acid added to neutrality, and the product precipitated in quantitative yield with 500 ml. of water. The material melted over the range 145–215° and was used directly for oxidation.

12a-Aza-C-homo-5α,22a-spirostane-3,12-dione (IX).—The total crude alcohol (0.14 mole) was dissolved in 500 ml. of 90% acetic acid and the solution cooled to 6°. Chromic oxide (14.0 g., 50% excess) in 100 ml. of 90% acetic acid was added dropwise with good stirring so that the temperature remained below 10°. The solution was allowed to stand at room temperature for three hours, diluted with water and the product isolated by chloroform extraction. The residue was crystallized from aqueous ethanol to give 54.6 g. (88%), m.p. 224–231°, in two crops. Recrystallization from aqueous ethanol yielded transparent blades, m.p. 234–236°; $[\alpha]_D$ −55°; λ_{max}^{KBr} 5.82(s), 6.02(s) μ.

Anal. Calcd. for $C_{27}H_{41}O_4N$: C, 73.09; H, 9.32; N, 3.16. Found: C, 73.01; H, 8.96; N, 3.01.

3β-Acetoxy-5α,22a-spirost-9(11)-en-12-one (V).—Selenous acid (7.7 g., 0.06 mole) was dissolved in 150 ml. of *t*-butyl alcohol and 15 ml. of acetic acid. Hecogenin acetate (9.5 g., 0.02 mole) was added and the mixture stirred and heated under reflux for 66 hours. The solvents were distilled, the residue taken up in benzene and chromatographed on silica gel. Elution with 5% ethyl acetate–benzene and crystallization from aqueous ethanol gave long needles, 3.4 g. (36%), m.p. 215–216° (lit.[15] 218–220°), $[\alpha]_D$ −0.1°; λ_{max}^{MeOH} 238 mμ, ε 13,200; λ_{max}^{KBr} 5.73(s), 5.96(s), 6.27(m) μ.

3β-Acetoxy-5α,22a-spirost-9(11)-en-12-one Oxime (VI).—The above acetate (1.9 g., 0.004 mole) was converted to the oxime by heating under reflux for two hours with 0.6 g. (0.008 mole) of hydroxylamine hydrochloride in 40 ml. of pyridine. The crude product on crystallization from aqueous ethanol yielded 1.7 g. (87%) of thin plates, m.p. 282–284°, $[\alpha]_D$ +36°; λ_{max}^{MeOH} 238 mμ, ε 13,600; λ_{max}^{KBr} 5.77(s), 6.20(w) μ.

Anal. Calcd. for $C_{29}H_{43}O_5N$: C, 71.72; H, 8.93; N, 2.88. Found: C, 71.32; H, 8.44; N, 3.13.

3β-Acetoxy-12a-aza-C-homo-5α,22a-spirost-9(11)-en-12-one (VII).—Oxime VI (0.9 g.) and 0.7 g. (approx. 2 molar equivalents) of *p*-toluenesulfonyl chloride were dissolved in 10 ml. of pyridine and allowed to stand at room temperature for 21 hours. Water was added, the product extracted with chloroform and the residue chromatographed on silica gel. Elution with 30% ethyl acetate–benzene and crystallization from aqueous ethanol yielded feathery clusters, 0.45 g. (50%), m.p. 225–231°. Recrystallization from aqueous ethanol gave irregular prisms, m.p. 228–231°, $[\alpha]_D$ −72°; λ_{max}^{MeOH} 220 mμ, ε 15,800; λ_{max}^{KBr} 5.75(s), 6.03(s), 6.21(m) μ.

Anal. Calcd. for $C_{29}H_{43}O_5N$: C, 71.72; H, 8.93; N, 2.88. Found: C, 71.32; H, 8.95; N, 3.00.

