solution of 9.25 g. of dimethyl acetylenedicarboxylate in 20 ml. of toluene was added in small portions 4.0 g. of N-(*p*)-tolylhydroxylamine. After the mixture had stood overnight, the precipitate of adduct was filtered off, washed with two 20-ml. portions of ether, and dried. The combined filtrate and washings were treated with 20 ml. of concd. hydrochloric acid in 50 ml. of methanol. The volume of the solution was reduced to half by distillation. After standing overnight, the precipitate of colorless crystals was removed by filtration and dried at 55° for two hours; m.p. 246–247°, yield 2.7 g. (36%).

Anal. Calcd. for $C_{12}H_{11}NO_4$: neut. equiv., 233.2. Found: neut. equiv., 231.0.

Dimethyl 5-Methylindole-2,3-dicarboxylate.—A 1.0-g. portion of the monomethyl ester was treated in 20 ml. of ether with diazomethane giving 1.0 g. (93%) from 5:1 methanol–water; m.p. 130.3–130.8°. For analysis a sample was dried at 100° for two hours.

Anal. Calcd. for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.26; H, 5.38; N, 6.04.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TULANE UNIVERSITY]

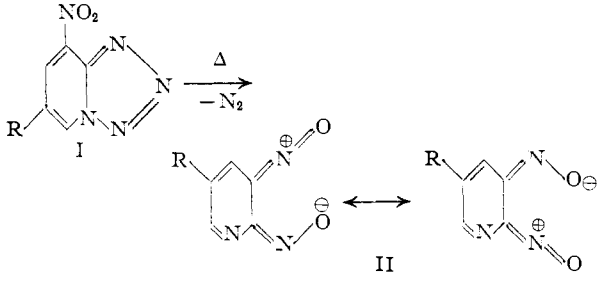
2,3-ψ-Dinitrosopyridines[1]

BY J. H. BOYER AND W. SCHOEN

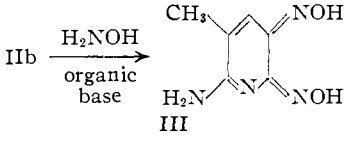
RECEIVED SEPTEMBER 12, 1955

Pyrolysis of appropriate derivatives of 8-nitropyridotetrazole brought about the formation of 5-methyl-, 5-carboxy- and 5-carbomethoxy-2,3-ψ-dinitrosopyridine. Hydroxylamine in diethylamine or in triethanolamine reduced ψ-*o*-dinitrosobenzene to a dioxime (presumably *amphi*) of *o*-benzquinone. Similar treatment of 5-methyl-2,3-ψ-dinitrosopyridine brought about reduction together with amination. The product appeared to be a dioxime of 3-aza-4-amino-5-methyl-*o*-benzquinone. Amination by hydroxylamine in aqueous alkali occurred at the 6-position for 2-amino-3-nitropyridine and 2-amino-3-nitro-5-methylpyridine but failed to occur with certain other derivatives of pyridine.

In the reported synthesis for ψ-2,3-dinitrosopyridine (IIa),[2] an essential step required the nitration of 2-amino or 2-hydroxypyridine at the 3-position. Undesirable alternate mononitration at the 5-position was eliminated in the present work with 2-hydroxy-5-carboxypyridine, the corresponding methyl ester and with 2-amino-5-methylpyridine. Usual procedures were employed to transform the nitration products into the corresponding derivatives of 8-nitropyridotetrazole (I). Interaction between the nitro group and a tetrazole nitrogen upon pyrolysis of each compound occurred with the formation of a 5-substituted-2,3-ψ-dinitrosopyridine (II).



a, R = H; b, R = CH_3; c, R = CO_2H; d, R = CO_2CH_3



Homocyclic aromatic ψ-*o*-dinitroso compounds have been reduced smoothly to dioximes by alkaline hydroxylamine.[3] Sensitivity of the nitroso compounds to alkaline degradation, however, has limited the usefulness of this reaction. A fairly rapid decomposition of ψ-1,2-dinitroso-3,5-dinitrobenzene, and apparently no reduction, occurred in both sodium and ammonium hydroxide which also contained hydroxylamine. In contrast, reduction to 1,2-diamino-3,5-dinitrobenzene occurred readily in hydroiodic acid. Presumably alkaline degradation also accounted for the difficulty in obtaining a reduction product from similar treatment of ψ-2,3-dinitroso-5-methylpyridine (IIb).

