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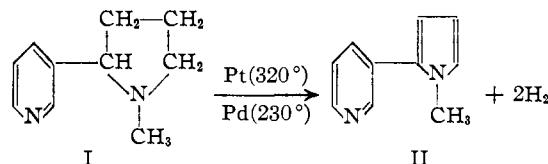
3,2'-Nicotyrine. Insecticidal Properties of Certain Azo Derivatives¹

BY ROBERT L. FRANK, ROBERT W. HOLLEY AND DONALD M. WIKHOLM

3,2'-Nicotyrine (II)² can now be obtained readily from nicotine (I) by catalytic dehydrogenation. Since both of these bases possess insecticidal properties,³ it seemed possible that dyes derived from them might also have this property and be useful as insect-proofing agents. In the present work a number of such dyes from 3,2'-nicotyrine have been prepared and tested.

The preparation of 3,2'-nicotyrine from nicotine has been accomplished by several methods. It was first carried out by Cahours and Étard⁴ by oxidation of natural nicotine with calcium ferricyanide in alkaline solution. Other methods which have been used since that time are oxidation of nicotine by means of silver oxide,⁵ silver acetate⁶ and electrolysis,⁷ but these are all unsatisfactory as preparative methods.

Wibaut and Overhoff⁷ have reported yields up to 92% by means of catalytic dehydrogenation of nicotine with platinum-on-asbestos catalyst at 320° in a heated tube. The catalytic dehydrogenation of nicotine by means of palladium-on-asbestos is reported in the present communication and has been found to provide a convenient method for the preparation of 3,2'-nicotyrine. It can be carried out either in the vapor phase in an electrically heated reaction tube (Procedure 1) or more simply by refluxing nicotine containing a suspension of palladium-on-asbestos (Procedure 2). These two procedures give approximately the same yields, but the latter is the more convenient.

**The vapor phase dehydrogenation (Procedure 1)**

(1) Presented before the Organic Division at the Buffalo meeting of the American Chemical Society, September 7-11, 1942.

(2) This is the name adopted by Wibaut and Overhoff for *N*-methyl-(3-pyridyl)-2-pyrrole.⁷ The compound is also referred to simply as nicotyrine, since it was the first of the *N*-methylpyridylpyrroles to be described.⁵

(3) LaForge, *THIS JOURNAL*, **50**, 2477 (1928); Richardson and Shepard, *J. Agr. Research*, **40**, 1007 (1930).

(4) Cahours and Étard, *Bull. soc. chim.*, **34**, 449 (1880).

(5) Blau, *Ber.*, **27**, 2535 (1894).

(6) Tafel, *ibid.*, **25**, 1619 (1892).

(7) Wibaut and Overhoff, *Rec. trav. chim.*, **47**, 935 (1928).

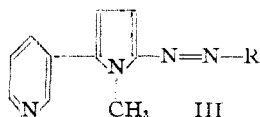
gives best yields, up to 41% of the nicotine which reacts, at 305-325°. Lowering the temperature lowers the yields.

In Procedure 2, on the other hand, dehydrogenation begins to take place at much lower temperatures, as evidenced by the evolution of hydrogen. Best results were obtained when nicotine and palladium-on-asbestos were heated to about 230° and the temperature was then allowed to rise gradually to 270-280°. When the reaction was carried out in this way, the yields were 30-35% and were almost as high after thirty minutes as after three hours. Very little nicotine was recovered. Several experiments were also made by this method in which lower temperatures were maintained by the addition of varying amounts of xylene to the reaction mixture. The yields were somewhat lower at temperatures varying from 185 to 230°, and the conversions were considerably lower. The yield was lowered sharply by carrying out Procedure 2 at temperatures higher than 250°.

The yields, ranging from 20 to 41% of the nicotine which reacted, are much lower than those reported by Wibaut and Overhoff, but the method should nevertheless be of value because of the rapidity of the reaction, the simplicity of the apparatus, the ready availability of nicotine, and the lower cost of palladium as compared to platinum.