Reduction.—The lactam VII (0.24 g.) in 15 ml. of acetic acid was hydrogenated over 0.10 g. of Adams platinum catalyst at atmospheric pressure and room temperature for 5 hours. Catalyst was removed by filtration, the filtrate diluted with water, extracted with chloroform and the residue from the chloroform precipitated from aqueous ethanol. The crude product, 0.19 g., was chromatographed on silica gel.[9] The material eluted with 30% ethyl acetate–benzene was crystallized from aqueous ethanol and yielded 0.084 g. of irregular plates, m.p. 230–233°. The melting point was not depressed on admixture with authentic 3β-acetoxy-12a-aza-C-homo-5α-22a-spirostan-12-one, and the infrared spectra of the two samples were identical.

SKOKIE, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

Syntheses of Pyrrocolines Unsubstituted in the Five-membered Ring[1]

BY V. BOEKELHEIDE AND R. J. WINDGASSEN, JR.[2]

RECEIVED SEPTEMBER 2, 1958

New methods for the synthesis of pyrrocolines having no substituents in the five-membered ring are presented. An unusually simple synthesis for pyrrocoline itself is described.

For the synthesis of cycl[3,2,2]azine described in an accompanying paper,[3] it was necessary to prepare 5-methylpyrrocoline (III). Unfortunately, the Chichibabin reaction,[4] which is the standard method, fails in the case of pyrrocolines bearing no substituents in the five-membered ring. For this reason new methods for the synthesis of pyrrocolines were investigated and it is the purpose of the present paper to report these findings.

The original synthesis of pyrrocoline by Scholtz[5] involved heating α-picoline with acetic anhydride to form "picolide" which, on hydrolysis, gave pyrrocoline. Even though the yields by this procedure are very low, it has persisted as a method of choice for preparing pyrrocoline itself and it seemed desirable in the present instance to subject 2,6-lutidine to the Scholtz procedure in order to obtain an authentic sample of 5-methylpyrrocoline. When 2,6-lutidine and acetic anhydride were heated at 215° in a sealed tube, two products were formed. The first of these was the expected 1,3-diacetyl-5-methylpyrrocoline (I) and the second was a monoacetyl derivative, presumably II. Acidic hydrolysis of II, as is usual for 1- or 3-acetylpyrrocolines, removed the acetyl group and gave the desired 5-methylpyrrocoline (III).

The assignment of structure II to the monoacetyl derivative is based on the further observation that treatment of 5-methylpyrrocoline with acetic anhydride gave a new monoacetyl derivative. Since simple alkylpyrrocolines are known to undergo acetylation at the 3-position,[6] the structure of this product has been assumed by analogy to be IV. Therefore, the monoacetyl derivative from the Scholtz reaction must be 1-acetyl-5-methylpyrrocoline (II). It is of interest that the mechanism proposed by Chichibabin and Stepanow[7] to explain the Scholtz reaction would require II as an intermediate in the formation of the diacetyl derivative I.

Recently, it was reported that the pyrolysis of 1-(2′-pyridyl)-1,3-diacetoxypropane provided a con-

(1) Supported in part by the Office of Ordnance Research, Army Ordnance Contract No. DA-30-115-O.R.D.-723.

(2) National Science Foundation Predoctoral Fellow, 1956–1958.

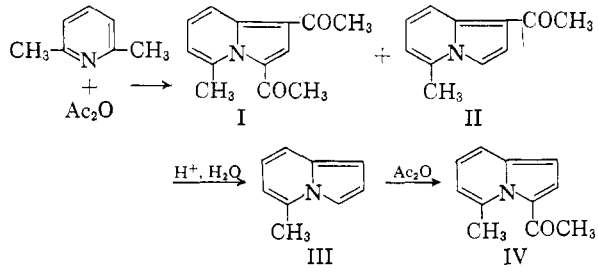
(3) R. J. Windgassen, Jr., W. H. Saunders, Jr., and V. Boekelheide, THIS JOURNAL, **81**, 1459 (1959).

