulfide (1.5 g) in dry pyridine (50 ml) was heated 12 hr under reflux. The resulting dark solution was poured into boiling water (600 ml). Upon cooling, **34** separated as a pale yellow precipitate (0.55 g, 69%). Two recrystallizations from acetic acid–ethanol yielded yellow prisms: mp >320°; nmr [$(CD_3)_2SO$] δ 1.2–2.2 (br, 11, C_6H_{11}), 8.08 (s, 1), 8.13 (s, 1), 8.80 (s, 1), 8.90 (s, 1); mass spectrum *m/e* 284 (M^+).

Anal. Calcd for $C_{15}H_{16}N_4S$: C, 63.35; H, 5.67; N, 19.70; S, 11.27. Found: C, 63.09; H, 5.76; N, 19.57; S, 11.45.

8-Amino-3-cyclohexylimidazo[4,5-*g*]quinazoline (30). A sealed tube containing **34** (0.1 g, 0.4 mmol) and 3 ml of ammonia–saturated ethanol was heated at 150° for 24 hr. Upon cooling, colorless needles of **30** were deposited (0.8 g, 85%). Recrystallization from hot dimethylformamide afforded analytically pure **30**: mp >320°; nmr [$(CD_3)_2SO$] δ 1.2–2.2 (br, 11, C_6H_{11}), 8.62 (s, 1), 9.04 (s, 1), 9.44 (s, 1), 9.56 (s, 1); $\lambda_{max}^{95\%\ EtOH}$ 231 nm (ε 46,700), 242 (sh), 260 (sh), 266 (17,100), 307 (sh), 319 (9100), 334 (11,700), 351 (9100); $\lambda_{max}^{0.1\ N\ HCl}$ (95% EtOH) 225 nm (ε 32,500), 233 (sh), 260 (13,600), 266 (sh), 307 (sh), 322 (10,200), 336 (13,400), 352 (12,600); $\lambda_{max}^{0.1\ N\ NaOH}$ (95% EtOH) 242 nm (sh), 260 (ε 18,000), 266 (sh), 307 (sh), 319 (9500), 334 (12,000), 351 (9500); mass spectrum *m/e* 267 (M^+).

Anal. Calcd for $C_{15}H_{17}N_5$: C, 67.39; H, 6.41; N, 26.20. Found: C, 67.30; H, 6.45; N, 25.96.

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Registry No.—**1**, 53449-12-0; 1 HCl, 53449-13-1; **6**, 31374-18-2; **7**, 53449-14-2; **8**, 53449-15-3; **9**, 53449-16-4; **10**, 53449-17-5; **11**, 53449-18-6; **12**, 53449-19-7; **13**, 53449-20-0; **14**, 53449-21-1; **15**, 53449-22-2; **16**, 53449-23-3; **17**, 53449-24-4; **18**, 53449-25-5; **19**, 53449-26-6; **20**, 53449-27-7; **21**, 53449-28-8; **22**, 53449-29-9; **23**, 53449-30-2; **24**, 53449-31-3; **25**, 53449-32-4; **26**, 53449-33-5; **27**, 53449-34-6; **28**, 53449-35-7; **29**, 53449-36-8; **30**, 53449-37-9; **31**, 53449-38-0; **32**, 53449-39-1; **33**, 53449-40-4; **34**, 53449-41-5; benzyl bromide, 100-39-0; benzylamine, 100-46-9; cyclohexylamine, 108-91-8.

