

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

**Petroleum Bases. I. Reactions of 2,3,8-Trimethylquinoline**

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Several polyalkyl pyridine and quinoline derivatives which are not easily accessible by synthetic approaches have become available recently by the separation of basic straight run and cracked petroleum fractions. Bailey and his co-workers<sup>1</sup> have published a long series of interesting articles dealing with the separation and the structure of individual nitrogen-containing constituents of these fractions. It seemed worth while to investigate whether some of the bases from kerosene containing the quinoline nucleus would lend themselves to the preparation of substances of pharmacological interest, since quinoline is the classical heterocyclic system encountered in a wide variety of medicinally important products.<sup>2</sup> One of the most readily available kerosene bases, 2,3,8-trimethylquinoline,<sup>3</sup> was chosen therefore as the starting material for our studies. This communication describes several reactions of this base leading to derivatives needed in the preparation of such substances which will be the subject of forthcoming publications from this Laboratory.

Nitration of 2,3,8-trimethylquinoline (I) with fuming nitric acid furnished 5-nitro-2,3,8-trimethylquinoline (II) in almost quantitative yield. Reduction of this nitro compound with stannous chloride led to the corresponding amine (III), while hydrogenation in neutral solvents in the presence of a platinum oxide catalyst not only reduced the nitro group, but also attacked the pyridine nucleus. When the reaction was interrupted after absorption of only three moles of hydrogen, the amino compound III could be isolated in yields of around 60%. Hydrogenation in the presence of Raney nickel recently recommended by Winterbottom<sup>4</sup> was abandoned when more than three moles of hydrogen was absorbed, and the unhydrogenated amine III could not be isolated from the reaction mixture.

The mono-hydrochloride of 2,3,8-trimethyl-5-aminoquinoline exhibits a deep brick-red color.

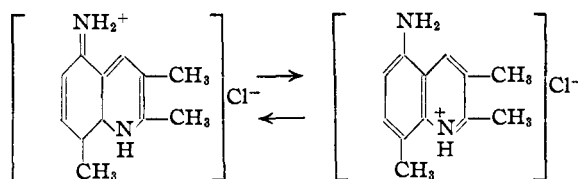
(1) Schenck and Bailey, *THIS JOURNAL*, **61**, 2613 (1939), and many preceding papers.

(2) Cf. von Oettingen, "Therapeutic Agents of the Quinoline Group," The Chemical Catalog Company, New York, 1933; Jensch, *Z. angew. Chem.*, **50**, 891 (1937); Houben, "Fortsschritte in der Heilstoffchemie," Part 2, Vol. III, Verlag Walter de Gruyter & Co., Berlin, 1939.

(3) Bailey and co-workers, *THIS JOURNAL*, **52**, 1239 (1930).

(4) Winterbottom, *ibid.*, **62**, 180 (1940).

When hydrochloric acid is added to the colored aqueous solution of this salt, the color disappears almost completely; when a sodium carbonate solution is added carefully to the resulting colorless acidic solution, the deep red color reappears, and vanishes only when the solution turns alkaline, and the base precipitates. The deep red color of the mono-hydrochloride may be explained by oscillation of the anion between the two nitrogen atoms; the salt may thus exist in resonating forms



A survey of some known 5- and 8-aminoquinoline derivatives revealed that a deepening of the color from diacidic toward monoacidic salts has been observed in several instances.<sup>5</sup> However, a similar change in color has been reported in the case of the salts of 6-aminolepidine.<sup>6</sup> In this case, a resonating system which would disappear upon addition of a second molecule of the acid cannot be held responsible for the deeper color of the monoacidic salts, because position-2 in the pyridine nucleus would be unable to hold a second hydrogen atom if the cyclic nitrogen atom assumed a positive charge.

