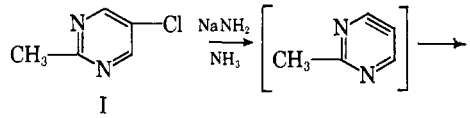
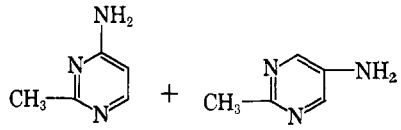
and hence less susceptible to reaction through the addition–elimination mechanism of substitution.

The chloro compound (I) was prepared by the decarboxylation of 2-methyl-4-carboxy-5-chloropyrimidine (II)[5] which was obtained from the condensation of acetamidine with mucochloric acid.

Treatment of I with sodium amide in liquid ammonia would be expected to yield 2-methyl-4-aminopyrimidine (III) and 2-methyl-5-aminopyrimidine (IV), providing the elimination–addition mechanism is operative.



I



III IV

Authentic samples of III and IV were prepared by the following procedures. Condensation of ethyl sodium formylacetate with acetamidine gave 2-methyl-4-hydroxypyrimidine (V).[6] Treatment of V with phosphorus oxychloride gave 2-methyl-4-chloropyrimidine (VI),[6] which was converted to III with aqueous ammonia. Urban and Schnider reported the preparation of IV by the reductive dehalogenation of 2-methyl-5-amino-4,6-dichloropyrimidine (VII).[7] We have synthesized IV by the decarboxylation of 2-methyl-4-carboxy-5-aminopyrimidine (VIII), which was obtained by the amination of 2-methyl-4-carboxy-5-bromopyrimidine (IX)[5] with aqueous ammonia. The bromo acid (IX) was prepared by condensing acetamidine with mucobromic acid.[5] The sample of IV obtained by the decarboxylation of VIII was identical with one prepared by the reduction of VII.[8]

2-Methyl-5-chloropyrimidine was treated with sodium amide in liquid ammonia for 2 hr., and the reaction mixture was analyzed by vapor phase chromatography. 2-Methyl-4-aminopyrimidine (III) was identified as a component of the mixture. This component was shown to have the same retention time as an authentic sample of III and when isolated exhibited an infrared spectrum identical with that of III. The presence of 2-methyl-5-aminopyrimidine (IV) can only be inferred. A component of the reaction mixture with a retention time identical with that of an authentic sample of IV was observed. The quantity obtained, however, was not sufficient for spectral comparison. Control experiments with III and IV indicated that interconversion of the two aminopyrimidines did not occur under the reaction conditions.

The formation of 2-methyl-4-aminopyrimidine (III) from I is consistent with a benzyne-type mechanism.[9] The determination of relative quantities of III and IV is precluded at this time by poor yields.

(5) Z. Budesinsky, *Collection Czech. Chem. Commun.*, **14**, 223 (1949).
(6) S. Gabriel, *Ber.*, **37**, 3638 (1904).
(7) R. Urban and O. Schnider, *Helv. Chim. Acta*, **41**, 1806 (1958).
(8) The authors are indebted to O. Schnider, R. Hoffmann-LaRoche and Co., Basel, Switzerland, for a sample of this compound.
(9) H. Heaney, *Chem. Rev.*, **62**, 81 (1962).

Experimental

Melting points were taken on a Mel-Temp apparatus. Infrared spectra were determined using a Beckman IR-5A spectrophotometer. All vapor phase chromatographic analyses were carried out on an F & M Model 500 gas chromatograph with a 0.25-in. o.d., 5-ft. stainless steel column packed with 8% Triton X-305 on Chromosorb W. The analyses were run isothermally at 153° using helium as a carrier gas (100 ml./min.).

Materials.—2-Methyl-5-chloropyrimidine (I),[5] 2-methyl-4-carboxy-5-chloropyrimidine (II),[5] 2-methyl-4-aminopyrimidine (III),[6] 2-methyl-4-hydroxypyrimidine (V),[6] 2-methyl-4-chloropyrimidine (VI),[6] 2-methyl-4-carboxy-5-aminopyrimidine (VIII),[5] and 2-methyl-4-carboxy-5-bromopyrimidine (IX)[5] were prepared according to procedures described in the literature.

2-Methyl-5-aminopyrimidine (IV) was prepared by heating 1.9 g. of VIII at 200° for 3 hr. in an oil bath. The reaction mixture was extracted for 12 hr. with benzene. Upon removal of the benzene *in vacuo* there was obtained a solid weighing 0.1 g. (8%), which was vacuum sublimed at 135° and 28 mm. The melting point of the sublimate was 155–157°. An authentic sample of IV[8] melted at 156–159° and exhibited an infrared spectrum identical with that of the product obtained from the decarboxylation of VIII.

