symmetry established by X-ray analysis requires the molecule to have a center of symmetry, two Pyronin B molecules would have to replace diagonally opposite chlorides in the iron dimer. On the basis of these data we propose the structure IV for Pyronin B. Symmetry and spatial considerations in the unit cell of the crystal eliminate all other chemically logical structures.

From the dialysis experiments, the differential solubility of the two major components of the crude dye in ethyl acetate suggested a simplified extraction procedure for the isolation of pure Pyronin B on a large scale. Extraction of 500 g. of crude dye in a Soxhlet extractor with ethyl acetate gave 120 g. of product which on re-extraction with ethyl acetate gave analytically pure Pyronin B, m.p. 176–178°, $\lambda_{max}^{50\%\ alc.}$ 555 mμ, $E_{1\ cm.}^{1\%}$ 2324. The purity by phase solubility is 99.8 ± 0.2%.

The absorption spectra of the dye was examined in 50% aqueous ethanol in a Beckmann DU spectrophotometer and a Cary recording spectrophotometer. It was found that solutions of the dye of concentrations greater than 10 mg./l. do no obey Beer's law. Principal absorption maximum is at 555 mμ with another at 521 mμ, and multiple absorption from 350 mμ to 210 mμ In addition, a fluorescent emission maximum appears at 580 mμ and an activation maximum at 530 mμ. These latter maxima give rise to erroneous results when measurements are made with the Beckmann DU spectrophotometer.

Experimental

Five hundred grams of commercial Pyronin B[5] was extracted in a Soxhlet extractor with 3-1. portions of ethyl acetate over a period of 14 days. The solvent was changed after the second, fifth, and ninth day. Each extract was worked up separately by concentrating to 500 ml., cooling in ice, filtering the product, washing with ether, and drying. In this way, 120 g. of product was obtained in four crops; 8 g. $\lambda_{max}^{50\%\ C_2H_5OH}$ 555 mμ, $E_{1\ cm.}^{1\%}$ 2185; 34 g. $\lambda_{max}^{50\%\ C_2H_5OH}$ 555 mμ $E_{1\ cm.}^{1\%}$ 2207; 51 g. $\lambda_{max}^{50\%\ C_2H_5OH}$ 555 mμ, $E_{1\ cm.}^{1\%}$ 2383; 27 g., $\lambda_{max}^{50\%\ C_2H_5OH}$ 555 mμ, $E_{1\ cm.}^{1\%}$ 2290.

The combined product was re-extracted with two 3-1. portions of ethyl acetate. The first extraction (7 days) was cooled in ice, filtered, and washed with ether to give 68 g. of metallic green needles, m.p. 176–177°; paper strip electrophoresis[6] (pH 2 buffer, 200 v.)—single spot; phase solubility—slope 1 ± 0.5; $\lambda_{max}^{50\%\ C_2H_5OH}$ 554 mμ, $E_{1\ cm.}^{1\%}$ 2428.

Anal. Calcd. for $C_{42}H_{54}N_4Cl_8O_2Fe_2$ (1,042.28): C, 48.40; H, 5.22; N, 5.38; Cl, 27.22. Found: C, 49.04; H, 5.35; N, 6.66; Cl, 27.33.

The second extraction (14 days) on cooling gave 39 g. of product as green metallic needles, m.p. 176–178°; paper strip electrophoresis (pH 2 buffer, 200 v.)—single spot; phase solubility–slope 0.2 ± 0.2; $\lambda_{max}^{50\%\ C_2H_5OH}$ 555 mμ, $E_{1\ cm.}^{1\%}$ 2324.

Anal. Calcd. for $C_{42}H_{54}N_4Cl_8O_2Fe_2$ (1,042.28): C, 48.40; H, 5.22; N, 5.38; Cl, 27.22; Fe, 10.71. Found: C, 48.60; H, 5.13; N, 5.85; Cl, 27.60; Fe, 10.86.

(5) National Aniline Division of Allied Chemical and Dye Corp. certified dye content 34%.

(6) Spinco Model RB, Durrum type.

Polarographic Analyses.—The half wave potential was determined on a Leeds and Northrup Electrochemograph Type E in 0.2 *M* potassium oxalate containing 0.004% gelatin against a saturated calomel electrode, $E_{1/2}$—0.25 V., i.d.—13.1 μA/mg. of iron added as Pyronin B, a standard Fe(III) solution under the same conditions, gave $E_{1/2}$—0.25V and i.d.—15.1 μA./mg. of iron.

X-Ray Diffraction.—Pyronin B crystallizes as needles, elongated along the *a* axis and developing the {010} and {011} forms. The ends of the needles are normally fractures rather than crystal faces. The crystals are quite opaque, being metallic green by reflected light. Observations on very thin crystals show them to be red by transmitted light.