The use of hydroxylamine in diethylamine or in triethanolamine was then found successful in reducing pseudonitroso groups. The dioxime of *o*-benzoquinone was obtained in this manner from ψ-*o*-dinitrosobenzene. Surprisingly, amination of the pyridine ring took place as well as reduction of the nitroso groups when ψ-2,3-dinitroso-5-methylpyridine was treated with hydroxylamine and an organic base. This unexpected facility in aminating a pyridine derivative was also observed in similar experiments with both 2-amino-3-nitropyridine and 2-amino-3-nitro-5-methylpyridine in aqueous alkali and hydroxylamine. In the former case the known 2,6-diamino-3-nitropyridine was obtained and, by analogy, the formation of 2,6-diamino-3-nitro-5-methylpyridine in the latter example was assumed. Attempts to aminate 2-hydroxy-3-nitropyridine, 2-amino-5-methylpyridine, pyridine and 3-methylisoquinoline with alkaline hydroxylamine were unsuccessful. In agreement with these reactions the above reduction–amination product was assigned the structure of the dioxime of 3-aza-4-amino-5-methyl-*o*-benzquinone (III). Configuration of the dioxime was not determined, but was assumed to be one of the two possible *amphi* forms.

Experimental[4]

Coumalic acid[5] was esterified with methanol in sulfuric

(1) Grants from the Research Corporation and the American Cyanamid Co. made this investigation possible and are gratefully acknowledged.

(2) Previously named pyrido-2,3-furoxane; see J. H. Boyer, D. I. McCane, W. J. McCarville and A. T. Tweedie, THIS JOURNAL, **75**, 5298 (1953), and J. H. Boyer, R. F. Reinisch, M. J. Danzig, G. A. Stoner and F. Sahhar, *ibid.*, **77**, 5688 (1955).

(3) T. Zincke and P. Schwarz, *Ann.*, **307**, 28 (1899).

(4) Analyses by Micro-tech Laboratories, Skokie, Ill. Infrared spectra were obtained through the courtesy of the Perkin-Elmer Corporation, New Orleans. Melting points are corrected unless otherwise specified; boiling points, uncorrected.

(5) R. H. Wiley and N. R. Smith, *Org. Syntheses*, **31**, 23 (1951).

acid.[6] Methyl coumalate was transformed by ammonium hydroxide into 6-hydroxynicotinic acid[7] (77% yield), m.p. 299–300° (uncor.). The preparation of 5-nitro-6-hydroxynicotinic acid[8] (34% yield), m.p. 291° (uncor., lit.[8] m.p. 279–280°) was realized upon nitration of 6-hydroxynicotinic acid with red fuming nitric acid. From the treatment of 5-nitro-6-hydroxynicotinic acid with phosphorus pentachloride in phosphorus oxychloride followed by the removal of excess phosphorus compounds and the addition of methanol, methyl 5-nitro-6-chloronicotinate,[8] m.p. 86.0–86.4° (lit.[8] m.p. 76°), was obtained in 85% yield.

Anal. Calcd. for $C_7H_5N_2O_2Cl$: Cl, 16.27. Found: Cl, 16.36.

Preparation of 6-Carbomethoxy-8-nitropyridotetrazole (Id).—To a solution of 0.54 g. (2.5 mmoles) of methyl 5-nitro-6-chloronicotinate in 15 ml. of methanol was added 0.65 g. (0.01 mole) of sodium azide dissolved in 2 ml. of water and 2 ml. of methanol and 1.25 ml. of 22% hydrochloric acid. The solution was refluxed for 8 hours. Concentration to about 5 ml. at room temperature under an air stream brought about separation of a crystalline solid which was filtered, washed with cold ethanol and dried overnight under vacuum. Extraction with hot petroleum ether and evaporation to dryness of the ether extract yielded 0.16 g. of starting material, m.p. 78–81°. The petroleum ether insoluble residue was dissolved in acetone and filtered. Yellow crystals were obtained by evaporating the acetone solution to dryness under an air stream followed by further drying at 40° under vacuum. The weight of crude 6-carbomethoxy-8-nitropyridotetrazole was 0.26 g. (65% based on unrecovered starting material), m.p. 105–107° dec. After three recrystallizations from hot ethanol the pale yellow crystals melted at 117° dec. Absorption in the infrared at 1653 cm.$^{-1}$ (6.05 μ) and at 1748–1730 cm.$^{-1}$ (5.72–5.78 μ) indicated the presence of the azomethine and carbonyl groups, respectively. Absorption at 1550–1532 cm.$^{-1}$ (6.45–6.53 μ) may be attributed to the nitro group.