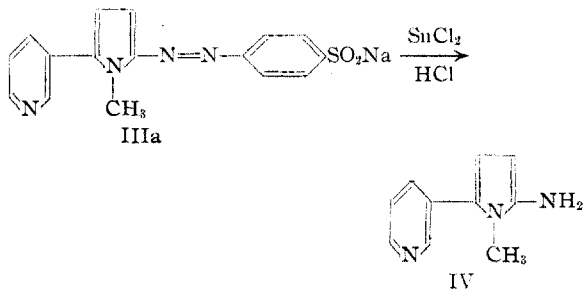
In addition to 3,2'-nicotyrine and recovered nicotine, two other fractions were isolated, one boiling at 48-70° (1 mm.) and the other, approximately as large as the yield of 3,2'-nicotyrine, boiling at 210-230° (1 mm.). This is interesting in view of the fact that Wibaut and Overhoff reported that there were no side products at all in the dehydrogenation with platinum. These fractions are being further investigated.

3,2'-Nicotyrine has been found to couple readily with diazonium salts and a number of the resulting azo dyes have been prepared (III, R equals *p*-C₆H₄SO₃Na, *m*-C₆H₄NO₂, *p*-C₆H₄NO₂, *p*-C₆H₄CO₂H, β-C₁₀H₇). These compounds are crystalline solids ranging in color from orange to purple. They are stable in acid solution and dissolve in boiling concentrated hydrochloric acid with no apparent decomposition.



The coupling reaction is believed to occur at the free alpha position of the 3,2'-nicotyrine rather than at one of the beta positions since Fischer and Hepp⁸ and Plancher and Soncini⁹ have found that substituted pyrroles undergo coupling in one of the alpha positions unless these are blocked.

One of these azo dyes was reduced to the corresponding aminonicotyrine, which, on the basis of the above evidence, probably has the structure IV. Sodium 5'-(3,2'-nicotyrine)-azo-*p*-benzenesulfonate (IIIa) was reduced to 5'-amino-3,2'-nicotyrine (IV) in 46% yield by means of stannous chloride and hydrochloric acid. The



product, a crystalline solid melting at 86–87°, could be purified only by distillation under reduced pressure. It is stable when kept out of contact with air, but gradually becomes dark and sticky when exposed. When heated in water, alcohol, ether or chloroform, it decomposes and a dark tar separates. It was possible to form a white hydrochloride by treating the amine with gaseous hydrogen chloride in anhydrous ether, but this decomposed rapidly when isolated. The picrate was found to be a stable derivative, however, although it could not be recrystallized.

The instability of this amine parallels the findings of Fischer and Rothweiler,¹⁰ who were unable to recrystallize 2,4,5-trimethyl-3-aminopyrrole.

Samples of wool cloth dyed with four of the compounds gave fast colors ranging from yellow to brown. These were subjected to the attack of the larvae of the black carpet beetle (*Attagenus Piceus*), and all were affected much less than a

sample of undyed wool. Details are included in the experimental part.¹¹

Experimental

Purification of Nicotine.—The technical product "Nicofume" of the Tobacco By-Products and Chemical Corporation of Louisville, Ky., containing 95% nicotine, was diluted with an equal volume of ethanol and refluxed over Raney nickel for three hours. The nickel was then removed by filtration and the filtrate was fractionally distilled, yielding a nicotine fraction boiling at 118–121° (18 mm.); n_D^{20} 1.5252.

Palladium-on-Asbestos Catalyst.—A catalyst containing 5 g. of palladium on 11 g. of asbestos wool was prepared from chloropalladic acid according to the directions of Linstead and Thomas.¹²

Dehydrogenation of Nicotine.—The dehydrogenation was carried out in two ways.

Procedure 1.—The vapor phase dehydrogenation was carried out by a procedure similar to that employed by Wibaut and Overhoff.⁷ The apparatus consisted of a vertical "Pyrex" glass catalyst tube equipped with an electrically heated jacket. A thermometer was inserted in the jacket next to the tube and the open ends of the jacket were then packed with asbestos wadding. A cold-finger condenser was attached by means of a ground-glass joint to the top of the catalyst tube and a side-arm at the top of this was connected by means of glass tubing to a buret. Nicotine was allowed to drop from this buret at a rate of 0.5–0.8 cc. per hour.

The brown-colored product was collected in a filter flask attached to the bottom of the reaction tube.

It was found necessary in filling the reaction tube with catalyst to take precautions to prevent spontaneous ignition of the catalyst. A slow stream of nitrogen was passed through the tube while it was being filled; it was then put into place immediately and the nitrogen was replaced by hydrogen, which was passed in from the top by means of a three-way stopcock between the condenser and the buret. Hydrogen was passed in slowly until the tube reached the desired temperature, after which the hydrogen was shut off and the nicotine passed in.