References and Notes

(1) (a) For example, see R. K. Robins, *J. Med. Chem.*, **7**, 186 (1964); (b) R. K. Robins, *Heterocycl. Compounds*, **8**, 162 (1967); (c) J. A. Montgomery, T. P. Johnson, and Y. F. Sheely in "Medicinal Chemistry," Part 1, 3rd ed, A. Burger, Ed., Wiley-Interscience, New York, N.Y., 1970; (d) D. Cole, University of Illinois Seminar Abstracts, Dec 14, 1972.
(2) The prefix *lin* refers to the linear disposition of the three rings in compound **1**; *prox* for proximal and *dist* for distal refer to the relationship of the amino group in compounds **2** and **3**, respectively, with respect to the imidazole ring. The numbering of the three ring systems is as shown.
(3) E. C. Taylor and W. R. Sherman, *J. Amer. Chem. Soc.*, **81**, 2464 (1959).
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(8) N. J. Leonard and D. Y. Curtin, *J. Org. Chem.*, **11**, 341 (1946); N. J. Leonard, W. V. Ruyle, and L. C. Bannister, *ibid.*, **13**, 617 (1948); N. J. Leonard and W. V. Ruyle, *ibid.*, **13**, 903 (1948).
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(11) J. H. Lister, *Chem. Heterocycl. Compounds*, **30**, 342 (1971).
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The Angular Benzoadenines. 9-Aminoimidazo[4,5-*f*]quinazoline and 6-Aminoimidazo[4,5-*h*]quinazoline

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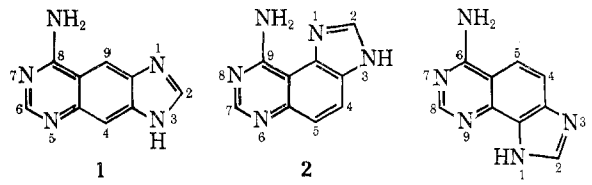
The synthesis of 9-aminoimidazo[4,5-*f*]quinazoline (**2**) and 6-aminoimidazo[4,5-*h*]quinazoline (**3**), angular benzologs of adenine which are given the descriptive names *prox*-benzoadenine and *dist*-benzoadenine, respectively, is reported. The proximal isomer of benzoadenine **2** is synthesized in several steps from 6-acetamido-4-quinazolone (**14**). The distal isomer of benzoadenine **3** is prepared *via* a related route from 7-chloro-8-nitro-4-quinazolone (**4**). The uv spectra of the *lin*-, *prox*-, and *dist*-benzoadenines are discussed in relation to the differing spatial arrangements of the three isomers.

We have undertaken the synthesis of a family of structural analogs of adenine in which a benzene ring has been "inserted" between the imidazole and pyrimidine moieties to form a "stretched-out" purine model. In the preceding paper,[1] we discussed the synthesis and chemical properties of the linearly extended analog, 8-aminoimidazo[4,5-*g*]quinazoline (**1**) for which we proposed the name *lin*-benzoadenine. In this paper we describe the synthesis of the two angular isomers of *lin*-benzoadenine, 9-aminoimidazo[4,5-*f*]quinazoline (**2**) and 6-aminoimidazo[4,5-*h*]quinazoline (**3**), for which we propose the descriptive names, *prox*-benzoadenine (**2**) and *dist*-benzoadenine, respectively.[2]

The similarity of the three isomeric benzoadenines (**1–3**) lies in the fact that they contain binding sites similar to the 1,N^6 binding sites found in adenine and related nucleosides and nucleotides. The differences reside (a) in the spatial re-



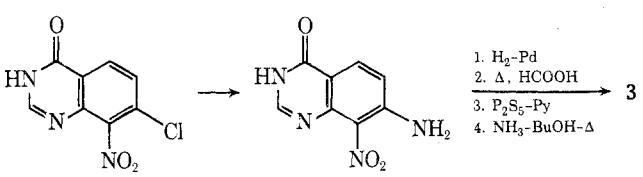
1 2 3

lationships of the pyrimidine and imidazole rings with respect to the central benzene ring and (b) in the extent to which internal hydrogen bonding is likely to occur in the three isomers. The structural differences may help elucidate the geometrical restraints placed upon the utilization of adenine benzologs as surrogates for naturally occurring adenine derivatives in biological systems.

The synthetic method utilized for the preparation of **2** and **3** was modeled after that employed for the synthesis of *lin*-benzoadenine (**1**).[1] The construction of the heterocyclic system contained in the angular compounds **2** and **3** was effected *via* the annelation of an imidazole ring onto a disubstituted quinazoline.