The unit cell dimensions were determined from rotation and Weissenberg photographs around the *a* and *c* axes. The density was measured by floatation. Monoclinic, a = 9.00, b = 20.84, C = 13.66, B = 108°. Volume of the unit cell = 2562 Å.^{3}. Density calculated = 1.421, measured = 1.398. Systematic absences: *hol* for odd indices of *l*, and *oho* for odd indices, space group $P2_1/c$.

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5-Pyrimidinecarboxylic Acid and Some of Its Derivatives

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The chemical literature seems to be devoid of suitable methods for the preparation of relatively large amounts of simple pyrimidines bearing a carboxy group or its derivative at position 5. In 1904 Gabriel and Colman[1] obtained a small amount of 5-pyrimidinecarboxylic acid during the course of degradative studies on quinazoline. Boarland and McOmie[2] converted this acid to the corresponding amide and methyl ester. Smith and Christensen[3] obtained the compound in 29% yield from the catalytic dehalogenation of 2,4-dichloro-5-pyrimidinecarboxylic acid ethyl ester using a palladium-carbon catalyst in an aqueous sodium hydroxide–ether system.

In our hands the ester was obtained in 60% yield by a modification of the Smith-Christensen procedure and was subsequently hydrolyzed to afford 5-pyrimidinecarboxylic acid. The acid was converted, *via* the acid chloride, to some amides whose counterpart in the pyridine series had been shown to possess biological activities. For example, treatment of a crude, ethereal solution of the acid chloride with diethylamine gave the *N*,*N*-diethylamide, analogous to "Coramine." A similar re-

(1) S. Gabriel and J. Colman, *Ber.*, **37**, 3643 (1904).

(2) M. P. V. Boarland and J. F. W. McOmie, *J. Chem. Soc.*, 1218 (1951).

(3) V. H. Smith and B. E. Christensen, *J. Org. Chem.*, **20**, 829 (1955).

action with *N,N*-diethylethylenediamine gave *N*-(2 - diethylaminoethyl) - 5 - pyrimidinecarboxamide, while the action of ammonia yielded 5-pyrimidinecarboxylic acid amide, resembling niacin.

Success in the dehalogenation of 2,4-dichloro-5-pyrimidinecarboxylic acid ester prompted attempts to extend this reaction to prepare 5-pyrimidinecarbonitrile from the corresponding dihalocyanopyrimidine. However, the hydrogenolysis of this compound, under conditions comparable to the ones employed in the reduction of the carbethoxy analog afforded 5-pyrimidinecarbonitrile in only 9% yield. This same nitrile could also be prepared by the dehydration of the carboxamide by means of phosphorus pentoxide. Furthermore the cyanopyrimidine was found to undergo hydrogen sulfide addition to give 5-pyrimidinethiocarboxamide.

Experimental

5-Pyrimidinecarboxylic Acid, Ethyl Ester.—A mixture of 125 g. (0.568 mole) of 2,4-dichloro-5-pyrimidinecarboxylic acid ester[3] in 1250 ml. of isopropyl alcohol was hydrogenated on a Parr shaker at 15.5 p.s.i. in the presence of 40 g. of calcium oxide and 5 g. of 5% palladium-on-carbon. Only a slight increase in temperature was noted in a run of this size, and the theoretical amount of hydrogen was absorbed after 3 hr. The solids were then filtered off and washed with several portions of fresh isopropyl alcohol. Stripping the filtrate of solvent *in vacuo* left a residue consisting of calcium chloride and product. Ether (500 ml.) was added to this mixture and the inorganic salts were removed by three washings with a minimum of ice-cold water. The organic phase was dried over sodium sulfate, and the solvent was subsequently removed. Very rapid vacuum distillation of the residual oil yielded 54 g. (63%) of crude carbethoxypyrimidine boiling at 80–85°/0.3 mm. which was collected in an ice-cooled receiver. The distillation was terminated when decomposition of the pot residue set in accompanied by the evolution of gases. Refractionation of the crude distillate through a Vigreux column gave 51 g. of pure 5-pyrimidinecarboxylic acid, ethyl ester, b.p. 102.5–103.5°/12 mm. The compound solidified when cooled on ice and melted at 16°. The yield of pure material was 60%.

Anal. Calcd. for $C_7H_8N_2O_2$: N, 18.42. Found: N, 18.15.