Anal. Calcd. for $C_7H_5N_5O_4$: C, 37.67; H, 2.26; N, 31.39. Found: C, 37.43; H, 2.01; N, 31.29.

Pyrolysis of 6-Carbomethoxy-8-nitropyridotetrazole.—In a 10-mm. test-tube was placed 0.100 g. (0.448 mmole) of 6-carbomethoxy-8-nitropyridotetrazole. The tetrazole was decomposed in an oil-bath at 106° and was heated at this temperature for 10 minutes after the initial vigorous reaction had subsided. After cooling to room temperature the yellow solid was extracted with ether which left a brown residue, m.p. >250°. The ether extract was filtered, evaporated to dryness and the residue dried overnight at 80°. The weight of crude ψ-2,3-dinitroso-5-carbomethoxypyridine (IId), m.p. 103–105°, was 0.085 g. (97.4%). After recrystallizing two times from ether, the yellow crystals melted at 106.5–107.5°. Strong absorption in the infrared occurred at 1623 cm.$^{-1}$ (6.16 μ) (azomethine linkage), 1735 cm.$^{-1}$ (5.76 μ) (carbonyl) and at 1529 cm.$^{-1}$ (6.54 μ) (possibly —N=O or $>\overset{+}{N}$=O).

Anal. Calcd. for $C_7H_6N_3O_4$: C, 43.08; H, 2.58; N, 21.53. Found: C, 42.95; H, 2.79; N, 21.67.

Preparation of 5-Nitro-6-chloronicotinic Acid.—To 3.68 g. (0.02 mole) of 5-nitro-6-hydroxynicotinic acid in a pear-shaped flask, equipped with a reflux condenser, was added 40 ml. of phosphorus oxychloride and 12 g. (0.058 mole) of phosphorus pentachloride. The mixture was heated on the steam-bath for 5 hours, excess phosphorus oxychloride was removed and 18 ml. of water was slowly added to the residue which was then allowed to stand for one hour. Upon cooling in an ice–salt-bath, a tan crystalline solid separated and was filtered, washed with ice-water and dried in a desiccator. The dry solid was extracted with hot benzene and, after decolorizing with charcoal, the benzene extract was evaporated to dryness. The weight of crude 5-nitro-6-chloronicotinic acid, m.p. 119–120°, was 2.74 g. (67.6%). After four recrystallizations from benzene, the tiny white needles melted at 126.5–127.5°.

Anal. Calcd. for $C_6H_3N_2ClO$: C, 35.58; H, 1.49; N, 13.83; Cl, 17.50. Found: C, 35.80; H, 1.73; N, 13.67; Cl, 17.80.

By following the procedure for the preparation of 6-carbomethoxy-8-nitropyridotetrazole, 5-nitro-6-chloronicotinic acid was transformed into **6-carboxy-8-nitropyridotetrazole (Ic)**, m.p. 189.5–190.0° dec. after recrystallization from ethanol, in 21% yield. The reflux time was shortened to 4 hours. Absorption in the infrared occurred at 1656–1653 cm.$^{-1}$ (6.04–6.05 μ) (azomethine group), at 1738–1730 cm.$^{-1}$ (5.75–5.78 μ) (carbonyl) and at 1555–1538 cm.$^{-1}$ (6.43–6.50 μ) (possibly the nitro group).

Anal. Calcd. for $C_6H_3N_5O_4$: C, 34.46; H, 1.45; N, 33.50. Found: C, 34.86; H, 1.56; N, 33.72.

