IIa with alcoholic ammonia at 110° under pressure[2,3] gave the corresponding adenine derivative (IIc) in 82% yield. Direct hydrolysis of the 6-chloropurine (IIa) with 12 *N* hydrochloric acid afforded 9H-hypoxanthin-9-ylpropionic acid (IIIe) in 43% yield; a similar acid hydrolysis of IIc gave the adeninepropionic acid (IIIc), isolated as a crystalline, quite water-soluble zwitterion. The less soluble 6-mercaptopurine-9-propionic acid (IIId) was isolated at 66% yield.

Experimental[6]

6-Chloro-9H-purin-9-ylpropionitrile (IIa).—To a magnetically stirred mixture of 10.3 g. (66 mmoles) of 6-chloropurine (I) (Burroughs Wellcome and Co.) and 100 ml. of dimethyl sulfoxide was added 22.2 ml. (330 mmoles) of acrylonitrile followed by 0.55 g. (4 mmoles) of anhydrous potassium carbonate. The mixture was stirred until solution was complete, then it was allowed to stand for 70 hr. protected from moisture. Diluted with 250 ml. of water, the mixture was extracted with five 100-ml. of chloroform. The combined extracts were washed with 100 ml. of water, dried with anhydrous magnesium sulfate, then spin evaporated *in vacuo;* the last of the dimethyl sulfoxide was removed at 1 mm. (bath 90°). Recrystallization from ethyl acetate gave 6.66 g. (48%) of light yellow crystals, m.p. 144–145°; a second crop of 1.83 g. (total 61%), m.p. 136–139°, was obtained that was suitable for further transformations. A second recrystallization of a pilot run gave light yellow crystals: m.p. 145–146°; ν_{max} 2250 (C≡N), 1915, 1765 (weak purine fine structure), 1590, 1560, 1500 cm.$^{-1}$ (C=C, C=N); λ_{max} 266 mμ.

Anal. Calcd. for $C_8H_6ClN_5$: C, 46.3; H, 2.91; Cl, 17.1. Found: C, 46.5; H, 3.05; Cl, 16.9.

Other conditions are listed in Table I.

6-Diethylamino-9H-purin-9-ylpropionitrile (IIb) Hydrochloride.—A solution of 104 mg. (0.5 mmole) of IIa and 110 mg. (1.5 mmoles) of diethylamine in 5 ml. of methanol was refluxed for 2 hr., then spin evaporated *in vacuo*. To a solution of the sirupy residue in 10 ml. of water was added 500 mg. of anhydrous potassium carbonate. The mixture was extracted with three 10-ml. portions of chloroform, then the combined extracts were washed with water, dried with magnesium sulfate, and spin evaporated *in vacuo*. The residue was dissolved in reagent ether and treated with hydrogen chloride. A gummy hydrochloride separated that solidified on standing overnight. Recrystallization from acetone–ethyl acetate gave 75 mg. (40%) of product, m.p. 168–170°. Recrystallization from the same solvent pair afforded the analytical sample as colorless needles: m.p. 173–176°; ν_{max} 3360 (NH+), 2700–2300 (broad acidic H), 2250 (C≡N), 2130, 1940 (weak purine fine structure), 1625, 1560 and 1540 cm.$^{-1}$ (C=C, C=N); λ_{max} (pH 1) 270 mμ (ε 17,500), (MeOH) 276 (18,000), (pH 13) 276 (18,200).[5] Since the compound lost hydrogen chloride on being dried at 100° under high vacuum, it was dried at room temperature under high vacuum for analysis.

Anal. Calcd. for $C_{12}H_{16}N_6 \cdot HCl$: C, 51.3; H, 6.10; N, 29.9. Found: C, 51.0; H, 6.20; N, 29.7.