(4) A. E. Chichibabin, *Ber.*, **60**, 1607 (1927).

(5) M. Scholtz, *ibid.*, **45**, 734 (1912); *cf.* E. T. Borrows and D. O. Holland, *Chem. Revs.*, **42**, 611 (1948), for a summary of the earlier methods.

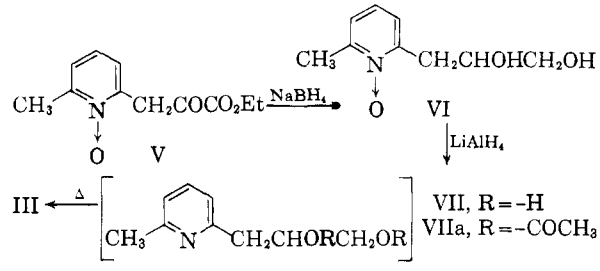
(6) E. T. Borrows, D. D. Holland and J. Kenyon, *J. Chem. Soc.*, 1083 (1946).

(7) A. E. Chichibabin and E. N. Stepanow, *Ber.*, **62**, 1068 (1929).

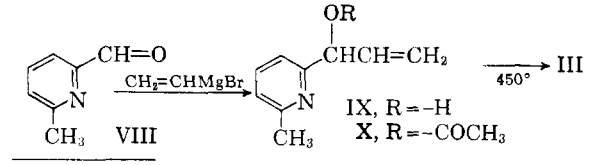


venient route to pyrrocoline.[8] To adopt this exact procedure for the preparation of 5-methylpyrrocoline did not seem feasible because of the difficulty presented in obtaining the necessary starting material, 1-(6′-methyl-2′-pyridyl)-1,3-diacetoxypropane. On the other hand, it seemed probable that the isomeric diacetate VIIa might undergo pyrolysis in a similar fashion and its synthesis appeared to be appreciably simpler. The condensation of 2,6-lutidine N-oxide with diethyl oxalate to give V was carried out following the general procedure described by Adams and Miyano[9] for the condensation of α-picoline N-oxide and diethyl oxalate.

As anticipated from previous experience in the quinaldine series,[10] the sodium borohydride reduction of the sodium enolate of V gave the corresponding diol VI in good yield. Removal of the N-oxide function was then accomplished with lithium aluminum hydride and the intermediate 1-(6′-methyl-2′-pyridyl)-2,3-propanediol (VII) was acetylated and pyrolyzed directly. Although 5-methylpyrrocoline was formed, the product was impure and the yield was very poor.



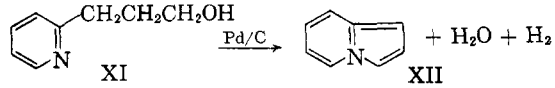
Finally, a practical scheme for the synthesis of 5-methylpyrrocoline was devised based on the commercially available 6-methylpyridine-2-carboxaldehyde(VIII) as starting material. Treatment of this aldehyde with vinylmagnesium bromide gave the vinylcarbinol IX in 68% yield. Conversion of this to the corresponding acetate X followed by pyrolysis at 450° gave 5-methylpyrrocoline in 30% yield. Despite the modest yield in the final step, the method is a practical one for preparing pyrrocolines which are unsubstituted in the five-membered ring and represents a marked improvement over the previous procedures in the literature.



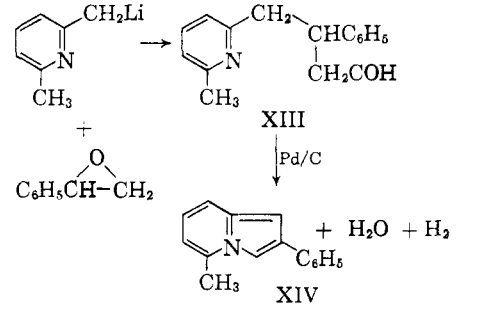
(8) V. Boekelheide and W. Feely, *J. Org. Chem.*, **22**, 589 (1957).
(9) R. Adams and S. Miyano, THIS JOURNAL, **76**, 3168 (1954).
(10) E. M. Roberts, M. D. Gates and V. Boekelheide, *J. Org. Chem.*, **20**, 1443 (1955).