Procedure 2.—Nicotine and palladium-on-asbestos were heated over a hot-plate in a round-bottomed flask equipped with a glass-jointed condenser and a side arm through which a thermometer was inserted. Dehydrogenation began somewhat below 230°, but became vigorous at this temperature. The evolution of hydrogen and the boiling of the liquid served to agitate the contents of the flask.

The mixture became dark in color as soon as the reaction began, and the refluxing temperature rose gradually to 270–280° (with the formation of higher-boiling products).

The reaction products were separated by slow fractional distillation in a modified Widmer column (those obtained by Procedure 2 were first filtered to remove the catalyst). A typical example using 28 g. of nicotine gave the following fractions: 2.2 g. boiling at 48–70° (1 mm.), 2.5 g. at 74–99° (1 mm.), 7.7 g. at 104–107° (1 mm.), and 7.6 g. at

(8) Fischer and Hepp, *Ber.*, **19**, 2251 (1886).

(9) Plancher and Soncini, *Atti Accad. Lincei*, **10**, 299 (1901); *Chem. Zentr.*, **72**, I, 1323 (1901).

(10) Fischer and Rothweiler, *Ber.*, **56**, 512 (1923).

(11) We are indebted to Dr. C. W. Kearns and Mr. Leroy Parker of the Department of Entomology of this University for testing the insecticidal activity of the dyed cloth.

(12) Linstead and Thomas, *J. Chem. Soc.*, 1127 (1940).

210–220° (1 mm.). Considerable residue was left in the distilling flask.

The fraction boiling at 74–99° (1 mm.) was mainly nicotine and that boiling at 104–107° (1 mm.) was 3,2'-nicotyrine, a colorless liquid, darkening somewhat on standing, very slightly soluble in water, soluble in alcohol and in acids, b. p. 150–152° (16 mm.); n_D^{20} 1.6057; d_4^{20} 1.241. A picrate melted at 168.5–169° (Wibaut and Overhoff reported 168–169°).

Sodium 5'-(3,2'-Nicotyrine)-azo-*p*-benzenesulfonate (IIIa).—Eleven grams (0.058 mole) of sulfanilic acid and 2.5 g. of sodium carbonate were dissolved in 100 cc. of water. Three and five-tenths grams (0.051 mole) of sodium nitrite dissolved in 20 cc. of water was added to the solution. After cooling to 3°, 7 cc. of concentrated hydrochloric acid was added with stirring. To the diazotized solution was added 7.8 g. (0.049 mole) of 3,2'-nicotyrine dissolved in 3 cc. of glacial acetic acid. After stirring for ten minutes, the solution was made alkaline by adding a solution of 7 g. of sodium hydroxide in 20 cc. of water. Some orange solid settled out, but the precipitation was made more nearly complete by the addition of 20 g. of sodium chloride. The orange-red solid was removed by filtration and allowed to dry. A yield of 15.0 g. (84%) was obtained.

The compound was crystallized from hot water, in which it was fairly soluble, and washed with alcohol and ether. It did not melt below 300°.

Anal. Calcd. for $C_{16}H_{13}O_3N_4SNa$: N, 15.38. Found: N, 15.35.

5'-(3,2'-Nicotyrine)-azo-*p*-nitrobenzene.—One and two-tenths grams (0.0087 mole) of *p*-nitroaniline was dissolved in 20 cc. of hot water and 3 cc. of concentrated hydrochloric acid. Twenty grams of ice was added and the solution cooled to 0°. To this was added 0.69 g. (0.01 mole) of sodium nitrite dissolved in 20 cc. of water.

One and four-tenths grams (0.0089 mole) of 3,2'-nicotyrine was dissolved in 25 cc. of alcohol and 3.0 g. of sodium acetate in 20 cc. of water was added to the alcoholic solution. The combined solution was added slowly with stirring to that of the diazonium salt. A red solid precipitated immediately. After standing thirty minutes, the solid was removed by filtration and recrystallized from hot alcohol. Two and four-tenths grams (90%) of beautiful purple-red needles was obtained. After two recrystallizations, these melted at 200–201°.

Anal. Calcd. for $C_{16}H_{13}O_2N_5$: N, 22.80. Found: N, 22.79.

Three other dyes were prepared in the same manner as 5'-(3,2'-nicotyrine)-azo-*p*-nitrobenzene from the corresponding aromatic amines. These are described as follows.