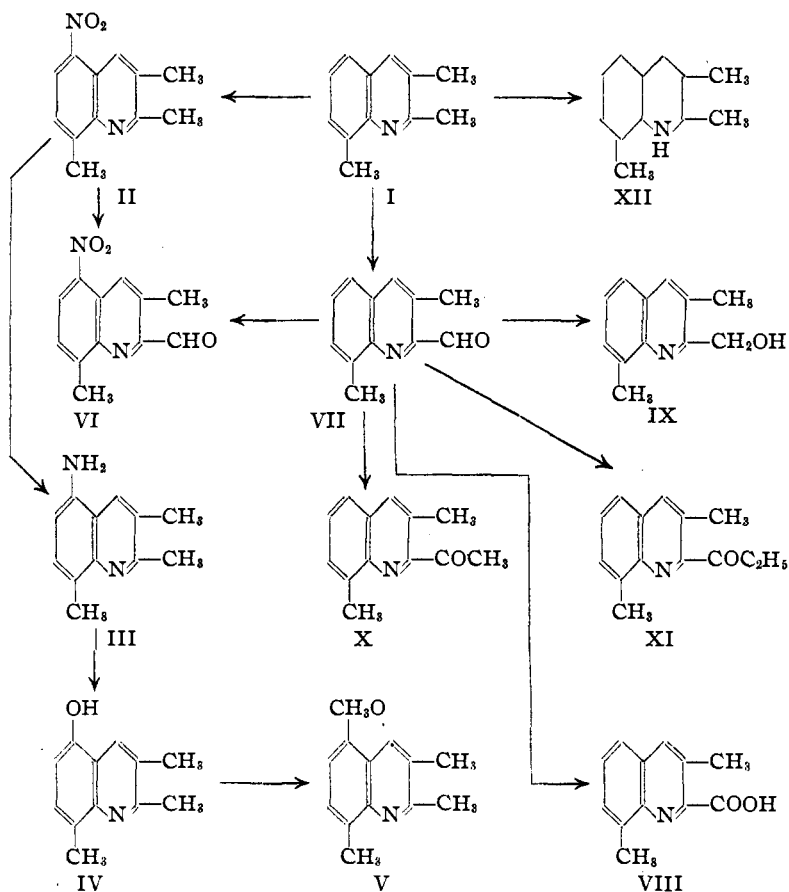
5-Hydroxy-2,3,8-trimethylquinoline (IV), prepared from the amine III by diazotization, was converted into the methyl ether (V) by the action of diazomethane. The structure of 5-methoxy-2,3,8-trimethylquinoline was established by synthesis from 4-methoxy-2-aminotoluene and tiglic aldehyde.<sup>7</sup> The base obtained in this condensation, and its picrate, proved to be identical with V, and its picrate, respectively. This also establishes the position of the functional substituents in the related nitro (II), amino (III), and hydroxy (IV) derivatives. Attempts to prepare 5-nitro-2,3,8-trimethylquinoline (II) by condensation of 2-amino-4-nitrotoluene with tiglic aldehyde failed

(5) Noelting and Trautmann, *Ber.*, **23**, 3674 (1890); cf. Doebner and v. Miller, *ibid.*, **17**, 1703 (1884); Seka, *Monatsh.*, **45**, 287 (1927).

(6) Koenigs, *Ber.*, **23**, 2671 (1890); Busch and Koenigs, *ibid.*, **23**, 2685 (1890).

(7) Cf. Rohde, *ibid.*, **20**, 1911 (1887).

to yield well-defined products, probably because the nitro group of the starting material is reduced during the dehydrogenation of the intermediate dihydroquinoline derivative. Addition of arsenic acid<sup>8</sup> during the condensation caused extensive formation of resins and failed to improve the yield.



2,3,8-Trimethylquinoline exhibits the normal reactivity of quinaldine derivatives: for example, the 2-methyl group may be condensed with carbonyl compounds.<sup>3</sup> This methyl group is also the only one which is attacked by selenium dioxide. Oxidation of the base with this reagent, previously employed in similar cases,<sup>9</sup> proceeded very smoothly and furnished 3,8-dimethylquinoline-2-aldehyde (VII) in good yield. The position of the aldehyde group was confirmed by oxidizing the compound with silver oxide<sup>10</sup> to 3,8-dimethylquinoline-2-carboxylic acid (VIII).<sup>3</sup> Concentrated nitric acid did not oxidize the aldehyde

(8) Knueppel, *Ber.*, **29**, 703 (1896); see also I. G. Farbenindustrie A.-G., French Patent 739,880 (1932) (*C. A.*, **27**, 2164).