6-Mercapto-9H-purin-9-ylpropionitrile (IId).—A solution of 207 mg. (1 mmole) of IIa and 76 mg. (1 mmole) of thiourea in 15 ml. of absolute ethanol was refluxed with magnetic stirring for 3 hr. during which time the product separated. The cooled mixture was filtered; the product was washed with water to yield 158 mg. (76%), m.p. 283–286° dec. Recrystallization from absolute ethanol gave buff-colored needles: m.p. 284–286° dec.; ν_{max} 2600–2300 (broad acidic H), 2250 (C≡N), 2000, 1850 (weak purine fine structure), 1590, 1560 (shoulder), 1540 cm.$^{-1}$ (C=C, C=N); λ_{max} 325 mμ.

Anal. Calcd. for $C_8H_7N_5S$: C, 46.8; H, 3.44; S, 15.6. Found: C, 46.8; H 3.30; S, 15.6.

9H-Adenin-9-ylpropionitrile (IIc).—To 2.08 g. (10 mmoles) of IIa in a steel bomb was added 44 ml. of ethanol saturated with ammonia at 0°. After being heated for 1 hr. in an oil bath at 110°, the bomb was cooled, and the mixture was spin evaporated *in vacuo*. Trituration of the residue with water gave 1.32 g. (71%) of white crystals, m.p. 243–247°. Recrystallization of a pilot run afforded the analytical sample: m.p. 247–250°; ν_{max} 3500, 3300, 3100 (NH), 2240 (C≡N), 1940, 1720 (weak purine fine structure), 1640, 1580, 1570, 1500 cm.$^{-1}$ (NH, C=C, C=N); λ_{max} 262 mμ.

Anal. Calcd. for $C_8H_8N_6$: C, 51.1; H, 4.28; N, 44.7. Found: C, 51.0; H, 4.39; N, 44.9.

9H-Hypoxanthin-9-ylpropionic Acid (IIIe).—A solution of 386 mg. (1.86 mmoles) of IIa in 12 ml. of 12 *N* hydrochloric acid was refluxed for 3 hr., then spin evaporated *in vacuo*. Trituration of the residue with 2 ml. of water gave 167 mg. (43%) of product, m.p. 275–280° dec.; no attempt was made to recover additional material from the filtrate. Recrystallization from water gave white crystals: m.p. 284–287° dec.; ν_{max} 2800–2300 (broad acidic H), 1720 (carboxyl C=O), 1660, 1580, 1550, 1510 (C=O, C=C, C=N), no C=N near 2250 cm.$^{-1}$; λ_{max} 251 mμ.

Anal. Calcd. for $C_8H_8N_4O_3$: C, 46.1; H, 3.87; N, 26.9. Found: C, 45.9; H, 3.73; N, 26.7.

6-Mercapto-9H-purin-9-ylpropionic Acid (IIId).—Hydrolysis of 390 mg. (1.9 mmoles) of IId as described for the preparation of IIIe gave 282 mg. (66%) of product, m.p. 261–262°. Recrystallization from water afforded opaque flakes: m.p. 262–264°; ν_{max} 2600–2200 (acidic H), 2000, 1925, 1875 (weak purine fine structure) 1710, (carboxyl C=O), 1640, 1600, 1575 (C=C, C=N), no C≡N near 2250 cm.$^{-1}$; λ_{max} 326 mμ.

Anal. Calcd. for $C_8H_8N_4O_2S$: C, 42.8; H, 3.59; N, 25.0. Found: C, 42.7; H, 3.59; N, 252.

9H-Adenin-9-ylpropionic Acid (IIIc).—A solution of 217 mg. (1.15 mmoles) of IIc in 8 ml. of 12 *N* hyrochloric acid was refluxed for 8 hr., then spin evaporated *in vacuo*. Recrystallization from 2.5 ml. of water gave 94 mg. (34%) of IIIc hydrochloride: m.p. 225–227° dec.; ν_{max} 3400, 3250, 3080 (NH), 2800–2400 (broad acidic H), 1720 (carboxyl C=O), 1690 (C=NH$^+$), 1630, 1600, 1550, 1520 cm.$^{-1}$ (NH, C=C, C=N); no attempt was made to recover additional material from the filtrate. Recrystallization from 50% aqueous ethanol gave 24 mg. of the zwitterion of IIIc as white crystals: m.p. 279–280° dec.; ν_{max} 3200–2600 (broad NH and acidic H), 2200–1800 (broad NH$^+$), 1690 (C=NH$^+$), 1670, 1570 (NH, C=C, C=N), no carboxyl C=O near 1720 cm.$^{-1}$; the shape of the curve and the band intensitities are quite different from those of the hydrochloride. The compound had λ_{max} 262 mμ.