5'-(3,2'-Nicotyrine)-azo-*m*-nitrobenzene.—The same amounts were used as in the preparation of 5'-(3,2'-nicotyrine)-azo-*p*-nitrobenzene. The yield was 2.1 g. of orange-red solid (79%), which melted at 156–157° after two recrystallizations from alcohol.

Anal. Calcd. for $C_{16}H_{13}O_2N_5$: N, 22.80. Found: N, 22.95.

5'-(3,2'-Nicotyrine)-azo-*p*-benzoic Acid.—One and two-tenths grams (0.0088 mole) of *p*-aminobenzoic acid was used. The yield was 1.9 g. (71%) of orange needles.

After five recrystallizations from hot alcohol, these melted with decomposition at 245–246°.

Anal. Calcd. for $C_{17}H_{14}O_2N_4$: N, 18.29. Found: N, 18.48.

β -Naphthaleneazo-5'-(3,2'-nicotyrine).—The amount of β -naphthylamine used was 2.86 g. (0.020 mole). The product crystallized from alcohol as red plates and weighed 5.2 g. (83%). After two recrystallizations, the crystals melted sharply at 148°.

Anal. Calcd. for $C_{20}H_{16}N_4$: N, 17.94. Found: N, 17.90.

5'-Amino-3,2'-nicotyrine (IV).—The reduction of sodium 5'-(3,2'-nicotyrine)-azo-*p*-benzenesulfonate was carried out according to the method of Smith, Opie, Wawzonek and Prichard.¹³ Twenty grams (0.055 mole) of the azo compound was dissolved in 200 cc. of 20% hydrochloric acid and warmed on a steam-bath. To this was added a solution of 24 g. (0.127 mole) of stannous chloride in 30 cc. of concentrated hydrochloric acid. The mixture was stirred and within one minute became light tan in color. After three minutes it was poured into a cooled solution of 100 g. of sodium hydroxide in 100 cc. of water and this mixture was further cooled. The alkaline mixture was extracted with eight 50-cc. portions of ether and the extract dried with solid potassium hydroxide. The ether was then removed and the black oil remaining was distilled at 166–167° (3 mm.). The light yellow distillate (4.4 g.; 46.2%) crystallized in the receiver with the evolution of much heat of crystallization, m. p. 86–87°. It was a light yellow solid which darkened on exposure, and was soluble (with decomposition when heated) in water, alcohol, chloroform and ether. It was insoluble in benzene.

Anal. Calcd. for $C_{10}H_{11}N_3$: N, 24.28. Found: N, 24.30.

A golden-yellow picrate of 5'-nicotyrineamine was formed by the method of Shriner and Fuson,¹⁴ with the exception that the solutions were not heated. It melted with decomposition at 173–174°.

Anal. Calcd. for $C_{22}H_{17}N_9O_{14}$: C, 41.84; H, 2.71; N, 19.97. Found: C, 42.21; H, 2.85; N, 19.89.

Azonicotyrine Dyes as Insect-Proofing Agents.—Four of the azo dyes prepared from 3,2'-nicotyrine were used for testing and the procedure with each was the same. Five-tenths of a gram of the dye was dissolved in 10 cc. of acetic acid and 25 cc. of warm water. To this solution was added 5 g. of sodium sulfate and 0.5 cc. of concentrated sulfuric acid and the combined solution was heated to 60°. A 1 × 3-inch strip of white wool cloth was then immersed in the dye solution and heated for one hour on a steam-bath. The cloth was then removed and rinsed with cold water.

The dyed strips were washed in boiling water and also in hot soapy water with no loss in color.

The wool strips, along with an undyed sample, were weighed and placed in separate cages, each containing ten larvae of the black beetle. After sixty-two days the samples were again weighed to determine the loss in weight

(13) Smith, Opie, Wawzonek and Prichard, *J. Org. Chem.*, **4**, 318 (1939).

(14) Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., second edition, 1940, p. 149.

due to attack by the larvae, and the number of larvae still alive was also recorded, as shown in Table I.

TABLE I
ACTION OF BLACK CARPET BEETLE LARVAE ON DYED WOOL
SAMPLES

Dye	Color of cloth	Mg. loss in wt. per 200 mg. cloth	% Larvae still alive
III, R = <i>p</i> -C ₆ H ₄ SO ₃ Na	Light yellow	21.2	80
III, R = <i>p</i> -C ₆ H ₄ NO ₂	Brown	18.4	100
III, R = <i>p</i> -C ₆ H ₄ CO ₂ H	Tan	14.2	60
III, R = β-C ₁₀ H ₇	Golden-yellow	12.2	40
Untreated sample	White	67.0	100

Summary

1. A convenient method for the preparation of 3,2'-nicotyrine from nicotine by means of palladium-on-asbestos catalyst is described.