(9) Monti, *Atti accad. Lincei*, **18**, 505 (1933); Henze, *Ber.*, **67**, 750 (1934); Kwartler and Lindwall, *THIS JOURNAL*, **59**, 524 (1937).

(10) Besthorn and Geisselbrecht, *Ber.*, **53**, 1017 (1920).

group but caused quantitative mono-nitration of the compound. The nitro derivative thus obtained proved to be identical with 5-nitro-3,8-dimethylquinoline-2-aldehyde (VI) which had been prepared by oxidation of 5-nitro-2,3,8-trimethylquinoline (II) with selenium dioxide. Thus, the para-orienting influence of the 8-methyl group, and the ortho-para-orienting effect of the heterocyclic nucleus combine to determine the position of the entering nitro group, regardless of the type of substituent in position-2.

Catalytic reduction of 3,8-dimethylquinoline-2-aldehyde (VII) yielded 3,8-dimethylquinoline-2-methanol (IX) which contains a  $\beta$ -amino alcohol arrangement,  $-\text{N}=\text{C}-\text{CH}_2\text{OH}$ , and may be expected to exert some influence on blood pressure and peristalsis. We attempted to prepare the 5-amino derivative of the alcohol IX by catalytic reduction of the nitro aldehyde VI, but although the calculated amount of hydrogen was absorbed, no crystalline reaction product could be isolated. Reduction of VI to the corresponding amino aldehyde by various methods did not furnish well-defined products either.

3,8-Dimethylquinoline-2-aldehyde (VII) served as a convenient starting material in the preparation of  $\alpha$ -quinolyl ketones. This class of compounds is not very easily accessible, and the reaction described here, namely, the action of diazoalkanes on a quinoline-2-aldehyde, may facilitate the approach to such substances. Diazomethane furnished a complex mixture containing moderate amounts of 3,8-dimethyl-2-quinolyl methyl ketone (X), while the main fraction consisted of high-boiling oils, perhaps polymers of the primary reaction products, namely, compounds of ethylene oxide character. Diazoethane gave a satisfactory yield of 3,8-dimethyl-2-quinolyl ethyl ketone (XI); both ketones were characterized by their oximes. The reaction of 3,8-dimethylquinoline-2-aldehyde with

diazoalkanes compares with that of some aromatic aldehydes, for example, piperonal,<sup>11</sup> which also reacts with diazomethane to yield ethylene oxide derivatives chiefly, while the corresponding aryl ethyl ketone is the main product of the reaction with diazoethane.

Taylor, Winckles and Marks<sup>12</sup> found that quinoline-2-aldoxime can form chelated metal compounds, and concluded that it must have the *cis* configuration. 3,8-Dimethylquinoline-2-aldoxime and its 5-nitro derivative also give color reactions and precipitates with a number of metallic ions. This would indicate that our aldoximes also are *syn*-oximes. The oximes of 3,8-dimethyl-2-acetylquinoline (X) and 3,8-dimethyl-2-propionylquinoline (XI), on the other hand, did not exhibit any reactions with metallic ions.

Hydrogenation of 2,3,8-trimethylquinoline in glacial acetic acid solution under ordinary pressure in the presence of a platinum oxide catalyst furnished 2,3,8-trimethyldecahydroquinoline (XII) in good yield. This compound may exist in a *cis*- and a *trans*-form. While the melting points of various fractions of the hydrochloride seem to indicate differences which may be attributed to a partial separation of the stereoisomers by fractional crystallization, a final evaluation of this separation must await future experimental results.

**Acknowledgment.**—The authors wish to thank Professor J. R. Bailey of the University of Texas, and the Union Oil Company of California for supplying the kerosene base used in this investigation.

