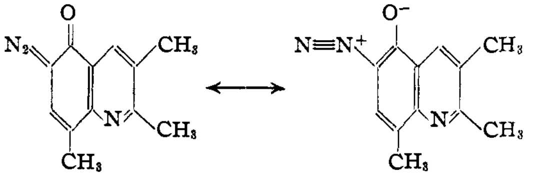
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Petroleum Bases. II.[1] Amino and Hydroxy Derivatives, and a Contribution to the Chemistry of Diazoöxides

BY LUTHER R. MODLIN, JR.,[2] AND ALFRED BURGER

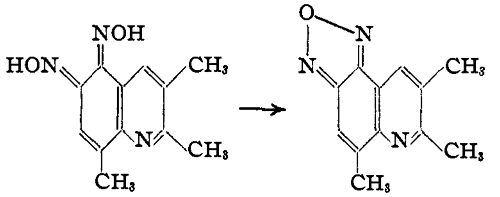
Nitration of 5-hydroxy-2,3,8-trimethylquinoline[1] (I) furnished 5-hydroxy-6-nitro-2,3,8-trimethylquinoline (II) which was methylated to the 5-methoxy derivative (III); this compound was obtained more easily by nitration of 5-methoxy-2,3,8-trimethylquinoline[1] (IV). Reduction of 5-methoxy-6-nitro-2,3,8-trimethylquinoline resulted in an 87% yield of the corresponding amine (V); this compound was demethylated to 5-hydroxy-6-amino-2,3,8-trimethylquinoline (VI) with boiling hydrobromic acid. The position of the nitro and amino groups in these compounds was to be demonstrated by converting the aminophenol VI to the corresponding dihydroxy derivative and proving the position of the phenolic hydroxyl groups by reactions typical of *o*-dihydroxy compounds. However, instead of the expected diphenol, diazotization of 5-hydroxy-6-amino-2,3,8-trimethylquinoline, and subsequent warming with dilute acid, yielded a deep red, alkali-insoluble compound (VII) of the formula $C_{12}H_{11}N_3O$. It lost two atoms of nitrogen on reduction with an alkaline solution of sodium hydrosulfite and was thereby converted into 5-hydroxy-2,3,8-trimethylquinoline (I). These reactions are in good agreement with the known behavior of "diazophenols," or, as they are usually called, diazoöxides.[3] This makes most probable position-6 for the amino group in the amines V and VI since only ortho and para diazoöxides are known, and the para position-8 is not available in our compounds. The structure of VII as a peri-diazooxide, placing the diazo group in position-4, is much less likely, because this position is extremely hard to nitrate, and 4-aminoquinolines cannot be diazotized under ordinary conditions.

Various formulas have been proposed for diazoöxides.[4] Most authors now advocate a quinoid type formula, while the stability of diazoöxides has been attributed[3] to resonance between such a quinoid, and a diazonium salt form. Our diazoöxide may therefore be expressed in the following way



VII

The compound is stable and can be recovered even after several hours boiling in ethanol in the presence of pyridine. In order to prove the presence of a carbonyl group we tried to prepare an *o*-diazoketoxime, but the *o*-quinone dioxime VIII was obtained instead. The structure of this dioxime was confirmed by its behavior toward dilute alkali solutions. It was easily dehydrated and converted to the furazan derivative IX.



VIII IX

This reaction is characteristic of other *o*-quinone or 1,2-diketone dioximes, for instance, β-naphthoquinone dioxime.[5]

As far as we are aware, the conversion of an *o*-diazoöxide into an *o*-quinone dioxime by means of hydroxylamine has not been observed before.

Catalytic hydrogenation of 5-amino-2,3,8-trimethylquinoline yielded 5-amino-2,3,8-trimethyl-1,2,3,4-tetrahydroquinoline (X). Diazotization converted this amine into 1-nitroso-2,3,8-trimethyl-5-hydroxy-1,2,3,4-tetrahydroquinoline (XI). The phenol XII was formed when 5-hydroxy-2,3,8-trimethylquinoline (I) was reduced by catalytically activated hydrogen. The alkali-insoluble fraction of the reduction products probably contained 5-hydroxy-2,3,8-trimethyl-5,6,7,8-tetrahydroquinoline, but it was so unstable that no attempt was made to isolate the cyclic alcohol.