Preparation of ψ-2,3-Dinitroso-5-carboxypyridine (IIc).—Special precautions were required for the pyrolysis of 6-carboxy-8-nitropyridotetrazole. Pure material would not pyrolyze below 190°, at which temperature extensive molecular destruction occurred. Decarboxylation as well as nitrogen elimination was suspected; however attempts to isolate ψ-2,3-dinitrosopyridine[2] were unsuccessful.

In a 10-mm. test-tube was placed about 10 mg. of crude tetrazole, m.p. 156–157°. The test-tube was set in an oil-bath at a sharp angle, fitted with a mechanical stirrer and was heated slowly with tumbling. At 148° decomposition occurred, but heating was continued to 161°, at which temperature the test-tube was removed from the oil-bath. This procedure was repeated until a total of 0.291 g. (1.4 mmole) of tetrazole was pyrolyzed. The reddish-brown solid in each tube was extracted with ether. Evaporation to dryness of the combined ether extracts yielded 0.216 g. (85.8%) of crude ψ-2,3-dinitroso-5-carboxypyridine, m.p. 173.5–175° dec. After two recrystallizations from ether, the yellow solid melted at 184–185° dec. Strong absorption in the infrared occurred at 1695 cm.$^{-1}$ (5.90 μ) (carbonyl), 1608 cm.$^{-1}$ (6.22 μ) (azomethine linkage) and at 1528 cm.$^{-1}$ (6.55 μ) (possibly —N=O or $>\overset{+}{N}$=O).

Anal. Calcd. for $C_6H_3N_3O_4$: C, 39.78; H, 1.67; N, 23.20. Found: C, 40.59; H, 1.90; N, 23.94.

Preparation of ψ-2,3-Dinitroso-5-methylpyridine (IIb).—According to the method of Seide,[9] 2-amino-5-methylpyridine was nitrated with 90% fuming nitric acid below 10°. A 31.8% yield of 2-amino-3-nitro-5-methylpyridine, m.p. 192–193°,[10] was obtained and was transformed by diazotization using a large excess of sodium nitrite into 2-hydroxy-3-nitro-5-methylpyridine, m.p. 253–255°,[10] in 88.3% yield. Upon treatment of the latter with phosphorus oxychloride, 2-chloro-3-nitro-5-methylpyridine, m.p. 47–48°,[10] was obtained quantitatively. This was then treated with an aqueous alcohol solution of sodium azide, to which a few ml. of hydrochloric acid were added, at reflux for 38 hours. Following the usual steps of isolation, 6-methyl-8-nitropyridotetrazole (Ib), m.p. 151–151.5° after recrystallization from ethanol, was obtained in 81.5% yield. Presence of the azomethine linkage was indicated by infrared absorption at 1656 cm.$^{-1}$ (6.04 μ). Absorption at 1555–1545 cm.$^{-1}$ (6.43–6.47 μ) may be attributed to the nitro group.

Anal. Calcd. for $C_6H_5N_5O_2$: C, 40.23; H, 2.81; N, 39.11. Found: C, 40.44; H, 2.85; N, 39.33.

The tetrazole was pyrolyzed in an oil-bath at 152–155° during a period of 10 minutes. Addition of ether to the product mixture left an insoluble residue, m.p. 300°. From the ether solution the yellow ψ-2,3-dinitroso-5-methylpyridine (IIb), m.p. 85.5–86.5° after further recrystallization from ether, was obtained in 93% yield. Strong infrared absorption occurred at 1619 cm.$^{-1}$ (6.17 μ (azomethine linkage) and at 1525 cm.$^{-1}$ (6.56 μ) (possibly —N=O or $>\overset{+}{N}$=O).

Anal. Calcd. for $C_6H_5N_3O_2$: C, 47.68; H, 3.33; N, 27.81. Found: C, 47.58; H, 3.51; N, 27.60.

Reduction of ψ-2,3-Dinitroso-5-methylpyridine (IIb).—To an ethanol solution of 0.50 g. (3.31 mmoles) of ψ-2,3-dinitroso-5-methylpyridine was added 1.75 g. (0.0252 mole) of hydroxylamine hydrochloride. Dropwise addition with stirring of a solution of 1.42 g. (0.0195 mole) of diethylamine in 15 ml. of water resulted in a red solution, gas evolution and an increase of temperature to a maximum of 36.5°. Stirring was continued for one hour after all the diethylamine was added. A red microcrystalline solid appeared

(6) H. von Pechmann, *Ann.*, **264**, 279 (1891).