### Experimental

**3,8-Dimethylquinoline-2-aldehyde (VII).**—A solution of 5 g. of 2,3,8-trimethylquinoline and 3.5 g. of selenium dioxide in 40 ml. of ethanol was boiled under reflux for six hours, and the precipitated selenium was filtered from the hot solution. The filtrate was concentrated and 3.3 g. of the aldehyde was collected as straw-colored needles. The mother liquor was precipitated with water, the reddish solid was filtered, dissolved in 10 ml. of benzene, and the solution shaken with 30 ml. of a saturated solution of sodium bisulfite for one hour. The crystalline addition product was filtered, washed with ether, and decomposed with a dilute sodium carbonate solution. Another 1.2 g. of the aldehyde was obtained in this manner, the yield totalling 82%. The aldehyde was purified by distillation under 1 mm. pressure, and recrystallization from ethanol. It appeared as long colorless needles, m. p. 107–108°.

(11) Mosettig, *Ber.*, **61**, 1391 (1928); **63**, 1271 (1929); Mosettig and Czadek, *Monatsh.*, **57**, 291 (1931).

(12) Taylor, Winckles and Marks, *J. Chem. Soc.*, 2778 (1931).

*Anal.*<sup>13</sup> Calcd. for C<sub>12</sub>H<sub>11</sub>NO: C, 77.80; H, 5.99. Found: C, 77.85; H, 6.18.

The oxime was prepared by the method of Bachmann and Boatner.<sup>14</sup> It crystallized from ethanol as almost colorless needles, m. p. 172–174°.

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O: C, 71.96; H, 6.04. Found: C, 71.87; H, 5.99.

The semicarbazone was prepared by heating equimolecular amounts of the aldehyde and semicarbazide hydrochloride in dilute ethanol solution for five minutes. The alcohol was boiled off, the solution neutralized with sodium bicarbonate and allowed to cool. The semicarbazone crystallized in little colorless needles which, after recrystallization from dilute ethanol, sintered at 185°, m. p. 190–192° (dec.).

*Anal.* Calcd. for C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>O: N, 23.14. Found: N, 23.82.

**3,8-Dimethylquinoline-2-methanol (IX).**—A solution of 5.0 g. of 3,8-dimethylquinoline-2-aldehyde in 150 ml. of ethanol was hydrogenated in the presence of 0.2 g. of a platinum oxide catalyst. Absorption of one mole of hydrogen was completed in ten minutes. After filtration from the catalyst, the solvent was evaporated under reduced pressure at 40°, and the crystalline residue was dissolved in low-boiling petroleum ether. A small amount of a white insoluble material was removed by filtration, the solution was concentrated, and the carbinol crystallized as colorless prisms, m. p. 68–69°. The yield was 90%.

*Anal.* Calcd. for C<sub>12</sub>H<sub>13</sub>NO: C, 76.96; H, 7.00. Found: C, 76.95; H, 7.34.

The hydrochloride was prepared by the action of ethanolic hydrogen chloride on the base and recrystallized from ethanol. It consisted of colorless water soluble crystals which sintered at 160°, m. p. 176–185° (dec.). The aqueous solution turned yellow on standing, but the color could be removed by extraction into ether.

*Anal.* Calcd. for C<sub>12</sub>H<sub>14</sub>ClNO: N, 6.27. Found: N, 6.57.

The acetyl derivative was obtained by allowing the carbinol to stand with an excess of acetic anhydride in pyridine solution overnight, and working up the mixture in the usual manner. It was recrystallized from dilute ethanol and appeared as colorless needles, m. p. 62–63°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>15</sub>NO<sub>2</sub>: C, 73.32; H, 6.60. Found: C, 73.46; H, 6.36.

**Oxidation of 3,8-Dimethylquinoline-2-aldehyde.**—Twentytenths gram of the aldehyde and 0.08 g. of freshly prepared silver oxide in 10 ml. of ethanol was heated under reflux for three hours. Alkaline water was added, the coagulated silver precipitate was filtered, and the filtrate was concentrated to 10 ml. Acidification with acetic acid and scratching caused 3,8-dimethylquinoline-2-carboxylic acid (VIII) to crystallize in good yield. Crystallization from a few milliliters of water yielded colorless needles, m. p. 154–155°. The melting point reported by Bailey<sup>3</sup> is 157°.