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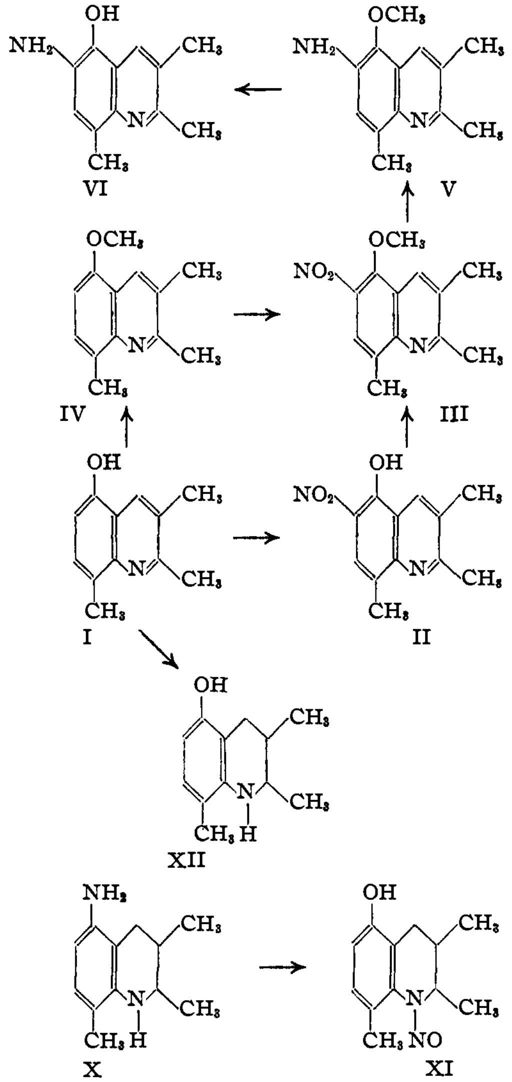
(1) First communication: Burger and Modlin, THIS JOURNAL, **62**, 1079 (1940).

(2) Du Pont Research Fellow.

(3) Sidgwick, "The Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1937, p. 422.

(4) Morgan and Porter, *J. Chem. Soc.*, **107**, 645 (1915); Morgan and Tomlins, *ibid.*, **111**, 497 (1917); Morgan and Evens, *ibid.*, **115**, 1126 (1919); Staudinger, *Helv. Chim. Acta*, **4**, 239 (1921).

(5) Goldschmidt and Schmidt, *Ber.*, **17**, 2066 (1884); *cf.* Angelico and Cusmano, *Gazz. chim. ital.*, **66** ,3 (1936).



Experimental

5-Hydroxy-6-nitro-2,3,8-trimethylquinoline (II).—By making alkaline the reaction mixture resulting from the diazotization of 5-amino-2,3,8-trimethylquinoline,[1] and clearing the solution with Norit, 5-hydroxy-2,3,8-trimethylquinoline (I) was obtained in a sufficient degree of purity to be used in subsequent reactions.

Five grams of 5-hydroxy-2,3,8-trimethylquinoline was added slowly and with stirring to 50 cc. of fuming nitric acid (d. 1.5) at 0° over a period of thirty minutes. After standing at this temperature for five minutes, the solution was poured onto 100 g. of ice, neutralized with a 20% sodium hydroxide solution, and stirred until the gummy precipitate became crystalline. The yield of crude product was 5.7 g. (92%), of pure product, after recrystallization from ligroin, 4.1 g. (66%). A sample, recrystallized from ethanol, contained one molecule of ethanol of crystallization. It melted at 152–152.5°.

Anal. Calcd. for $C_{12}H_{12}N_2O_3 \cdot C_2H_5OH$: N, 10.07. Found: N, 10.46.

The solvent of crystallization was removed by heating to 100° under 1 mm. pressure for one hour. The melting point was unchanged.

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21. Found: C, 61.66; H, 5.10.

5-Methoxy-6-nitro-2,3,8-trimethylquinoline (III).—(a) 5-Methoxy-2,3,8-trimethylquinoline (IV), which had been obtained from the hydroxy compound (I) with diazomethane,[1] could be prepared in larger amounts by methylation of I with dimethyl sulfate and strong alkali in acetone solution.[6] The yield was 95%.

The nitration of the methyl ether IV was carried out as described above for the hydroxy derivative. The reaction mixture was allowed to stand at −10° for thirty minutes, decomposed with ice, and neutralized with a strong sodium hydroxide solution; the precipitate was filtered immediately and washed well with water. After recrystallization from methanol, the nitro compound was obtained as yellow needles, m. p. 128–129°. The yield was 87%.

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73. Found: C, 63.39; H, 5.80.