(7) H. von Pechmann and W. Welsh, *Ber.*, **17**, 2384 (1884).

(8) A. H. Berrie, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 2590 (1951).

(9) O. Seide, *Ber.*, **57**, 791 (1924).

(10) S. J. Childress and R. L. McKee, THIS JOURNAL, **73**, 3504 (1955).

upon chilling. It was filtered, washed with cold water and dried under vacuum over anhydrous calcium chloride. The yield of crude, red 3-aza-4-amino-5-methyl-*o*-benzoquinone dioxime (III) was 0.30 g. (53.8%) m.p. >215°. After four recrystallizations from water, clusters of tiny red needles, m.p. >250°, were obtained.

In a spot test with sodium pentacyanoaquoferrate the development of a green color indicated the presence of a primary aromatic amine.[11]

Infrared absorption occurred at 1650–1678 cm.$^{-1}$ (6.06–5.96 μ) (azomethine linkage). Absorption was absent in the 6.5 μ region.

Anal. Calcd. for $C_6H_6N_4O_2 \cdot H_2O$: C, 38.71; H, 5.41; N, 30.10; mol. wt., 186. Found: C, 38.81; H, 5.22; N, 30.22; mol. wt., 255.[12]

A sample was dried at 110° and analyzed again.

Anal. Calcd. for $C_6H_8N_4O_2$: C, 42.85; H, 4.80; N, 33.32. Found: C, 42.76; H, 5.00; N, 33.21.

In a similar experiment, *ψ*-*o*-dinitrosobenzene was reduced by hydroxylamine in diethylamine to the dioxime of *o*-benzquinone in 29.6% yield. The substitution of triethanolamine for diethylamine in both cases brought about a lower yield of product.

Reduction of *ψ*-1,2-Dinitroso-3,5-dinitrobenzene.—To 50 g. of 48% hydroiodic acid, small portions of *ψ*-1,2-dinitroso-3,5-dinitrobenzene, m.p. 172°,[13] was added at such a rate that the temperature was held at 50° and until a total of 4.5 g. (0.02 mole) had been added. The mixture was cooled to room temperature and iodine was removed with the addition of sodium sulfite. The dark red precipitate, 1,2-diamino-3,5-dinitrobenzene, separated from methanol as red prisms or needles, m.p. 214–215°,[14] wt. 2.8 g. (60%). The diacetyl derivative was prepared in refluxing acetic anhydride and was recrystallized from alcohol from which it separated as colorless needles, m.p. 244–245°.[15]

Amination of 2-Amino-3-nitropyridine.—To a warm solution of 1.0 g. (7.2 mmoles) of 2-amino-3-nitropyridine in 60 ml. of ethanol was added with swirling 2.50 g. (0.036 mole) of hydroxylamine hydrochloride. While maintaining the mixture at about 50–60° a solution of 5.0 g. (0.09 mole) of potassium hydroxide in 30 ml. of methanol was added over a one hour period. The mixture was warmed for an additional hour and then concentrated on the steam-bath. Addition of small amounts of water resulted in a clear solution which was concentrated until substantially all the alcohol was removed. Separation of 2,6-diamino-3-nitropyridine occurred upon chilling in an ice-bath. It was filtered, washed with water and dried at 80°, wt. 0.10 g. (9.0%), m.p. 235–237° dec. Recrystallization from methanol gave yellowish-green crystals, m.p. 236–236.5° dec. (lit.[16] m.p. 230° dec.).

In a similar manner, 2,6-diamino-3-nitro-5-methylpyridine, m.p. 282° (uncor.) after recrystallization from nitromethane, was obtained in 21% yield from 2-amino-3-nitro-5-methylpyridine.

Anal. Calcd. for $C_6H_8N_4O_2$: C, 42.85; H, 4.80; N, 33.32. Found: C, 42.95; H, 5.05; N, 33.15.