**3,8-Dimethyl-2-quinolyl Methyl Ketone (X).**—A solution of 1 g. of 3,8-dimethylquinoline-2-aldehyde in 20 ml. of

(13) C and H micro determinations by Mrs. Elizabeth Johnson Mathers.

(14) Bachmann and Boatner, *This Journal*, **59**, 2097 (1933).

ether and 4 ml. of methanol was treated with an ethereal solution of about 0.6 g. of diazomethane. Nitrogen began to evolve soon, and the solvent was evaporated after sixteen hours. The semi-oily residue was fractionated under 1 mm. pressure. A mostly crystalline fraction distilled first; the major fraction consisted of a brown oil of high boiling range. The crystalline fraction was recrystallized from dilute methanol and yielded 0.2 g. of yellowish needles, m. p. 90°.

*Anal.* Calcd. for  $C_{13}H_{13}NO$ : C, 78.35; H, 6.58. Found: C, 78.58; H, 6.66.

The *oxime*, prepared in ethanol-pyridine solution,<sup>13</sup> was crystallized from dilute methanol; colorless, m. p. 153–154°.

*Anal.* Calcd. for  $C_{13}H_{14}N_2O$ : C, 72.85; H, 6.59. Found: C, 72.80; H, 6.59.

**3,8-Dimethyl-2-quinolyl Ethyl Ketone (XI).**—Fifteen-tenths gram of 3,8-dimethylquinoline-2-aldehyde was dissolved in a solution of diazoethane (from 2 ml. of nitrosoethylurethane) in 30 ml. of ether. A vigorous reaction started soon and was completed by addition of 2 ml. of methanol. After standing overnight, the decolorized solution was evaporated, and the crystalline residue was recrystallized from slightly dilute methanol. The ketone appeared as colorless prisms, m. p. 80°. The yield was 52%.

*Anal.* Calcd. for  $C_{14}H_{15}NO$ : C, 78.83; H, 7.09. Found: C, 79.01; H, 7.10.

The *oxime* was obtained from dilute methanol as colorless crystals, m. p. 146–148°.

*Anal.* Calcd. for  $C_{14}H_{16}N_2O$ : C, 73.64; H, 7.07. Found: C, 73.49; H, 6.96.

**5-Nitro-2,3,8-trimethylquinoline (II).**—Twenty grams of 2,3,8-trimethylquinoline was added gradually to 200 ml. of fuming nitric acid (*d* 1.49). The solution became hot and was heated on a steam-bath for five hours. It was poured into 200 ml. of water, and the mixture was made alkaline with sodium hydroxide solution. Recrystallization from dilute ethanol rendered pale yellow needles, m. p. 124°, in a yield of 98%.

*Anal.* Calcd. for  $C_{12}H_{12}N_2O_2$ : C, 66.63; H, 5.60; N, 12.96. Found: C, 66.69; H, 5.60; N, 12.91.

**5-Nitro-3,8-dimethylquinoline-2-aldehyde (VI).**—(a) Thirteen and two-tenths grams of 3,8-dimethylquinoline-2-aldehyde was boiled under reflux with 132 ml. of fuming nitric acid (*d* 1.49) for five hours, and the solution was poured into ammoniacal water. The nitro-aldehyde was crystallized from dilute ethanol and appeared as almost colorless felted needles, m. p. 165°. The compound contained one molecule of ethanol of crystallization. The yield was 85%.

*Anal.* Calcd. for  $C_{12}H_{10}N_2O_3 \cdot C_2H_6O$ : C, 60.84; H, 5.84. Found: C, 60.71; H, 5.63.

Ethanol of crystallization was lost when the compound was heated at 100° under 1 mm. pressure for one hour. The substance melted at 167°.

*Anal.* Calcd. for  $C_{12}H_{10}N_2O_3$ : C, 62.58; H, 4.38. Found: C, 62.39; H, 4.05.