Reaction of 2-Methyl-5-chloropyrimidine (I) with Sodium Amide in Liquid Ammonia.—The reaction conditions were similar to those by Pieterse and den Hertog employed in the amination of 3-chloropyridine.[10] Sodium amide was prepared from 0.37 g. of sodium, 12 ml. of anhydrous liquid ammonia, and 0.1 g. of ferric nitrate.[11] 2-Methyl-5-chloropyrimidine (I, 0.97 g.) was added cautiously to the stirred mixture. After the mixture was stirred and refluxed for 2 hr., the reaction was quenched with 1.0 g. of ammonium chloride. The ammonia was allowed to evaporate, and the resulting residue was extracted with benzene for 36 hr. The benzene was removed *in vacuo*, and the resulting residue was dissolved in methanol and diluted to 1 ml. Authentic samples of 2-methyl-4-aminopyrimidine (III) and 2-methyl-5-aminopyrimidine (IV) were found to have retention times of 13.0 and 14.8 min., respectively, under the column conditions stated above. The methanolic solution contained a component with a retention time of 13.0 min. When this component was collected, it exhibited an infrared spectrum identical with that of III. A component with a retention time identical with that of IV was detected, but it was not present in sufficient amounts for collection and spectral comparisons. By means of a quantitative correlation between weight of pyrimidine and chromatogram peak area, in which authentic samples of the aminopyrimidines were employed, the reaction mixture was found to contain these pyrimidines in only small amounts (<5%).

Control Experiments on 2-Methyl-4-aminopyrimidine (III) and 2-Methyl-5-aminopyrimidine (IV).—The aminopyrimidines were recovered in amounts up to approximately 50% when refluxed with sodium amide in liquid ammonia at −33° for 2 hr. The column conditions for the analysis were the same as those described above. In each instance, the aminopyrimidine under investigation was found to be the only component present in the reaction mixture.

(10) M. J. Pieterse and H. J. den Hertog, *Rec. trav. chim.*, **80**, 1376 (1961).
(11) T. H. Vaughn, R. R. Vogt, and J. Nieuwland, *J. Am. Chem. Soc.*, **56**, 2120 (1934).

Synthesis of 3,5-Diaminopyrazole Hydrochlorides

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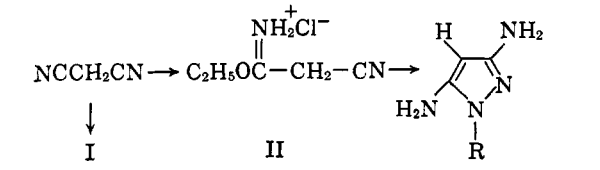
In 1894, von Rothenburg[1] reported that the condensation of malononitrile and hydrazine yielded a compound believed to be 3,5-diaminopyrazole (IIIa).

(1) R. von Rothenburg, *Chem. Ber.*, **27**, 685 (1894).

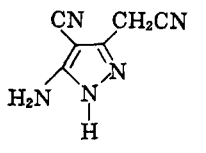
Subsequent reinvestigation by Taylor and Hartke[2] demonstrated that the actual product was 5-amino-4-cyano-3-cyanomethylpyrazole (IV), which was formed by the addition of hydrazine to the dimer of malononitrile, 1,1,3-tricyano-2-aminopropene-1. No authentic simple 3,5-diaminopyrazoles appear to have been described in the literature. An interest in new heterocyclic systems led us to investigate a synthetic route to this class of compounds.

When ethyl cyanoacetimidate hydrochloride (II)[3,4] was allowed to react with phenylhydrazine in ethanol, 3,5-diamino-1-phenylpyrazole hydrochloride (IIIb) was obtained. Similarly, the action of phenethylhydrazine on II gave 3,5-diamino-1-phenethylpyrazole hydrochloride (IIIc). Regrettably, the action of hydrazine itself on II failed; only intractable tars were formed.

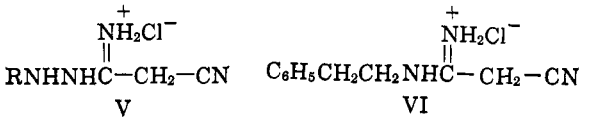


I II

IIIa, R = H
b, R = C_6H_5,·HCl
c, R = $C_6H_5CH_2CH_2$,·HCl

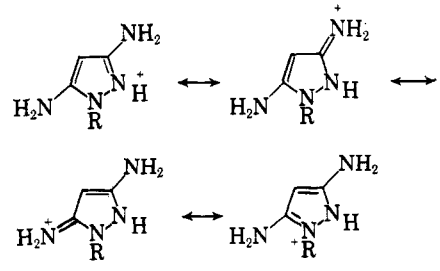


IV



V VI

Alternative structures for the products, the isomeric amidrazones V, were excluded on the basis of the n.m.r. spectra. In D_6-dimethyl sulfoxide solution, IIIb exhibits sharp singlets at 4.73 (1 proton) and 2.38 τ (5); IIIc exhibits singlets at 4.97 (1) and 2.55 τ (5), and triplets at 5.83 (2) and 7.05 τ (2). These chemical shifts differ markedly from those displayed by a reasonable model for V, cyano-N-phenethylacetamidine hydrochloride (VI).[4] The n.m.r. spectrum of VI exhibits resonance at 2.55 (5), 5.70 (2, singlet), 6.30 (2, triplet), and 7.05 τ (2, triplet). The absence of a two-proton singlet at 5.7 τ and the appearance of a one-proton singlet at 4.73 or 4.97 τ clearly excludes structure V and supports the cyclic structures IIIa and IIIb. The absence of nitrile bands in the infrared spectra of IIIa and IIIb is consistent with this interpretation.