5-Pyrimidinecarboxylic Acid.—To 11.5 g. (0.758 mole) of the ester was added 40 ml. (0.080 mole) of 2 *N* sodium hydroxide solution. A mildly exothermic reaction set in, causing the temperature to rise to 50° as the oil went into solution. After a few minutes one equivalent of 1 *N* hydrochloric acid was added, causing immediate precipitation of the acid. The mixture was cooled and filtered to give 8.3 g. (88%) of product, melting at 268–270°. Lit. value: 268–270°.[3]

5-Pyrimidinecarboxylic Acid Chloride.—A mixture of 8.3 g. (0.067 mole) of the acid was refluxed in 50 ml. of reagent grade thionyl chloride until all the material had dissolved. The excess thionyl chloride was removed in vacuum. One equivalent of quinoline was added to the residue which was then distilled to yield 8.1 g. of acid chloride, boiling at 80–85°/3 mm. Atmospheric exposure caused this material to be instantaneously converted to a viscous gum, but it was quite stable if kept in tightly sealed containers. Analytical results were unsatisfactory.

***N*-(2-Diethylaminoethyl) - 5 - pyrimidinecarboxamide.**—A solution of purified 5-pyrimidinecarboxylic acid chloride (8.1 g., 0.056 mole) in 50 ml. reagent grade chloroform was added slowly to an ice-cold solution of 13.2 g. (0.114 mole) of *N,N*-diethylethylenediamine in 30 ml. chloroform. The reaction was allowed to proceed for several days at room temperature, and it was then poured on ice water containing 12 ml. (0.06 mole) of 5 *N* sodium hydroxide solution. The chloroform layer was separated and dried. Stripping of solvent followed by vacuum distillation of the residue yielded 5.5 g. of the amide as a yellow oil boiling at 145–150°/0.160 mm. This corresponds to a 44% yield.

Anal. Calcd. for $C_{11}H_{18}N_4O$: C, 59.43; H, 8.17. Found: C, 59.50; H, 8.51.

***N,N*-Diethyl-5-pyrimidinecarboxamide.**—A crude ethereal solution of 5-pyrimidinecarboxylic acid chloride was prepared by allowing 6.0 g. (0.0485 mole) of the acid to react with 30 ml. of thionyl chloride; the excess thionyl chloride was removed in vacuum and replaced with anhydrous ether.

This solution was added slowly to an ice-cold solution of 24 ml. of diethylamine in 150 ml. dry ether. After allowing the reaction mixture to stand for 1 hr. at room temperature, 3 g. of diethylamine hydrochloride was removed by filtration. The filtrate solvent was subsequently removed and the oily residue was subjected to vacuum distillation to yield 4.5 g. (52% yield) of a pale yellow oil, boiling at 108–113°/0.2 mm.

Anal. Calcd. for $C_9H_{13}N_3O$: N, 23.45. Found: N, 23.50, 23.30.

5-Pyrimidinecarboxamide.—This compound had been previously prepared "in low yield" by the action of aqueous ammonia upon the acid chloride.[2] An improved method is given below.

A crude solution of 5-pyrimidinecarboxylic acid chloride was prepared from 12 g. (0.097 mole) of the acid, as described above. This solution was added dropwise to ether previously saturated with excess gaseous ammonia. The solids, a mixture of product and ammonium chloride, were filtered off after 1 hr. Recrystallization of the solids from 20 ml. of water gave 7.4 g. of the amide. The mother liquor was taken to dryness. The residue was recrystallized from 6 ml. of hot water to give an additional 0.60 g. of product. Both crops melted at 212–213° and the combined yield of 8.0 g. represents 67% of the theoretical amount.

5-Pyrimidinecarbonitrile. A. By the Dehydration of 5-Pyrimidinecarboxamide.—An intimate mixture of 2.5 g. of phosphorus pentoxide and 2.0 g. (0.016 mole) of 5-pyrimidinecarboxamide was placed in a 50-ml. flask equipped with facilities for rapid vacuum distillation. A slight vacuum (50–100 mm.) was applied to the system and the flask was gently heated in a metal bath. At a bath temperature of 250° the product started to distill, boiling at 140°/80 mm., and solidifying in the receiver, which was cooled in an ice bath. The distillate weighed 1.3 g. (77% yield) and melted between 75° and 80°. One recrystallization from alcohol yielded an analytically pure product, m.p. 83.5–84° which weighed 0.80 g. The material crystallized as very long, stout needles.

Anal. Calcd. for $C_5H_3N_3$: C, 57.14; H, 2.87. Found: C, 57.27; H, 3.23.