(b) One half gram of 2,3,8-trimethyl-5-nitroquinoline was heated with 0.3 g. of selenium dioxide in 20 ml. of ethanol for fifty hours. After filtration from selenium, the solution was concentrated, and a brown oil precipitated which solidified on standing. After several crystallizations from ethanol-water the nitro-aldehyde was obtained in a yield of 38%; m. p. 164–165°. A mixture melting point with the substance obtained by procedure (a) showed no depression.

The *oxime* crystallized from dilute ethanol as a slightly yellow powder, m. p. 180–181°.

*Anal.* Calcd. for  $C_{12}H_{11}N_3O_3$ : C, 58.75; H, 4.52. Found: C, 58.64; H, 4.64.

The oximes of the aldehydes VI and VII undergo a number of reactions with metallic ions which are listed in Table I furnished by Dr. Lyle G. Overholser.

**2,3,8-Trimethyl-5-aminoquinoline (III).**—Two grams of 2,3,8-trimethyl-5-nitroquinoline was added to a solution of 8.5 g. of stannous chloride in 16 ml. of 17% hydrochloric acid, and the solution was heated on a steam-bath for three hours. A small amount of an orange-colored double salt separated out and was brought into solution by dilution with 25 ml. of water. The amino compound was precipitated by the addition of strong sodium hydroxide solution and was purified by sublimation at 100° under 0.1 mm. pressure. The yield was 97%. Recrystallization from dilute ethanol furnished yellow needles, m. p. 110–111°.

TABLE I

Metallic ion	3,8-Dimethylquinoline-2-aldoxime	3,8-Dimethyl-5-nitroquinoline-2-aldoxime
$Ag^{+1}$	Slight reduction on prolonged standing	Pale yellow color; pale yellow-greenish color in $NH_4OH$
$Au^{+3}$	Yellow color within one minute, yellow precipitate on standing	Pale yellow precipitate
$Ce^{+4}$	Yellow color, fades soon	
$Cu^{-}(NH_3)$	Green precipitate, soluble in strong $NH_4OH$	Slight precipitate in weak $NH_4OH$ , no reaction in 1 <i>M</i> $NH_4OH$
$Hg^{+2}$		Slightly yellow precipitate
Ni	Pale green color in neutral solution, slight yellow-green precipitate in $NH_4OH$ solution	Same reaction as with $Cu^{-}(NH_3)$
$OsCl_6^{-}$	Green color in HCl solution	Pale yellow precipitate in HCl, pale yellow color in KOH solution
$Pd^{+2}$	Stable green color	
$Pt^{+4}$	Pale yellow-green color in HCl solution	
$S^{-}$		Pale yellow color
$Sm^{+3}$		Orange-pink color in HCl solution

*Anal.* Calcd. for  $C_{12}H_{14}N_2$ : C, 77.36; H, 7.58. Found: C, 77.56; H, 7.45.

The **mono-hydrochloride**, prepared in ethereal solution, and recrystallized from ethanol, appeared as brick-red needles which sublimed at high temperatures without melting.

*Anal.* Calcd. for  $C_{12}H_{13}ClN_2$ : N, 12.59. Found: N, 12.13.

The **di-hydrochloride** was obtained as pale yellow crystals by treating the mono-hydrochloride with an excess of ethanolic hydrogen chloride. It loses hydrogen chloride slowly in the dry state, more rapidly in alcoholic solution, turning deep red.

Acetylation of the amine with acetic anhydride in pyridine solution yielded **2,3,8-trimethyl-5-acetaminoquinoline**, light colorless needles, m. p. 234–235°.

*Anal.* Calcd. for  $C_{14}H_{16}N_2O$ : C, 73.64; H, 7.07. Found: C, 73.73; H, 6.97.