(11) F. Feigl, "Qualitative Analysis by Spot Tests," Elsevier Publishing Co., New York, N. Y., 3rd ed., 1947, pp. 381–383.

(12) The molecular weight was determined by the ebullioscopic method in acetic acid by the Huffman Micro-analytical Laboratories, Wheatridge, Colorado. These results indicate that an association with one molecule of acetic acid occurred: $C_6H_8N_4O_2 \cdot H_2O \cdot C_2H_4O_2$ has calcd. mol. wt. 246.

(13) P. Drost, *Ann.*, **307**, 49 (1899).

(14) R. Nietzki and H. Hagenback, *Ber.*, **30**, 539 (1897).

(15) L. M. Norton and J. F. Elliot, *ibid.*, **11**, 327 (1878).

(16) A. E. Tschitschibabin and O. A. Zeide, *J. Russ. Phys. Chem. Soc.*, **50**, 522 (1920); *C. A.*, **18**, 1496 (1924).

NEW ORLEANS, LOUISIANA

[CONTRIBUTION FROM ROHM AND HAAS CO.]

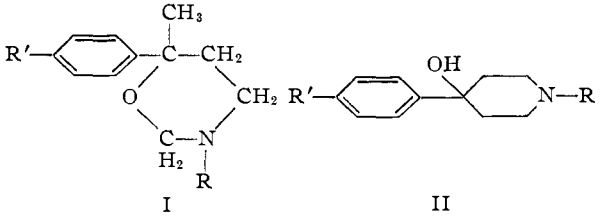
The Aminomethylation of Olefins. IV. The Formation of 1-Alkyl-4-aryl-1,2,3,6-tetrahydropyridines

BY CLAUDE J. SCHMIDLE AND RICHARD C. MANSFIELD

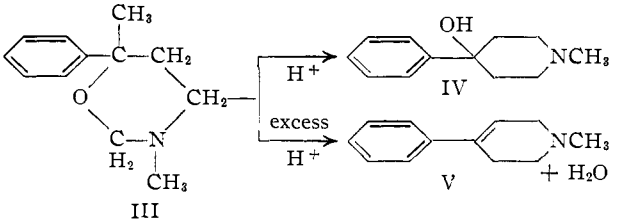
RECEIVED JULY 25, 1955

1-Alkyl-4-aryl-1,2,3,6-tetrahydropyridines and 1-alkyl-4-aryl-4-piperidinols have been obtained by the acid-catalyzed rearrangement of 3-alkyl-6-methyl-6-aryltetrahydro-1,3-oxazines. 1-Alkyl-4-aryl-4-piperidinols have been obtained by hydration of 1-alkyl-4-aryl-1,2,3,6-tetrahydropyridines.

The discovery that 3-alkyl-6-methyl-6-aryltetrahydro-1,3-oxazines (I)[1] and 1-alkyl-4-aryl-4-piperidinols (II)[2] are the principal products of the reaction of α-methylstyrenes, formaldehyde and primary amine salts suggested the possibility that 3-alkyl-6-methyl-6-aryltetrahydro-1,3-oxazines (I) could be converted to 1-alkyl-4-aryl-4-piperidinols (II). The rearrangement of 3,6-dimethyl-6-phenyltetrahydro-1,3-oxazine (III) was effected using either sulfuric acid or hydrochloric acid. Under relatively mild reaction conditions some 1-methyl-4-phenyl-4-piperidinol (IV) was obtained. The principal product with excess acid was 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (V).



I II



III IV V

Under conditions similar to those employed for the rearrangement of 3,6-dimethyl-6-phenyltetrahydro-1,3-oxazine (III) to 1-methyl-4-phenyl-1,2,-3,6-tetrahydropyridine (V), 1-methyl-4-phenyl-4-piperidinol (IV) is known[2,3] to undergo dehydration to 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (V). When α-methylstyrene, formaldehyde and methylamine hydrochloride reacted and then were treated with excess sulfuric acid, 1-methyl-4-

(1) H. D. Hartough, J. J. Dickert, Jr., and S. L. Meisel, U. S. Patent 2,647,117 (July 28, 1953); *C. A.*, **48**, 8265 (1954).

(2) C. J. Schmidle and R. C. Mansfield, THIS JOURNAL, **77**, 5698 (1955).