Results and Discussion

The nitration of 7-chloro-4-quinazolone,[3] as described in the previous paper, gave a mixture of two isomeric chloronitroquinazolines. The minor isomer, 7-chloro-8-nitro-4-quinazolone (**4**), was heated with ammonia-saturated butanol in a sealed tube to afford the corresponding amine **5**. Compound **5** was hydrogenated in formic acid to generate the diamino compound, and subsequent heating of the reaction mixture produced the tricyclic imidazoquinazolone. Treatment with phosphorus pentasulfide in refluxing pyridine led to the isolation of 6-mercaptoimidazo[4,5-*h*]quinazoline. The thiation proceeded slowly, requiring 3 days for complete reaction, apparently due to the intermediate formation of an insoluble complex between phosphorus pentasulfide and imidazo[4,5-*h*]quinazolin-6-one. The mercapto compound was then converted to *dist*-benzoadenine, 6-aminoimidazo[4,5-*h*]quinazoline (**3**), by treatment with ammonia-saturated butanol.



4 5

For the preparation of the proximal isomer of benzoadenine (**2**), it was anticipated that 6-chloro-4-quinazolone (**6**)[4] could be used as a starting material in a route to **2** analogous to that described above. Nitration of **6** yielded a single product, 6-chloro-5-nitro-4-quinazolone (**7**) as shown by the nmr spectrum, but reaction of **7** with ammonia in butanol at 175° led to displacement of nitro rather than chloro, with the formation of 5-amino-6-chloro-4-quinazolone (**8**). Conversion of the activated 5-carbon from sp^2 to sp^3 in the transition state must be accompanied by sufficient relief of steric compression between the nitro and the coplanar adjacent carbonyl and chloro groups as to supervene over the $sp^2 \rightarrow sp^3$ conversion at the competing activated 6-carbon. By contrast, coplanarity of the amino group with the adjacent carbonyl and chloro groups will be energetically favored in the product **8**. Since further nucleophilic displacement of the 6-chloro substituent of **8** seemed unfavorable, a modified approach was adopted.

Nitration of 6-acetamido-4-quinazolone (**9**)[5] gave 6-acetamido-5-nitro-4-quinazolone (**10**) as the sole product. The acetamido function was hydrolyzed to the corresponding

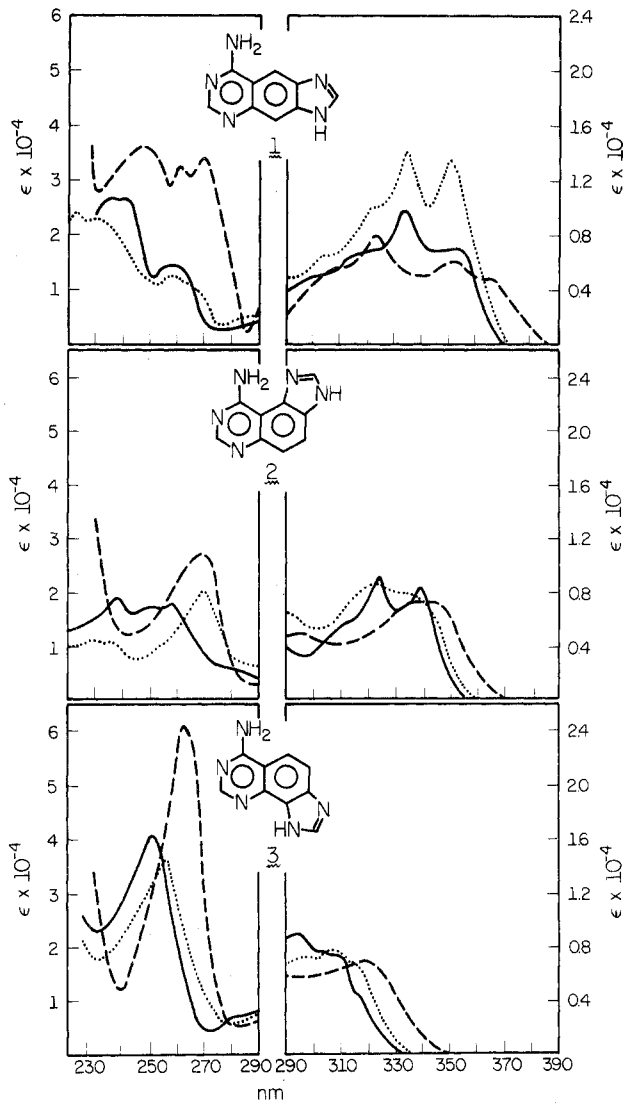
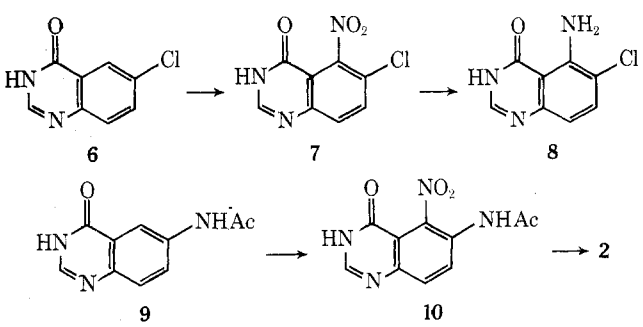