Anal. Calcd. for $C_8H_9N_5O_2$: C, 46.4; H, 4.38; N, 33.8. Found: C, 46.2; H, 4.59; N, 33.6.

(6) Melting points were determined in capillary tubes on a Mel-Temp block and those below 230° are corrected. Infrared spectra were run in KBr pellet with a Perkin-Elmer 137B spectrophotometer. Ultraviolet spectra were run with a Perkin-Elmer 202 spectrophotometer in ethanol, unless otherwise indicated.

Reaction of 2,3-Diphenylquinoxaline with Amide Ion. An Unusual Ring Contraction[1]

EDWARD C. TAYLOR AND ALEXANDER MCKILLOP

Department of Chemistry, Princeton University, Princeton, New Jersey

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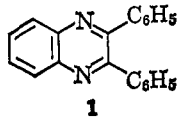
In 1931, Ogg and Bergstrom described a series of investigations designed to demonstrate possible analogies between heterocyclic systems and their acyclic and alicyclic counterparts.[2] Quinoxaline, for example, was described as an "ammono glyoxal," and 2,3-diphenylquinoxaline (**1**) was considered to be the heterocyclic equivalent of benzil. In an attempt to justify this hypothesis, the authors treated 2,3-diphenylquinoxaline (**1**) with potassium amide in liquid ammonia, anticipating a reaction similar to the benzil → benzilic acid rearrangement, which would lead to the formation of 2,2-diphenyl-3-amino-1,2-dihydroquinoxaline (**2**). The conditions chosen for

(1) This work was supported by a research grant to Princeton University from the Smith Kline and French Laboratories, Philadelphia, Pa.

(2) R. A. Ogg, Jr., and F. W. Bergstrom, *J. Am. Chem. Soc.*, **53**, 1846 (1931).

the reaction (*vide infra*) did, in fact, lead to a new product in approximately 30% yield and the recovery of about 60% of unchanged **1**. Data for this new compound A were summarized by Ogg and Bergstrom as follows: the alleged 2,2-diphenyl-3-amino-1,2-dihy-



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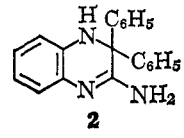

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droquinoxaline melted at 287° (uncor.), formed a hydrochloride, and was unaffected by nitrous acid or by HCl and ethanol at 150°.

Anal. Calcd. for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.41, 80.28; H, 5.42, 5.50; N, 14.16, 14.11.

This evidence, taken in conjunction with the above analogy, was regarded by Ogg and Bergstrom as good proof for the formulation of A as **2**. The failure of A to react with nitrous acid, despite the presence of both a primary and a secondary amino group, was curious and unexplained.

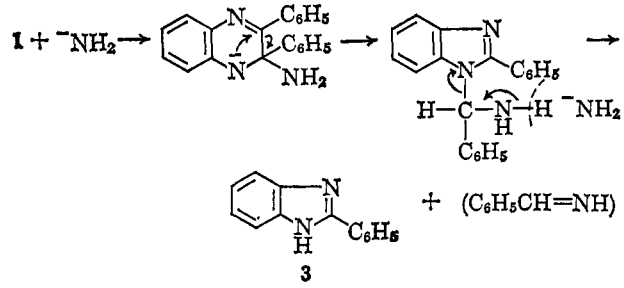
As a consequence of this discrepancy and our general interest in dihydroquinoxalines, we have reinvestigated the "rearrangement" of **1** to **2** and wish to report that the product is in actuality 2-phenylbenzimidazole (**3**), formed by an unusual ring contraction reaction.