(b) A solution 0.5 g. of 5-hydroxy-6-nitro-2,3,8-trimethylquinoline (II) in 5 cc. of methanol and 20 cc. of ether was treated with an ethereal solution of diazomethane (from 2 g. of nitrosomethylurea[7]) and allowed to stand overnight. The reaction mixture was worked up in the usual manner; the yield was 96%.

5-Methoxy-6-amino-2,3,8-trimethylquinoline (V).—Two grams of 5-methoxy-6-nitro-2,3,8-trimethylquinoline was added to a warm solution of 8.6 g. of stannous chloride in 16 cc. of 17% hydrochloric acid, and the mixture was warmed on a steam-bath for five minutes. It was cooled by addition of 20 g. of ice and made alkaline with a strong sodium hydroxide solution. A small amount of sodium bisulfite was added to retard oxidation. The crude dark-brown solid (yield, 1.5 g.) (87%) was sublimed at 100° under 0.1 mm. pressure and recrystallized from dilute methanol. It appeared as nearly colorless rhombic crystals, m. p. 137–138°. The yield was 1 g. (57%).

Anal. Calcd. for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46. Found: C, 72.51; H, 7.26.

The monohydrochloride crystallized from ethanol as red-orange needles, m. p. 255–259° (dec.).

Anal. Calcd. for $C_{13}H_{17}ClN_2O$: N, 11.09. Found: N, 10.92.

5-Hydroxy-6-amino-2,3,8-trimethylquinoline (VI).—A solution of 7 g. of 5-methoxy-6-amino-2,3,8-trimethylquinoline in 110 cc. of 40% hydrobromic acid was boiled under reflux for four hours. The hot solution was decolorized with Norit, and filtered through a sintered glass funnel. The filtrate was concentrated to 60 cc. when 6.8 g. of a yellow hydrobromide crystallized out. Another 2 g. of the same salt was obtained by further concentration. The total yield was 75%. It was extracted with ethanol in which it was sparingly soluble; its color deepened to red indicating a loss of hydrogen bromide.[1] Recrystallization from hot water rendered brick-red needles, m. p. 330–335° (dec., in vacuum).

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(6) *Cf.* Stevens and Tucker, *J. Chem. Soc.*, **123**, 2140 (1923).

(7) Arndt, Loewe and Avan, *Ber.*, **73**, 606 (1940).

Anal. Calcd. for $C_{12}H_{15}BrN_2O$: C, 50.89; H, 5.34. Found: C, 50.93; H, 4.98.

The free aminophenol was unstable.

2,3,8-Trimethylquinoline-6-diazo-5-oxide (VII).—Four grams of crude 5-hydroxy-6-amino-2,3,8-trimethylquinoline dihydrobromide, dissolved in 90 cc. of 17% hydrochloric acid, was diazotized at −5° with a solution of 1.3 g. of sodium nitrite in 10 cc. of ice-water. The clear solution was allowed to stand at −5° for fifteen minutes, excess nitrous acid was decomposed with urea, and the solution was poured into 200 cc. of boiling water. No nitrogen was evolved during this operation. After neutralization with sodium bicarbonate, the red precipitate was filtered and recrystallized from boiling ethanol. The diazoöxide was obtained as long red needles which darkened at 167° and decomposed at 228° in an evacuated tube. The yield was 2.1 g. (90%).

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.53; H, 5.27; N, 20.29.

Reduction of the Diazoöxide VII.—An alkaline solution of 1.2 g. of sodium hydrosulfite in 20 cc. of water was added to a solution of 0.3 g. of the diazoöxide in 25 cc. of ethanol, and the mixture was boiled for ten minutes. It was cooled, acidified with dilute hydrochloric acid, and 5-hydroxy-2,3,8-trimethylquinoline (I) was precipitated with sodium bicarbonate. The yield was 0.25 g. (95%). The phenol was purified by repeated sublimation at 140° and 0.1 mm. pressure, and recrystallization from benzene. It melted at 219°.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00. Found: C, 76.62; H, 7.57.

Methylation with diazomethane yielded 5-methoxy-2,3,8-trimethylquinoline, m. p. 80–81°.

Mixture melting points of the phenol I with a sample of 5-hydroxy-2,3,8-trimethylquinoline,[1] and of the methoxy compound with a sample of the 5-methoxy derivative, showed no depression.