Figure 1. The uv spectra of *lin*-, *prox*-, and *dist*-benzoadenine in 95% ethanol (———), 0.1 *N* HCl in 95 ethanol (·····), and 0.1 *N* NaOH in 95% ethanol (- - - - -).

amine with dilute hydrochloric acid. Reduction of the nitro group and subsequent condensation of the diamino intermediate with formic acid afforded imidazo[4,5-*f*]quinazolin-9-one. Thiation with phosphorus pentasulfide in pyridine yielded 9-mercaptoimidazo[4,5-*f*]quinazoline which was converted to *prox*-benzoadenine, 9-aminoimidazo[4,5-*f*]quinazoline (**2**), by heating in ammonia-saturated butanol. The final conversion could also be effected by treatment with hydrazine followed by hydrogenolysis.[6]



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The ultraviolet spectra of benzoadenines **1–3** are shown in Figure 1. In general, the spectra of heteraromatic compounds can usually be related to absorption properties of their carbocyclic analogs.[7] Accordingly, *lin*-benzoadenine **1**

is formally related to anthracene; the angular benzoadenines **2** and **3** can be related to phenanthrene. Aromatic systems of the linear type (such as **1**) generally exhibit lower energy electronic transitions than isomers of the angular type (such as **2** and **3**).[8] Thus, the low energy bands for the distal isomer **3** are shifted 30 nm to shorter wavelength relative to the corresponding bands for *lin*-benzoadenine (**1**), and those for the proximal isomer **2** exhibit a hypsochromic shift of 10 nm relative to **1**. It is apparent that a countering bathochromic effect is occurring in the latter isomer; otherwise the shift would have been expected to be greater, *i.e.*, closer to that for **3**, namely 30 nm. Accordingly, one looks for a unique structural basis in **2** to account for the comparative electronic absorption data. In compound **2**, intramolecular hydrogen bonding between N^9 and N-1 will assist in maintaining the NH_2 group coplanar with the heterocyclic ring system, thereby extending the π-electron system and lowering the excitation energy, whereas in compounds **1** and **3**, the steric interaction between NH_2 and the peri hydrogen (8-NH_2 and 9-H for **1**; 6-NH_2 and 5-H for **3**) tends for force the NH_2 out of coplanarity, resulting in less effective overlap between the lone pair electrons and the π system. Among the three benzoadenines, *prox*-benzoadenine **2** is the most ready to give up its imidazole hydrogen, exhibiting a pK_a in 66% dimethylformamide of 11.4, while *dist*-benzoadenine **3** is least ready to give up its imidazole hydrogen, with a pK_a of 12.25, and *lin*-benzoadenine **1** is intermediate, pK_a = 11.7. This pattern is consistent with stabilization by intramolecular hydrogen bonding of the anion of **2** and of the free base **3**. In addition, the latter (**3**) is also the least ready to protonate, pK_a 4.9, *vs.* 5.2 for isomer **2** and 5.6 for isomer **1**.

In sequels we shall discuss the ribosidation and the preparation of further substituted derivatives of the benzoadenines to test various concepts concerning structure and biological activity.