VII

(2) E. C. Taylor and K. S. Hartke, *J. Am. Chem. Soc.*, **81**, 2452 (1959).
(3) A. H. Cook, G. Harris, and A. L. Levy, *J. Chem. Soc.*, 3227 (1949).
(4) W. J. Fanshawe, V. J. Bauer, E. F. Ullman, and S. R. Safir, *J. Org. Chem.*, **29**, 308 (1964).

Although the structures of the bases corresponding to III have been represented as 3,5-diaminopyrazoles, alternative tautomeric forms cannot be excluded. However, protonation of any tautomer can lead to VII, the most probable structure for the pyrazole salts III, in which a high degree of charge distribution is possible.

Experimental[5]

3,5-Diamino-1-phenylpyrazole Hydrochloride (IIIb).—To a solution of 7.4 g. (0.05 mole) of ethyl cyanoacetimidate hydrochloride[3,4] and 100 ml. of ethanol was added with stirring under nitrogen 5.4 g. (0.05 mole) of phenylhydrazine. After 30 min. the mixture was filtered, and the filtrate was evaporated under reduced pressure to a brown tar which crystallized from ethanol–ether. One recrystallization gave 2.3 g. (22%) of colorless needles, m.p. 230–231.5° dec. Two additional recrystallizations from ethanol–ether followed by a third recrystallization from ethanol afforded the analytical sample, m.p. 231–233° dec., λ_{max}^{MeOH} 249 mμ (ϵ 18,300).

Anal. Calcd. for $C_9H_{11}ClN_4$: C, 51.31; H, 5.23; Cl, 16.86; N, 26.60. Found: C, 51.37; H, 5.35; Cl, 17.19; N, 26.63.

3,5-Diamino-1-phenethylpyrazole Hydrochloride (IIIc).—To a solution of 1.48 g. (0.01 mole) of ethyl cyanoacetimidate hydrochloride[3,4] and 20 ml. of ethanol was added with stirring under nitrogen 1.4 g. (0.01 mole) of phenethylhydrazine.[6] After 30 min. the mixture was filtered, and the filtrate was evaporated under reduced pressure to a tan pasty solid. Two recrystallizations from acetonitrile gave 0.21 g. (9%) of colorless prisms, m.p. 160–162°. An additional recrystallization afforded the analytical sample, m.p. 160–161°, λ_{max}^{MeOH} 237 mμ (ϵ 13,300).

Anal. Calcd. for $C_{11}H_{15}ClN_4$: C, 55.35; H, 6.29; Cl, 14.88; N, 23.48. Found: C, 55.14; H, 6.42; Cl, 14.45; N, 23.97.

(5) Melting points were determined with a Hershberg apparatus and are uncorrected. Ultraviolet spectra were determined with a Cary 11 spectrophotometer. N.m.r. spectra were determined with a Varian Associates A-60 spectrometer by Mr. W. Fulmor and associates. Microanalyses were performed by Mr. L. M. Brancone and associates.
(6) Phenethylhydrazine, b.p. 108–113° (1–1.5 mm.), was liberated from the commercially available sulfate salt with ethanolic sodium methoxide.

The Synthesis of 2-Bromopyrimidines and 2,2′-Bipyrimidines

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Received August 21, 1963

The syntheses of 2-bromopyrimidine and 2,2′-bipyrimidine have been reported recently,[3] as well as a study of 2,2′-bipyrimidine as a color forming agent in analytical chemistry.[4] The purpose of the present study was to determine whether the reverse addition diazotization method for converting 2-aminopyrimidine to 2-bromopyrimidine[3] could be generalized for preparing new substituted 2-bromopyrimidines, and to determine whether the resulting substituted 2-bromopyrimidines could, in general, be coupled, with the elimination of bromine, to form new substituted 2,2′-bipyrimidines.

This study was successful as far as it was carried out. Additional work on the project had to be suspended,

(1) The author gratefully acknowledges a postdoctoral fellowship granted to him by Eli Lilly and Co., which financially supported this work.
(2) To whom correspondence should be addressed at Carothers Research Laboratory, E. I. du Pont de Nemours and Co., Experimental Station, Wilmington, Del.
(3) D. D. Bly and M. G. Mellon, *J. Org. Chem.*, **27**, 2945 (1962).
(4) D. D. Bly and M. G. Mellon, *Anal. Chem.*, **35**, 1386 (1963).