2. 3,2'-Nicotyrine couples readily with diazonium salts to form azo dyes which show activity as insect-proofing agents.

3. Sodium 5'-(3,2'-nicotyrine)-azo-*p*-benzene-sulfonate has been reduced to 5'-amino-3,2'-nicotyrine.

URBANA, ILLINOIS

RECEIVED AUGUST 21, 1942

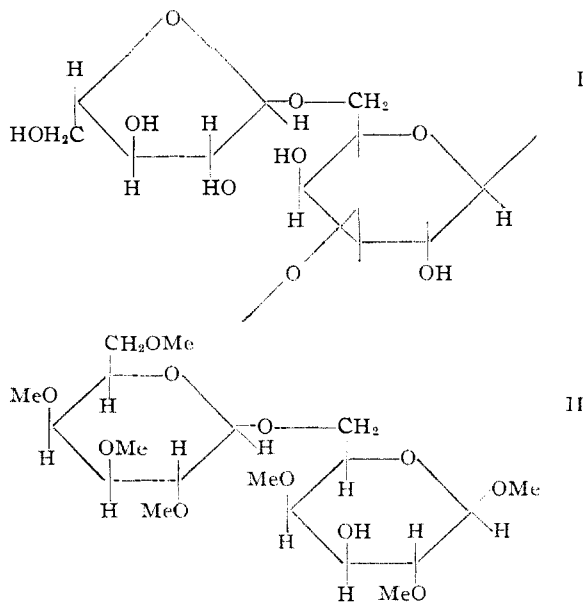
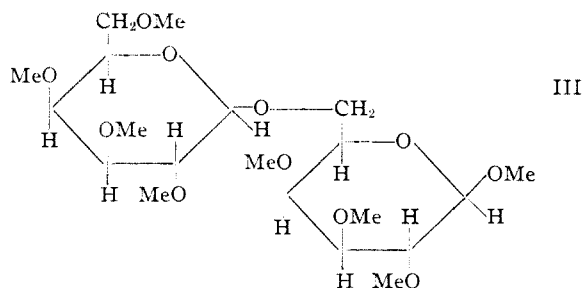
[CONTRIBUTION FROM THE WOOD CONVERSION LABORATORY OF THE UNIVERSITY OF IDAHO]

The Constitution of Arabo-galactan. IV. The Structure of the Repeating Unit

By E. V. WHITE

In the previous papers of this series^{1a,b,c} it has been shown that the water-soluble gum extracted from western larch, *Larix occidentalis*, yields the glycosides of 2,4-dimethyl-*d*-galactose (3 parts), 2,3,4-trimethyl-*d*-galactose (1 part), 2,3,4,6-tetramethyl-*d*-galactose (2 parts), and 2,3,5-trimethyl-*l*-arabinose (1 part) upon methanolysis of the methyl ether derivative^{1a}. The furanopenose unit is joined by oxygen linkage through the reducing carbon to the 6-position of an adjacent galactose residue as an arabofuranosido-galactan I^{1c} and this, together with the separation of two crystalline disaccharides, heptamethyl-6-*d*-

galactosidogalactose II and octamethyl-6-*d*-galactosidogalactose III from the partial methanolysis



(1) (a) White, THIS JOURNAL, 63, 2871 (1941); (b) 64, 302 (1942); (c) 64, 1507 (1942).

products of methylated arabogalactan^{1b} establishes the position of linkage of the terminal units of the polysaccharide. It is also apparent, since two of the three 2,4-dimethyl-methylgalactoside residues found in the complete methanolysis products are united through position 6 to terminal units in I and II, that these residues are joined by 1-3 linkage to dimethyl substituted units in the original methyl ether.

In the event that the third dimethylated residue is joined in a similar manner the repeating unit structure IV would be suggested wherein each unit of the 1-3 linked main chain galactose anhydrides is substituted in position 6 by the radicals R, respectively, *l*-arabinose, *d*-galactose, and 6-*d*-galactosidogalactose. However, if the above third residue is not part of the main chain but is located rather in a side-chain the radicals R become of polysaccharide character and the nature of the main chain linkage is open to question.

Preliminary experiments, reported in Part II, showed that some of the galactose residues oc-