Experimental Section

Melting points were determined with a Thomas-Hoover capillary melting apparatus and are corrected. The nmr spectra were recorded on Varian Associates A-60 or A-56/60 spectrometers by Mr. Robert Thrift and his associates using tetramethylsilane (TMS) as an internal standard. The ultraviolet spectra were obtained on a Cary Model 15 spectrophotometer.[9] Microanalyses were performed by Mr. Joseph Nemeth and his associates, who also weighed samples for the quantitative electronic absorption spectra, and by Midwest Microlab, Inc., Indianapolis, Ind. Mass spectra were obtained on a Varian-MAT CH-5 spectrometer coupled with a 620i computer and Statos recorder by Mr. J. Carter Cook and associates. Infrared spectra were determined on a Perkin-Elmer 337 spectrophotometer. Thin-layer chromatograms were run on Eastman Chromagram Sheet 6060 (silica gel with fluorescent indicator).

7-Amino-8-nitro-4-quinazolone (5). A sealed tube containing **4** (1 g, 4.5 mmol) and ammonia-saturated methanol was heated at 175° for 24 hr. Reduction in volume until the appearance of a precipitate and cooling yielded 0.8 g of 7-amino-8-nitro-4-quinazolone (**5**, 87%). Recrystallization several times from ethanol afforded an analytical sample: mp 293–295°; nmr [$(CD_3)_2SO$] δ 6.79 (s, 2, disappears on D_2O shake, NH_2), 6.99 and 7.90 (AB quartet, 2, J = 9 Hz), 8.05 (s, 1); mass spectrum m/e 206 (M^+).

Anal. Calcd for $C_8H_6N_4O_3$: C, 46.61; H, 2.93; N, 27.18. Found: C, 46.57; H, 3.03; N, 26.91.

Imidazo[4,5-*h*]quinazolin-6-one. A solution of **5** (6.6 g, 32 mmol) in formic acid (150 ml) was hydrogenated over 0.6 g of 10% palladium on carbon at 3 atm for 3 hr. After removal of the catalyst by filtration, the solution was refluxed under nitrogen for 2 hr. About 50 ml of water was added, and the volume of the solution was reduced until a white precipitate appeared. On cooling, 4.7 g of white crystals of imidazo[4,5-*h*]quinazolin-6-one was obtained. The mother liquor, on adjustment to pH 8 with ammonia, afforded a further 0.1 g (total 4.8 g, 81%). An analytical sample was obtained by recrystallization several times from water: mp >320°; nmr (TFA) δ 8.14 and 8.74 (AB quartet, 2, J = 9 Hz), 9.37 (s, 1), 9.60 (s, 1); mass spectrum m/e 186 (M^+).

Anal. Calcd for $C_9H_6N_4O$: C, 58.06; H, 3.25; N, 30.09. Found: C, 58.15; H, 3.30; N, 30.25.

6-Mercaptoimidazo[4,5-*h*]quinazoline. A slurry of imidazo[4,5-*h*]quinazolin-6-one (1 g, 5.4 mmol) and phosphorus pentasulfide (5.0 g) in dry pyridine (50 ml) was heated at reflux under nitrogen for 72 hr. After 24 hr the mixture had become clear. The orange solution was poured into hot water (175 ml) and allowed to stand, with the separation of yellow crystals (0.76 g, 70%). Recrystallization from acetic acid–dimethylformamide afforded pale yellow crystals: mp >320°; nmr (TFA) δ 8.17 and 8.92 (AB quartet, 2, J = 9 Hz), 9.00 (s, 1), 9.47 (s, 1); mass spectrum m/e 202 (M^+).

Anal. Calcd for $C_9H_6N_4S$: C, 53.45; H, 2.99; N, 27.70; S, 15.85. Found: C, 53.51; H, 3.25; N, 27.88; S, 15.84.