2,3,8-Trimethylquinoline-5,6-quinone Dioxime (VIII).—A solution of 1 g. of the diazoöxide VII, 14 cc. of pyridine, and 1.4 g. of hydroxylamine hydrochloride in 40 cc. of absolute ethanol was boiled under reflux for four hours, the solvent was evaporated under reduced pressure, the oily residue was dissolved in ethanol and precipitated with water. Recrystallization from dilute ethanol yielded 0.8 g. (74%) of light-yellow needles, m. p. 189–190° (dec., in vacuum).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.32; H, 5.67; N, 18.17. Found: C, 62.34; H, 5.56; N, 18.30.

The dioxime gave colored precipitates with eight different heavy metal ions.

2,3,8-Trimethyl-5,6-quinolinofurazan (IX).—A solution of 0.15 g. of 2,3,8-trimethylquinoline-5,6-quinone dioxime in 20 cc. of 10% sodium hydroxide solution was boiled for two minutes, when a crystalline product precipitated almost quantitatively. It was recrystallized from dilute ethanol and appeared as almost colorless needles, m. p. 130°.

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20. Found: C, 67.74; H, 5.14.

5 - Amino - 2,3,8 - trimethyl - 1,2,3,4 - tetrahydroquinoline (X).—A solution of 0.22 g. of 5-amino-2,3,8-trimethylquinoline in 10 cc. of ethanol was shaken under one atmosphere of hydrogen pressure in the presence of 0.2 g. of a platinum oxide catalyst. Two moles of hydrogen was absorbed. The residue from the alcohol solution was purified by distillation at 110° under 0.1 mm. pressure. The distillate consisted of a colorless viscous oil which darkened on standing in the air.

Anal. Calcd. for $C_{12}H_{18}N_2$: C, 75.74; H, 9.54. Found: C, 75.70; H, 9.57.

The same results were obtained by using a Raney nickel catalyst. The yield in both cases was 90%. The amine X was also prepared by hydrogenation of 5-nitro-2,3,8-trimethylquinoline in ethanol solution in the presence of a platinum oxide catalyst. Five moles of hydrogen was absorbed, and the reaction mixture was worked up as described above to give a yield of 90%.

The colorless **dihydrochloride** crystallized from boiling absolute ethanol. It decomposed above 300°.

Anal. Calcd. for $C_{12}H_{20}Cl_2N_2$: C, 54.75; H, 7.66. Found: C, 54.83; H, 7.76.

1 - Acetyl - 1,2,3,4 - tetrahydro - 5 - acetamino - 2,3,8-trimethylquinoline, prepared by the action of acetic anhydride and pyridine on the amine X, was sublimed at 150° under 0.1 mm. pressure, and recrystallized from benzene. It appeared as colorless needles, m. p. 152°.

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08. Found: C, 69.90; H, 8.18.

1 - Nitroso - 1,2,3,4 - tetrahydro - 5 - hydroxy - 2,3,8-trimethylquinoline (XI).—Three grams of 5-amino-2,3,8-trimethyl-1,2,3,4-tetrahydroquinoline dihydrochloride, dissolved in 60 cc. of 5 *N* hydrochloric acid, was diazotized with a solution of 0.9 g. of sodium nitrite in 30 cc. of water at −5°. The mixture was allowed to stand at this temperature for one hour, 1 g. of urea was added, and the solution was poured into 270 cc. of 5% sulfuric acid at 70°. The mixture was heated at 65° for thirty minutes, boiled gently for one hour, cooled, made alkaline with sodium hydroxide solution, filtered from impurities, acidified with hydrochloric acid, and the phenolic nitroso compound was liberated with sodium bicarbonate. The yield was 0.9 g. (35%). It crystallized from benzene–petroleum ether as red needles which decomposed at high temperatures.

Anal. Calcd. for $C_{12}H_{18}N_2O_2$: C, 65.43; H, 7.32. Found: C, 65.91; H, 7.28.

5 - Hydroxy - 1,2,3,4 - tetrahydro - 2,3,8 - trimethylquinoline (XII).—One gram of 5-hydroxy-2,3,8-trimethylquinoline (I) in 50 cc. of ethanol absorbed two moles of hydrogen in the presence of 0.2 g. of a platinum oxide catalyst. The oily reduction product was dissolved in ether, and the phenolic fraction was extracted into a dilute sodium hydroxide solution. The phenol XII was isolated in the customary way; it was oily and therefore converted to the hydrochloride in acetone–ethanol solution. Recrystallization from acetone–ethanol gave colorless needles, m. p. 258–263° (dec.). The yield was 65%.

Anal. Calcd. for $C_{12}H_{18}ClNO$: C, 63.28; H, 7.97. Found: C, 63.26; H, 7.74.