**2,3,8-Trimethyl-5-hydroxyquinoline (IV)**.—Five-tenths gram of 2,3,8-trimethyl-5-aminoquinoline, dissolved in 50 ml. of 5 *N* hydrochloric acid, was diazotized at 0° with a solution of 0.25 g. of sodium nitrite in 40 ml. of water. A small amount of urea was added, the solution heated to boiling, cooled, neutralized with sodium bicarbonate, and the phenolic base filtered. The yield was 76%. Sublimation at 125° and 0.1 mm. pressure yielded colorless rods, m. p. 219–219.5°.

*Anal.* Calcd. for  $C_{12}H_{13}NO$ : C, 76.96; H, 7.00. Found: C, 76.77; H, 6.81.

**2,3,8-Trimethyl-5-methoxyquinoline (V)**.—(a) Methylation of the phenolic base IV with diazomethane in methanol-ether solution yielded the methoxy compound as colorless prisms, which were purified by sublimation at 75° and 0.01 mm. pressure, and recrystallization from dilute methanol; m. p. 80°.

*Anal.* Calcd. for  $C_{13}H_{15}NO$ : C, 77.56; H, 7.52. Found: C, 77.53; H, 7.31.

The **picrate** crystallized from methanol as short yellow prisms, m. p. 198–199°.

*Anal.* Calcd. for  $C_{19}H_{18}N_4O_8$ : C, 53.02; H, 4.22. Found: C, 53.19; H, 4.53.

(b) 2-Amino-4-methoxytoluene<sup>15</sup> was prepared by reduction of 2-nitro-4-methoxytoluene<sup>16</sup> with hydrogen in the presence of a platinum oxide catalyst in ethanol solution; the yield was 95%, m. p. 45°.

A solution of 4.2 g. (0.031 mole) of 2-amino-4-methoxy-

toluene and 3.5 ml. (0.031 mole) of tiglic aldehyde in 65 ml. of concentrated hydrochloric acid was heated on a steam-bath for two hours. The dark solution was diluted with water, and some unchanged methoxytoluidine was removed by diazotization and extraction of the resulting 2-hydroxy-4-methoxytoluene into ether. The solution was then made alkaline and 5-methoxy-2,3,8-trimethylquinoline was extracted into ether. It was purified by sublimation and crystallization and melted at 80°. The yield was 8%.

*Anal.* Calcd. for  $C_{18}H_{19}NO$ : C, 77.56; H, 7.52. Found: C, 77.64; H, 7.42.

The **picrate** melted at 197–199°.

*Anal.* Calcd. for  $C_{19}H_{18}N_4O_8$ : C, 53.02; H, 4.22. Found: C, 53.47; H, 4.34.

The mixture melting point of the 5-methoxytrimethylquinoline derivatives obtained (a) by degradation and (b) by synthesis, and that of their respective picrates, showed no depression.

**2,3,8-Trimethyldecahydroquinoline (XII)**.—Five grams of 2,3,8-trimethylquinoline in 30 ml. of purified glacial acetic acid was hydrogenated in the presence of 0.4 g. of a platinum oxide catalyst. Another 0.3 g. of the catalyst had to be added to carry hydrogen absorption to completion. Five moles of hydrogen was absorbed in twenty-four hours. The catalyst was filtered, the solution was made alkaline, and the decahydro base was extracted into ether. It was fractionated under 10 mm. pressure, and the main fraction, a colorless oil of b. p. (10 mm.) 89–91°, was collected.

*Anal.* Calcd. for  $C_{12}H_{23}N$ : C, 79.48; H, 12.79. Found: C, 79.35; H, 12.39.

The **hydrochloride** was prepared in acetone-ether solution. It appeared as colorless crystals, m. p. 251–275° (dec.).

*Anal.* Calcd. for  $C_{12}H_{24}ClN$ : N, 6.44. Found: N, 6.53.

### Summary

A number of reactions of the kerosene base, 2,3,8-trimethylquinoline, involving mainly positions 2 and 5 of the quinoline system, have been studied. The derivatives obtained in these reactions will serve as starting materials in the syntheses of compounds containing pharmacologically interesting groups.

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(15) Knecht, *Ann.*, **215**, 83 (1882).

(16) Ullmann and Dootson, *Ber.*, **51**, 19 (1918).