6-Aminoimidazo[4,5-*h*]quinazoline (3). A sealed tube containing 6-mercaptoimidazo[4,5-*h*]quinazoline (0.1 g, 0.6 mmol) and ammonia-saturated butanol (10 ml) was heated at 200° for 24 hr. The reaction mixture was filtered, and the crystals were dissolved in water by the addition of formic acid and reprecipitated with ammonia to yield 0.056 g (50%) of **3** as a white powder. Recrystallization from acetic acid–ethanol gave analytically pure white crystals: mp >320°; nmr [$(CD_3)_2SO$] δ 7.80 and 8.42 (AB quartet, 2, J = 9 Hz), 8.28 (s, 1), 8.42 (s, 1); $\lambda_{max}^{95\%\ EtOH}$ 251 nm (ϵ 40,700), 280 (sh), 295 (9000), 303 (sh), 309 (sh), 315 (sh); $\lambda_{max}^{0.1\ N\ HCl}$ (95% EtOH) 255 (35,700), 295 (sh), 307 (7700), 315 (sh); $\lambda_{max}^{0.1\ N\ NaOH}$ (95% EtOH) 262 (61,200), 320 (6900); mass spectrum m/e 185 (M^+).

Anal. Calcd for $C_9H_7N_5$: C, 58.37; H, 3.81; N, 37.82. Found: C, 58.10; H, 3.84; N, 37.75.

6-Chloro-5-nitro-4-quinazolone (7). A mixture of 6-chloro-4-quinazolone (**6**,[4] 5 g, 28 mmol), 10 ml of fuming nitric acid, and 10 ml of concentrated sulfuric acid was heated on a steam bath for 3 hr. When the mixture was poured into ice water, 3.4 g of crude yellow material was obtained. Recrystallization from acetic acid afforded 1.5 g of **7** as white crystals. Reduction in volume yielded a second crop (0.1 g, total 1.6 g, 26%): mp 308°; nmr [$(CD_3)_2SO$] δ 7.83 and 8.10 (AB quartet, 2, J = 9 Hz), 8.23 (s, 1, 2-H); mass spectrum m/e (rel intensity) 225 (100) and 227 (36).

Anal. Calcd for $C_8H_4ClN_3O_3$: C, 42.49; H, 1.79; Cl, 15.72; N, 18.63. Found: C, 42.67; H, 1.91; Cl, 15.60; N, 18.55.

5-Amino-6-chloro-4-quinazolone (8). A sealed tube containing compound **7** (5 g, 22 mmol) and ammonia-saturated butanol (70 ml) was heated at 175° for 24 hr. The crystals that separated during the course of the reaction were collected and dried to give 3.6 g (83%) of **8**: mp 278–279°; nmr [$(CD_3)_2SO$] δ 6.72 and 7.55 (AB quartet, 2, J = 9 Hz), 7.19 (br s, disappears on D_2O shake, NH_2), 7.95 (s, 1); mass spectrum m/e (rel intensity) 195 (100) and 197 (36).

Anal. Calcd for $C_8H_6ClN_3O$: C, 49.12; H, 3.09; Cl, 18.21; N, 21.48. Found: C, 49.06; H, 2.98; Cl, 18.24; N, 21.51.

6-Acetamido-5-nitro-4-quinazolone (10). 6-Acetamido-4-quinazolone (**9**,[5] 10 g, 48 mmol) was added to a mixture of red fuming nitric acid (100 ml) and concentrated sulfuric acid (100 ml) in portions such that the temperature did not exceed 10°. The solution was stirred 30 min longer at 0–10° and then poured into 1 l. of ice water. After refrigeration for several hours, yellow crystals of **10** deposited and were recrystallized from water (500 ml) to give 5.9 g (40%) of pure material: mp 311–312° dec; nmr [$(CD_3)_2SO$] δ 2.11 (s, 3, $COCH_3$), 7.84 and 8.08 (AB quartet, 2, J = 9 Hz), 8.20 (s, 1, 2-H); mass spectrum m/e 248 (M^+).

Anal. Calcd for $C_{10}H_8N_4O_4$: C, 48.39; H, 3.25; N, 22.57. Found: C, 48.33; H, 3.07; N, 22.72.