B. By the Dehalogenation of 2,4-Dichloro-5-pyrimidinecarbonitrile.—A solution of 52.2 g. (0.301 mole) of dihalide (*vide infra*) in 1200 ml. of isopropyl alcohol was shaken under an atmosphere of hydrogen (11 p.s.i.) in the presence of 30 g. of calcium oxide and 3 g. of 5% palladium-on-carbon. The theoretical amount of hydrogen was absorbed after 4 hr. Removal of the solids by filtration, followed by solvent stripping *in vacuo* left a solid residue. This was repeatedly extracted with warm ether as the solids were filtered off. Evaporation of the ether from the filtrate left a residue, but this material failed to yield any 5-pyrimidinecarbonitrile upon distillation. However, when the ether-insoluble material was subjected to exhaustive vacuum sublimation, 2.8 g. (9% yield) of product could be obtained. This material melted at 83–84° and was spectrally identical with 5-pyrimidinecarbonitrile obtained from the dehydration of the amide.

Thio-5-pyrimidinecarboxamide.—A slow stream of hydro-

gen sulfide was passed through a mixture of 0.250 g. (0.0024 mole) of 5-pyrimidinecarbonitrile in 3 ml. of alcohol previously saturated with ammonia. After a short time all the solids went into solution and the product started crystallizing. The hydrogen sulfide addition was continued for another 15 min. Cooling and filtration of the mixture gave 0.230 g. of yellow, well defined crystals melting at 169–170°. An analytical sample prepared from 30 parts of alcohol melted at 170–170.5°.

Anal. Calcd. for $C_5H_5N_3S$: C, 43.15; H, 3.62. Found: C, 43.25; H, 3.68.

2,4-Dichloro-5-pyrimidinecarbonitrile.—A mixture of 123 g. (0.90 mole) of 2,4-dihydroxy-5-pyrimidinecarbonitrile,[4] 290 ml. of diethylaniline, and 720 ml. of phosphoryl chloride was stirred without the application of heat for *ca.* 0.5 hr. After the initial exothermic reaction had subsided, the dark solution was heated under reflux for an additional 1–2 hr. Removal of the excess phosphoryl chloride *in vacuo* and keeping the internal temperature below 65° left a viscous residue. This material was poured on ice and was caused to crystallize by prolonged stirring. The crude product was removed by filtration, and melted between 50° and 58°. Further purification was achieved by dissolving the material in 800 ml. of ether, washing with dilute sodium bicarbonate solution, and drying the ether phase. Subsequent removal of the solvent left a red crystalline mass which was distilled to give 101 g. of a yellow product, b.p. 110–112°/2 mm. solidifying in the receiver. An analytical sample was prepared from isooctane to give lemon-yellow needles, m.p. 62–63°.

Anal. Calcd. for $C_5HCl_2N_3$: N, 24.15. Found: N, 24.19.

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(4) G. Shaw, *J. Chem. Soc.*, 1827 (1955).

Formation of Copper Phthalocyanine

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It has remained an open question in the formation of copper phthalocyanine from phthalic anhydride and urea whether the α-carbon atoms in the maleic anhydride ring of phthalic anhydride are replaced by the carbon atom in urea, or whether the α-carbon atoms in the maleic anhydride ring in phthalic anhydride remain intact to constitute the eight porphin carbons in the tetraazaporphin ring.

This question relates to the formation of phthalonitrile which has been considered to be a reaction intermediate but the presence of which remains to be detected.[1,2] If the α-carbons supplied by the

TABLE I

Material	Run No. 1			Run No. 2			Run No. 3		
	Weight in G.		Activity counts/ min./mg.	Weight in G.		Activity counts/ min./mg.	Weight in G.		Activity counts/ min./mg.
	Initial	Final		Initial	Final		Initial	Final	
C-14 urea	8.0×10^{-5}	...	...	8.0×10^{-5}	...	...	8.0×10^{-5}	...	...
Urea mix	2.000	...	12 ± 2	2.000	...	12 ± 2	2.000	...	12 ± 2
Phthalic anhydride	1.250	...	0	1.250	...	0	1.250	...	0
Reaction mixture	3.540	...	6.5 ± 1	3.540	...	6.5 ± 1	3.540	...	6.5 ± 1
Reaction crude	...	1.8459	3.2 ± 1	...	1.9090	3.4 ± 1		1.8132	3.2 ± 1
Copper phthalocyanine	...	0.792	0	...	Lost during purification			0.382	0
Drierite	14.9959	15.2425	0	11.7162	11.9406	0	10.9004	11.1839	0
Ascarite in tower	42.4878	43.7240	0.44 ± .05	40.9385	42.0769	0.46 ± .05	42.8473	44.0681	0.41 ± .05
Ascarite in tube	12.4081	12.5040	0	13.6144	13.6912	0	14.1807	14.2718	0
Ammonia in H_2SO_4 tower	0	0.1104	...	0	0.1621	...	0	0.2098	...