Treatment of pure 2,3-diphenylquinoxaline with freshly prepared potassium amide in liquid ammonia in a sealed tube at 140° yielded a crude product, m.p. 260–285°, in 32% yield which, upon rigorous purification, was obtained in the form of colorless needles, m.p. 289–290°, in substantial agreement with the published value. The ultraviolet spectrum of this product (A) showed a distinct bathochromic shift compared with the spectrum of 2,3-diphenylquinoxaline, and was substantially altered by addition of either acid or base. The infrared spectrum of A exhibited diffuse absorption in the range 3010–2500 cm.$^{-1}$, indicative of strong N–H bonding, bands at 698 and 735 cm.$^{-1}$, indicative of a monosubstituted benzene ring, and a band at 760 cm.$^{-1}$, confirming the additional presence in A of a 1,2-disubstituted benzene ring. Otherwise, the spectrum was remarkably simple, especially in the fingerprint region; this feature is often associated with a highly symmetrical molecule. The n.m.r. spectrum of A was similarly nondefinitive, showing only aromatic protons which exhibited complex splitting.

The structure of A was readily determined, however, by inspection of its mass spectrum.[3] The parent peak appeared at *m/e* 194, with the P + 1 and P + 2 peaks well defined. Microanalysis confirmed the new molecular formula of $C_{13}H_{10}N_2$ (Calcd.: C, 80.38; H, 5.19; N, 14.42. Found: C, 80.25; H, 5.03; N, 14.56); the fortuitous correspondence of these values with those calculated for the alleged $C_{20}H_{17}N_3$ formula is remarkable. It was clear from this result that the "rearrangement" of 2,3-diphenylquinoxaline with amide ion had in actuality resulted in the extrusion of a C_7 fragment. The only possible structure for compound A compatible with this spectroscopic evidence was thus 2-phenylbenzimidazole (**3**), and this conclusion was confirmed by direct comparison (mixture melting point determination and identity of n.m.r., ultraviolet, and infrared spectra) with an authentic sample prepared by the condensation of *o*-phenylenediamine with benzaldehyde in the presence of cupric acetate.[4]

The formation of 2-phenylbenzimidazole (**3**) from 2,3-diphenylquinoxaline (**1**) and potassium amide must involve initial addition of amide ion at C-2 (as postulated by Ogg and Bergstrom), but with subsequent ring contraction, presumably with elimination of benzylidenimine, to give the very stable, symmetrical, observed product **3**, rather than phenyl migration of the benzil acid-rearrangement type.

Attempts to effect ring contraction of **1** to **3** with other bases (potassium hydroxide in water or ethanol, sodium methoxide in methanol, sodium hydride in toluene) were unsuccessful; the efficacy of potassium amide appears to be specific.



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Experimental

Reaction of 2,3-Diphenylquinoxaline with Potassium Amide in Liquid Ammonia. Formation of 2-Phenylbenzimidazole (3).—2,3-Diphenylquinoxaline[5] was treated with potassium amide, and the crude product was separated from unchanged starting material as previously described.[2] It was recrystallized from ethanol, with the use of Norit, then sublimed at 260° (0.1 mm.) and the sublimate was recrystallized three times from ethanol to give colorless needles, m.p. 289–290° (lit.[4] m.p. 290°).

(3) We are deeply indebted to Dr. Frank Hochgesang of the Socony Oil Co., Paulsboro, N. J., for the determination of the mass spectrum.

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Substituent Effects on the Long-Range Nitrogen-14 Coupling in Alkylammonium Salts[1]

PAUL G. GASSMAN AND DAVID C. HECKERT[2]

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

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The H^1–N^{14} long-range coupling in ammonium salts has been noted by several workers.[3–8] In general, these authors have attributed the existence of this

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