6-Amino-5-nitro-4-quinazolone. A mixture of *N*-acetyl derivative **10** (0.1 g, 0.4 mmol) and 10 ml of 1 *N* HCl was heated at reflux under nitrogen for 2 hr. The solution was reduced in volume and, upon cooling, red crystals were deposited and recrystallized from aqueous ethanol (0.064 g, 75%): mp 310–311°; nmr [$(CD_3)_2SO$] δ 7.28 and 7.60 (AB quartet, 2, J = 8 Hz), 8.14 (s, 1, 2-H); mass spectrum m/e 206 (M^+).

Anal. Calcd for $C_8H_6N_4O_3$: C, 46.61; H, 2.93; N, 27.18. Found: C, 46.64; H, 2.88; N, 27.05.

Imidazo[4,5-*f*]quinazolin-9-one. A mixture of 6-amino-5-nitro-4-quinazolone (3 g, 16 mmol) and formic acid (100 ml) was hydrogenated over 0.3 g of 10% palladium on carbon at 3 atm for 30 min. The catalyst was removed by filtration, and the solution was heated at reflux under nitrogen for 2 hr. The solvent was removed *in vacuo*. The residue was dissolved in water (30 ml), the pH was adjusted to 8 with dilute ammonia, and the solution was chilled. The white crystals were deposited and recrystallized from

water (2.0 g, 69%): mp >320°; nmr (TFA) δ 8.22 and 8.63 (AB quartet, 2, J = 9 Hz), 10.92 (s, 1), 10.97 (s, 1); mass spectrum m/e 186 (M^+).

Anal. Calcd for $C_9H_6N_4O$: C, 58.06; H, 3.25; N, 30.09. Found: C, 58.06; H, 3.44; N, 30.00.

9-Mercaptoimidazo[4,5-*f*]quinazoline. Phosphorus pentasulfide (2.4 g) was dissolved in pyridine (36 ml) with heating, 0.6 g (3 mmol) of imidazo[4,5-*f*]quinazolin-9-one was added, and the mixture was heated at reflux for 17 hr. The volume was reduced to 12 ml by removal of the solvent *in vacuo*, and the solution was poured into boiling water (500 ml). The yellow crystals that were deposited were recrystallized from aqueous dimethyl sulfoxide (0.5 g, 78%): mp >320°; nmr (TFA) δ 8.15 and 8.56 (AB quartet, 2, J = 9 Hz), 10.63 (s, 1), 10.91 (s, 1); mass spectrum m/e 202 (M^+).

Anal. Calcd for $C_9H_6N_4S$: C, 53.45; H, 2.99; N, 27.70; S, 15.85. Found: C, 53.69; H, 3.00; N, 27.47; S, 15.91.

9-Aminoimidazo[4,5-*f*]quinazoline (2). A. *Via* 9-Hydrazinoimidazo[4,5-*f*]quinazoline. A solution of 9-mercaptoimidazo[4,5-*f*]quinazoline (1 g, 5 mmol) in hydrazine hydrate (6 ml) and methyl cellosolve (4 ml) was heated at 100° for 2 hr. The reaction mixture was poured into ethanol (20 ml) and upon cooling, tan crystals of 9-hydrazinoimidazo[4,5-*f*]quinazoline were obtained (1 g, 100%): mp 225° dec; mass spectrum m/e 200 (M^+). The hydrazino derivative was dissolved in hot methyl cellosolve (300 ml), and the solution was refluxed for 2 hr with addition of 2-ml portions of Raney nickel suspension every 20 min. The catalyst was removed by filtration, and the volume was reduced to 40 ml. Upon cooling, tan crystals of **2** were obtained (0.336 g, 37%). Recrystallization from ethanol yielded an analytical sample: mp >320°; nmr [$(CD_3)_2SO$] δ 7.73 and 8.25 (AB quartet, 2, J = 9 Hz), 8.72 (s, 1), 8.82 (s, 1); $\lambda_{max}^{95\%\ EtOH}$ 238 nm (ε 19,000), 251 (17,300), 258 (18,000), 278 (sh), 312 (5900), 324 (9300), 335 (sh), 339 (8500); $\lambda_{max}^{0.1\ N\ HCl}$ (95% EtOH) 229 (11,000), 237 (10,800), 270 (20,500), 290 (sh), 324 (8600), 335 (sh); $\lambda_{max}^{0.1\ N\ NaOH}$ (95% EtOH) 269 (27,700), 296 (4900), 333 (7600), 346 (sh); mass spectrum m/e 185 (M^+).