Heer and Hoffmann have prepared some highly substituted pyrrocolines in the steroid series by a rather similar reaction path.[11] In their case cyclization of the unsaturated carbinol was accomplished using phosphorus tribromide and pyridine. Our attempts to effect the conversion of the carbinol IX to 5-methylpyrrocoline using these conditions were completely unsuccessful.

After the work requiring 5-methylpyrrocoline was completed, a superior method for the synthesis of pyrrocoline itself was discovered. The basis for this discovery was the known instability of 3-(2′-pyridyl)-propionaldehyde[12] coupled with the fact that this compound is at the correct oxidation level to form pyrrocoline by simple loss of the elements of water. When 3-(2′-pyrydyl)-1-propanol (XI) was heated in the presence of a dehydrogenation catalyst, water and hydrogen were eliminated to give pyrrocoline (XII) directly in 50% yield. The simplicity of the method plus the commercial availability of the starting material easily makes this the method of choice for preparing pyrrocoline, and for the first time, this interesting heterocycle is readily accessible.



Although the generality of this pyrrocoline synthesis is still under investigation, the preparation of 2-phenyl-5-methylpyrrocoline has been accomplished by the same cyclization procedure. From the reaction of 2,6-lutidyllithium and styrene oxide, the carbinol XIII was obtained in 55% yield.[13] When this was heated with a palladium-on-charcoal catalyst, water and hydrogen were eliminated to give 2-phenyl-5-methylpyrrocoline (XIV), identical in all respects with a sample of this compound prepared by the standard Chichibabin procedure.[3]



Experimental[14]

Reaction of 2,6-Lutidine and Acetic Anhydride.—A mixture of 15.0 g. of 2,6-lutidine and 80.0 g. of acetic anhydride was heated at 210–215° for 5 hr. in a sealed tube. Although the tube was cooled in Dry Ice before it was opened, there

(11) J. Heer and K. Hoffmann, *Helv. Chim. Acta*, **39**, 1820 (1956).
(12) M. G. J. Beets and J. P. Wibaut, *Rec. trav. chim.*, **60**, 905 (1941).
(13) Although it would have been anticipated (*cf.* S. J. Cristol, J. R. Douglass and J. S. Meek, THIS JOURNAL, **73**, 816 (1951)) that attack of the 2,6-lutidyllithium would have been on the β-rather than the α-carbon of styrene oxide, the carbinol must have structure XIII in view of its cyclization to XIV. Also in another connection (R. J. Windgassen, Ph.D. Thesis, University of Rochester, 1958) the alternate carbinol has been prepared independently and shown to be different.
(14) All melting points are corrected. Analyses by Miss A. Smith and the Micro-Tech Laboratories.

was still appreciable pressure present. The contents of the tube, a black solid, were boiled for one hr. with a liter of water. The insoluble material was collected and washed with water and then the aqueous filtrate and washings were extracted with ether. Evaporation of the dried ether extracts gave a dark solid. Recrystallization of this from diisopropyl ether gave 1.4 g. (4.7%) of 1,3-diacetyl-5-methylpyrrocoline (I) as yellow needles which, after another recrystallization from benzene–diisopropyl ether melted at 161–162°. The carbonyl absorption in the infrared occurred at 6.12μ.

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.94; H, 6.34.

The mother liquor from the recrystallization of 1,3-diacetyl-5-methylpyrrocoline from diisopropyl ether was evaporated to dryness, and the residue was treated with charcoal in a mixture of water and methanol. After removal of the charcoal, the solution was concentrated until most of the methanol had been evaporated. Extraction of the concentrated solution with ether, followed by evaporation of the dried ether extracts, gave a solid. Recrystallization of this from diisopropyl ether gave 1.3 g. (5.4%) of 1-acetyl-5-methyl-pyrrocoline (II) as nearly white needles, m.p. 70–71°. The carbonyl absorption in the infrared occurred at 6.15 μ.