The alkali-insoluble fraction of the reduction mixture was obtained as an unstable oil from its ether solution. No crystalline hydrochloride could be prepared.

Summary

A number of amino and hydroxy derivatives of the kerosene base 2,3,8-trimethylquinoline have been prepared.

Diazotization of 5-hydroxy-6-amino-2,3,8-trimethylquinoline furnished 2,3,8-trimethylquinoline-6-diazo-5-oxide which was converted by the action of hydroxylamine to 2,3,8-trimethylquinoline-5,6-quinone dioxime. Such a reaction of *o*-diazoöxides has not been observed before.

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The Treatment of Simple Aliphatic Amines with Nitrous Acid

BY FRANK C. WHITMORE AND R. S. THORPE

It might be assumed that low molecular weight primary aliphatic amines would react easily with nitrous acid to form primary alcohols with liberation of nitrogen according to the equation

$$RNH_2 + HNO_2 \longrightarrow ROH + N_2 + H_2O$$

This reaction takes place with *n*-butylamine to the extent of 25%.[1] However, very little study has been made of the reaction of the simple amines with nitrous acid. The purpose of the present work was to study the effect of nitrous acid on methylamine, ethylamine and *n*-propylamine under conditions similar to those used in the successful reaction of nitrous acid with *n*-butylamine.[1]

In sixteen experiments using methylamine and nitrous acid under a wide variety of conditions neither methyl alcohol nor any other reaction products could be isolated from the reaction mixtures. In every reaction attempted, some methylamine was recovered unchanged. The amount of unreacted amine was never less than 25%, and in some experiments the recovery was greater than 90%. This was in spite of the fact that conditions like those employed with *n*-butylamine[1] were used in several cases. The usual variations of concentrations and temperature were tried. Other solvents than water were used. Even a reaction in the gas phase between methylamine and "nitrogen trioxide" in presence of traces of moisture was attempted.

We believe that the failure to obtain methyl alcohol or any related product from methylamine and nitrous acid is because the nitrite of the amine is more readily hydrolyzed than decomposed.

We were able to confirm the earlier workers by producing small amounts of methyl alcohol from silver nitrite and methylamine hydrochloride.

Ethylamine with nitrous acid gave a 60% yield of ethyl alcohol. *n*-Propylamine gave 7% *n*-propyl alcohol, 32% isopropyl alcohol and 28% propylene. Traces of ethers were also formed with ethyl and propyl amines.

Experimental

Preparation of Reagents.—Methylamine was prepared by the Hofmann degradation of acetamide with H. T. H. according to the directions of Hauser and Renfrow.[2] It was necessary to allow several hours for the formation of the N-chloroamide before heating to degradation temperature. With this modification it was possible to prepare methylamine and convert it to methylamine hydrochloride, m. p. 230–231°, consistently in 78% yield. For solutions of methylamine in water, free amine gas was bubbled through cold water; the amine strength was determined by titration with standard acid.

Ethylamine was purchased from the Sharples Solvents Corporation as a 33.3% solution in water. Propylamine was prepared by the action of ammonia on *n*-propyl bromide. The propylamine salts were neutralized and the free amines were fractionally distilled. Two fractionations were carried out using a 1.5 × 65 cm. packed column and taking the fraction b. p. 47–49°.

U. S. P. sodium nitrite was used. Silver nitrite was prepared from sodium nitrite and silver nitrate.

Methylamine and Nitrous Acid.—Only a few of the sixteen experiments are given. Methylamine hydrochloride dissolved in water was placed in a 3-liter flask fitted with a mechanical stirrer, dropping funnel and an outlet for gas. At the gas outlet a spiral condenser was arranged and fitted with a receiver cooled with ice. A trap immersed in dry-ice and acetone was used to condense any low boiling material. Alkaline permanganate was used to absorb nitrogen oxides, and finally a graduated carboy was arranged to collect gases. Sodium nitrite solution was introduced through the dropping funnel. Recovery of methylamine was accomplished by finally combining all solutions possibly containing unreacted amine, neutralizing with alkali, distilling the free amine into hydrochloric acid, and evaporating the resulting solution to dryness.

Approximately one-mole amounts of methylamine were mixed with nitrous acid prepared in various concentrations from sodium nitrite and hydrochloric acid. The fact that

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(1) Whitmore and Langlois, THIS JOURNAL, **54**, 3441 (1932).

(2) Hauser and Renfrow, *J. Chem. Education*, **14**, 542 (1938).