Anal. Calcd for $C_9H_7N_5$: C, 58.37; H, 3.81; N, 37.82. Found: C, 58.20; H, 3.91; N, 37.53.

B. *From* 9-Mercaptoimidazo[4,5-*f*]quinazoline. A sealed tube containing the mercapto compound (0.5 g, 2.5 mmol) and ammonia-saturated butanol (20 ml) was heated at 220° for 24 hr. The crystals were filtered and dissolved in water (10 ml) by the addition of formic acid. Upon adjusting to pH 8 with ammonia, *prox*-benzoadenine was obtained as colorless crystals (0.38 g, 67%), identical with material synthesized in part A (ir, tlc).

pK_a Determinations. In 66% dimethylformamide (34% water) the following pK_a values were observed: *lin*-benzoadenine (**1**), 5.6, 11.7; *prox*-benzoadenine (**2**), 5.2, 11.4; *dist*-benzoadenine (**3**), 4.9, 12.25.

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Registry No.—**2,** 53449-43-7; **3,** 53449-44-8; **4,** 53449-15-3; **5,** 53449-45-9; **6,** 16064-14-5; **7,** 53449-46-0; **8,** 53449-47-1; **9,** 16064-11-2; **10,** 53449-48-2; imidazo[4,5-*h*]quinazolin-6-one, 53449-49-3; 6-mercaptoimidazo[4,5-*h*]quinazoline, 53449-50-6; 6-amino-5-nitro-4-quinazolone, 53449-51-7; imidazo[4,5-*f*]quinazolin-9-one, 53449-52-8; 9-mercaptoimidazo[4,5-*f*]quinazoline, 53449-53-9; 9-hydrazinoimidazo[4,5-*f*]quinazoline, 53500-17-7.

References and Notes

(1) N. J. Leonard, A. G. Morrice, and M. A. Sprecker, *J. Org. Chem.*, preceding paper.
(2) The prefix *lin* refers to the linear relationships of the three rings in compound **1**; *prox* for proximal and *dist* for distal refer to the spatial relationship of the amino group in compounds **2** and **3**, respectively, with respect to the imidazole ring. The term "benzo" presents no ambiguity for only when the ring is central does it contain no nitrogens and is accordingly "benzo."
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Cyclization of 1-Acetylanthraquinone[1]

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1-Acetylanthraquinone (**1b**) cyclizes under alkaline conditions to give 1-methoxy-2,6-aceanthrylenedione (**2b**). The mechanism of the reaction is discussed.

Anthraquinone (**1a**) is, of course, the parent substance of an extensive family of polycyclic quinones,[2] but one of the simplest possible members of the family, 2,6-aceanthrylenedione (**2a**), has never been prepared. This is simply a cyclic vinylog of anthraquinone and, as such, might be capable of reversible reduction to the dihydro or "vat" form (**3**), corresponding to anthrahydroquinone (**4**).

We have attempted the synthesis of **2a** by cyclodehydration of 1-acetylanthraquinone (**1b**), but this reaction does not succeed under a variety of acidic and basic conditions that were tried. The cyanoacetyl derivative (**1c**) might be expected to cyclize more easily, but we were unable to prepare this compound in working quantities. Bromination of **1b** to **1d** proceeded smoothly, but replacement of Br by CN did not.

We then found that **1b** is readily cyclized in dimethyl sulfoxide containing "Triton B." The product is not, indeed, **2a,** but (as shown by analysis and molecular weight determination) a methoxy derivative of it, and since oxidation of this product gives a mixture of 1-anthraquinonecarboxylic acid (**1e**) and the glyoxylic ester (**1f**), it is evidently the 1-methoxy derivative (**2b**). Two other structures (**5b** and **6b**) can be written for a methoxyaceanthrylenedione capable of oxidation to **1e,** but neither system is a plausible cyclization product of **1b,** and neither would be capable of oxidation to **1f.** In addition, we have synthesized isomer **5b**