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40. Found: C, 75.89; H, 6.54.

The yields in the above reaction were not reproducible. The description given is typical of the best runs. In many cases none of the desired pyrrocolines could be isolated.

Conversion of 1-Acetyl-5-methylpyrrocoline (II) to 3-Acetyl-5-methylpyrrocoline (IV).—A solution of 0.4 g. of 1-acetyl-5-methylpyrrocoline in 3 ml. of concentrated hydrochloric acid was boiled under reflux for 50 min. Neutralization of the acid with aqueous sodium carbonate, followed by steam distillation of the resulting aqueous solution, gave 0.15 g. (49%) of 5-methylpyrrocoline as an oil, purified by bulb to bulb distillation. A portion of this oil was reserved for spectral determinations and the remainder was reacetylated. A mixture of 100 mg. of 5-methylpyrrocoline and 200 mg. of sodium acetate in 3 ml. of acetic anhydride was boiled under reflux for 2 hr. It was then neutralized with aqueous sodium carbonate and extracted with ether. The dried ether extracts were concentrated to give a solid which was taken up in benzene and chromatographed over alumina. From the benzene–ether eluate, a solid resulted which, after recrystallization from diisopropyl ether, yielded 45 mg. (29%) of 3-acetyl-5-methylpyrrocoline (IV) as yellow crystals, m.p. 56.5–57°. The carbonyl absorption in the infrared occurred at 6.15μ.

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40. Found: C, 76.37; H, 6.63.

Ethyl (6-Methyl-2-pyridyl)-pyruvate N-Oxide (V).—In the initial preparation the general procedure of Adams and Miyano[9] was followed without change and gave V in 81% yield. In later preparations it was found more convenient to modify the directions as follows. To a mixture of 92.0 g. of 2,6-lutidine N-oxide and 110 g. of diethyl oxalate in 100 ml. of benzene there was added 80.0 g. of a 25% suspension of sodium hydride in mineral oil. After a brief induction period hydrogen evolution became rapid and cooling of the mixture was necessary to moderate the reaction. When hydrogen was no longer being evolved, the yellow solid, which had separated, was collected and washed with benzene. The yellow solid was then dissolved in a liter of water and this was extracted with ether to remove neutral organic material. After the aqueous solution had been neutralized by the addition of dilute hydrochloric acid, it was extracted with chloroform. When the chloroform extract was dried and concentrated, there separated 161.0 g. (91)% of yellow crystals, m.p. 51–53°. These, after recrystallization from ethanol, melted at 56.5–58.5.

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87. Found: C, 59.54; H, 6.08.

3-(6′-Methyl-2′-pyridyl)-1,2-propanediol N-Oxide (VI).—To a solution of 4.75 g. of the sodium enolate of V (directly as it separated from the reaction mixture above) in 25 ml. of methanol there was added 3.0 g. of sodium borohydride in 25 ml. of methanol. After the initial spontaneous reaction had subsided, the solution was boiled under reflux for 4 hr. The methanol was then removed, 25 ml. of water was added, and the solution was extracted with chloroform using a continuous extractor. Concentration of the chloroform extract gave 2.24 g. (56%) of white crystals, m.p. 96–106°. These, on recrystallization from absolute ethanol, gave crystals melting at 113–114°.

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 59.00; H, 7.15. Found: C, 58.99, 58.65; H, 7.33, 7.32.

Conversion of VI to 5-Methylpyrrocoline.—A mixture of 30.0 g. of 3-(6′-methyl-2′-pyridyl)-1,2-propanediol N-oxide in 60 ml. of tetrahydrofuran was added to a solution of 8.0 g. of lithium aluminum hydride in 280 ml. of tetrahydrofuran. After the mixture had boiled under reflux for 3 hr., it was allowed to stand overnight. The excess lithium aluminum hydride was decomposed by adding ethyl acetate and then a saturated aqueous solution of sodium sulfate was added until the granular precipitate of metallic hydroxides separated cleanly. The organic layer was extracted with ether, dried and concentrated. The residual oil weighed 22.0 g. and had an infrared spectrum consistent with structure VII. This oil was then taken up directly in 50 ml. of acetic anhydride containing 20 g. of sodium acetate and the resulting mixture was allowed to stand overnight. After the mixture had been rendered basic with aqueous sodium carbonate, it was extracted with chloroform. Concentration of the chloroform extracts gave 31.1 g. of an oil whose infrared spectrum showed the absence of hydroxyl absorption and the presence of the typical acetate absorption at 5.78 and 8.25μ. Pyrolysis of this oil at 450° following the procedure used previously for pyrrocoline[8] gave 2.8 g. of a light yellow oil, after steam distillation. Further purification by chromatography over alumina gave a small amount of an oil whose infrared spectrum was in general agreement with that of the sample of 5-methyl-pyrrocoline obtained by hydrolysis of II, although the presence of an appreciable amount of impurities was indicated. This approach was therefore abandoned.

Vinyl-(6′-methyl-2′-pyridyl)-carbinol (IX).—A solution of vinylmagnesium bromide was prepared by adding gaseous vinyl bromide to a mixture of 16.2 g. of magnesium turnings in 400 ml. of tetrahydrofuran at a rate sufficient to cause the tetrahydrofuran to boil gently. A Dry Ice condenser was employed to prevent excessive loss of vinyl bromide. The solution of vinylmagnesium bromide was cooled in an ice–acetone-bath and vigorously stirred while 60.0 g. of freshly distilled 6-methylpyridine-2-carboxyaldehyde[15] in 100 ml. of tetrahydrofuran was added. After the addition was complete, the mixture was stirred for an additional half hour. This mixture was then stirred with 100 ml. of water for one-half hour, and the precipitated magnesium hydroxide was collected and washed with tetrahydrofuran. The combined tetrahydrofuran filtrate and washings were concentrated *in vacuo*, and then 300 ml. of water was added to the residue. This aqueous solution was extracted with methylene chloride, the methylene chloride extract was concentrated and the residual oil was distilled to give 50.2 g. (68%) of a colorless oil, b.p. 72–74° at 0.7 mm.

Anal. Calcd. for $C_9H_{11}NO$: C, 69.09; H, 6.85. Found: C, 69.37; H, 6.86.

Vinyl-(6′-methyl-2′-pyridyl)-carbinyl Acetate (X).—To a mixture of 90 g. of acetic anhydride and 9 g. of sodium acetate was added 60.0 g. of vinyl-(6′-methyl-2′-pyridyl)-carbinol. The mixture was maintained at room temperature for 6 hr., heated at 100° for 2 hr. and finally allowed to stand for 12 hr. Aqueous sodium carbonate was then added to neutralize the acid, and the resulting mixture was extracted with ether. Concentration of the ether extracts *in vacuo* followed by distillation of the residue gave 53.4 g. (68%) of colorless oil, b.p. 91–94° at 2 mm.

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 72.45; H, 7.43. Found: C, 72.12; H, 7.43.

5-Methylpyrrocoline (III).—At the top of a tube, 20 mm. in diameter and 150 mm. long and heated at 450°, there was introduced under an atmosphere of nitrogen 25.0 g. of IX at the rate of 5 drops per minute. The pyrolysis products were flushed through the tube with a stream of nitrogen and collected in a flask containing an aqueous solution of sodium carbonate. When the pyrolysis was complete, the material in the collection flask was subjected to steam distillation. The distillate was extracted with ether and the ethereal extract was dried and concentrated. The residual oil was carefully distilled using a spinning band column and gave two fractions. The first fraction, b.p. 102–104° at 30 mm.,

(15) Supplied by Aldrich Chemical Co., Milwaukee, Wisconsin.

weighed 2.26 g. (13%) and its identification as 6-methyl-2-propenylpyridine is discussed later. The second fraction, b.p. 82–83° at 4 mm., was a yellow oil weighing 5.15 g. (30%). Its infrared spectrum was in good agreement with the spectrum of 5-methylpyrrocoline obtained by hydrolysis of II. Also, its ultraviolet absorption spectrum showed maxima, in mμ (log ε) at 344 (3.42), 294 (3.74), 288 (3.46), 281 (3.59) and 232 (4.53) as would be expected for 5-methylpyrrocoline.[8]

Anal. Calcd. for C_9H_9N:: C, 82.40; H, 6.92; N, 10.88. Found: C, 82.00; H, 7.15; N, 10.93.

Acetylation of this sample of 5-methylpyrrocoline by the procedure described earlier gave yellow crystals, m.p. 56.5–57°, undepressed by admixture of a sample of 3-acetyl-5-methylpyrrocoline (IV) from the previous preparation. Also, the infrared spectra of the two samples were superimposable.

That the oil obtained as the first fraction in the above distillation was **6-methyl-2-propenylpyridine** was shown both by its ultraviolet absorption spectrum (max. 286 (log ε 3.88) and 240 (log ε 4.07)) which was quite similar to that of 2-vinylpyridine and its composition.

Anal. Calcd. for $C_9H_{11}N$: C, 81.14; H, 8.34. Found: C, 81.10; H, 8.52.

The picrate of 6-Methyl-2-propenylpyridine formed readily in ethanol and was obtained after recrystallization from the same solvent as yellow needles, m.p. 146.5–147.5°.

Anal. Calcd. for $C_{15}H_{14}N_4O_7$: C, 49.73; H, 3.90. Found: C, 50.23; H, 4.23.

As final proof of structure of the 6-methyl-2-propenylpyridine, it was prepared by an independent synthesis. When 2,6-lutidyllithium in ether was treated with acetaldehyde and the lithium salt of the adduct, obtained after removal of the ether, was dry-distilled, a colorless oil, b.p. 105–107° at 39 mm., resulted. The infrared spectrum of this oil was superimposable with that of the sample of 6-methyl-2-propenylpyridine obtained before. Also, the picrate of this oil melted at 146–147°, undepressed by admixture of the picrate from the former sample.

Preparation of Pyrrocoline (XII) from 3-(2-Pyridyl)-1-propanol (XI).—Into a 25-ml. flask were introduced 12.0 g. of redistilled 3-(2-pyridyl)-1-propanol, 0.5 g. of a 10% palladium-on-charcoal catalyst and a small porcelain boiling stone. A fine capillary was inserted into the liquid, and nitrogen was passed though the capillary at the rate of 3 l. per hr. After the system had been flushed with nitrogen, the mixture was boiled vigorously under reflux by heating it at 280° for 12 hr. In the initial period of heating, the water which formed was removed. At the end of the period of heating, the contents of the flask were steam distilled. The solid which separated from the distillate, was collected and recrystallized from a minimum amount of methanol to give 5.5 g. (50%) of white crystals, m.p. 73–74°. These were identical in all respects with an authentic sample of pyrrocoline.[8]

3-(6-Methyl-2-pyridyl)-2-phenyl-1-propanol (XIII).—To a cold solution of phenyllithium, prepared by dissolving 2.31 g. of lithium in a mixture of 25.7 g. of bromobenzene and 130 ml. of ether, was added 17.8 g. of 2,6-lutidine. After this solution had been allowed to stand for 0.5 hr., it was stirred and cooled in an ice-bath while 20.0 g. of styrene oxide was added. Stirring was continued for 0.5 hr. after the addition was complete. The ether solution was then washed with water, dried and concentrated *in vacuo*. Distillation of the residue gave 21.0 g. (55%) of a colorless oil, b.p. 157–160° at 0.3 mm. The distillate slowly solidified and recrystallization from methylcyclohexane gave white plates, m.p. 74–75°.

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.31; H, 7.56. Found: C, 79.08; H, 7.95.

Conversion of 3-(6-Methyl-2-pyridyl)-2-phenyl-1-propanol (XIII) to 2-Phenyl-5-methylpyrrocoline (XIV).—A mixture of 5.0 g. of 3-(6-methyl-2-pyridyl)-2-phenyl-1-propanol and 0.5 g. of a 10% palladium-on-charcoal catalyst was heated at 290° for 6 hr. A stream of nitrogen was passed into the mixture to stir it and to carry off hydrogen evolved. The residue was then taken up in benzene and chromatographed on alumina. From the eluate there was isolated a fluorescent solid. This, on recrystallization from methanol, gave 1.3 g. (28%) of white needles, m.p. 80–81°. These were shown both by infrared spectral comparison and by a mixed melting point determination to be identical with an authentic sample of 2-phenyl-5-methyl-pyrrocoline.[3]

ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

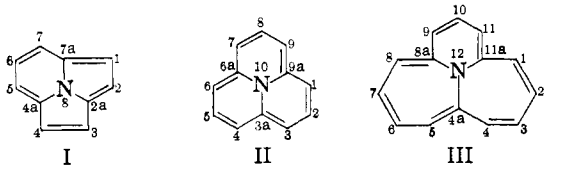
Cyclazines. A New Class of Aromatic Heterocycles[1]

BY R. J. WINDGASSEN, JR.,[2] W. H. SAUNDERS, JR., AND V. BOEKELHEIDE

RECEIVED SEPTEMBER 2, 1958

The synthesis of cycl[3,2,2]azine (I), its properties, and some of its substitution reactions are described. Molecular orbital calculations for systems of this type are presented and their correlation with the experimental findings is discussed.

We have for some time been interested in the requirements for aromaticity, particularly in large rings and in polycycles.[3,4] One synthetic goal to which we have devoted our attention is the synthesis of a large conjugated carbocycle which would be held planar by bonding to an internal atom. With nitrogen as the internal atom, the type of molecules under consideration are exemplified by structures I, II and III. For ease of discussion and naming we propose that this new class of heterocycles be given the trivial name cyclazines.[5] It is the purpose of the present communication to report the synthesis of cycl[3,2,2]azine (I) as well as to discuss the implications from molecular orbital theory for all three of these aromatic systems.



I II III

Of the possible routes to a synthesis of cycl[3,2,-2]azine, the most obvious utilize pyrrocoline deriv-

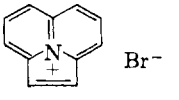
(1) Supported in part by the Office of Ordnance Research, Army Ordnance Contract No. DA-30-115-O. R. D.-723.

(2) National Science Foundation Predoctoral Fellow, 1956–1958.

(3) V. Boekelheide and W. G. Gall, *J. Org. Chem.*, **19**, 499 (1954).

(4) V. Boekelheide and G. K. Vick, THIS JOURNAL, **78**, 653 (1956).

(5) In this proposal of nomenclature, the word cyclazine would refer to the general case of a conjugate, unsaturated cycle held planar by three covalent bonds to an internal nitrogen atom. The individual members would be distinguished by placing in brackets numerals corresponding to the number of atoms on the peripheral cycle between points of bonding to the internal nitrogen. Thus, in this scheme structure I would be cycl-[3,2,2]-azine, II would be cycl-[3,3,3]-azine and III would be cycl-[4,4,3]-azine. This system would also accommodate ionic structures such as IV, which would be named cycl-[3,3,2]-azinium bromide. The numbering has been designed to conform with the lowest possible numbers for simple substitution products.



IV