nesium bromide in accord with the experiments of Sherwood and Short.[5] This lack of reactivity is readily explained by the steric hindrance exerted by the angular methyl group.

Experimental[6]

Diphenyl-*t*-dehydroabietinol (I).—A solution of 38 g. of methyl dehydroabietate in 100 ml. of dry ether was added to a refluxing ethereal solution of phenylmagnesium bromide prepared from 7 g. of magnesium turnings and 43 g. of bromobenzene in 200 ml. of dry ether. The mixture was refluxed for two hours, the ether was removed and the viscous residue heated on the steam-bath for two hours. After standing overnight the mass was hydrolyzed with 10% sulfuric acid and ice with stirring under a layer of ordinary ether. Both layers were transferred to a separatory funnel and the acidic layer removed. After washing the ether layer with several portions of 10% sulfuric acid and finally with distilled water to neutrality, solvent ether was removed and the residue was steam distilled to remove diphenyl. The mass was next dried in ether over sodium sulfate and then vacuum distilled, the main fraction of carbinol distilling between 186–191° (8–9 mm.) as a pale yellow oil; yield 33.5 g. (63%).

Anal.[7] Calcd. for $C_{32}H_{38}O$: C, 87.61; H, 8.73. Found: C, 87.22, 87.65; H, 8.54, 8.69.

Diphenyl-*t*-6-hydroxydehydroabietinol (II).—Methyl 6-methoxydehydroabietate (8.6 g.) in 20 ml. of absolute ether was added to an ether solution of phenylmagnesium turnings. The procedure was the same as above. Cleavage of the ether linkage seems to have occurred during hydrolysis with 10% sulfuric acid, after which the crude hydroxy carbinol residue was steam distilled to remove diphenyl and dried in ether. After removal of the ether the residue was crystallized three times from methanol giving 2.8 g. (24.5%) of transparent prisms of diphenyl-*t*-6-hydroxydehydroabietinol; m. p. 194–196°. Repeated recrystallization from glacial acetic acid did not alter the melting point.

Anal.[8] Calcd. for $C_{32}H_{38}O_2$: C, 84.53; H, 8.42. Found: C, 84.70, 84.45; H, 8.85, 8.82.

Acknowledgment.—The assistance of Mr. A. F. Ray and Mrs. M. S. King in the experimental work is gratefully acknowledged. The author also wishes to thank Ridbo Laboratories, Inc., for permission to publish this paper.

Summary

The synthesis of diphenyl-*t*-dehydroabietinol and diphenyl-*t*-6-hydroxydehydroabietinol by the Grignard method has been described. Further proof of the *trans* configuration of the C_1 carboxyl group in dehydroabietic acid through the preparation of these compounds is also given.

(5) Sherwood and Short, *J. Chem. Soc.*, 1006 (1938).

(6) The carbinols reported here are being submitted to pharmacological tests.

(7) Analysis by the author.

(8) Analysis by Mrs. B. G. Zeiss.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Heterocyclic Basic Compounds. X. 4,8-Diaminoquinoline and Derivatives

BY R. W. GOULEY,[1] G. W. MOERSCH[1,2a] AND HARRY S. MOSHER[2b]

Of all the quinoline derivatives which have been tested as antimalarials, only the derivatives of 4-amino- and 8-aminoquinolines have shown any appreciable activity. For this reason it was decided to investigate derivatives of 4,8-diaminoquinoline. Although other diaminoquinoline compounds, particularly derivatives of 4,6-diaminoquinoline, have shown promise in chemotherapy,[3] no reports appear in the literature on the synthesis and properties of 4,8-diaminoquinoline and its derivatives. Considerable difficulty was experienced in this work and it was necessary to abandon several proposed methods of synthesis before a successful route was uncovered.

The synthesis of 4-hydroxy-8-nitroquinoline was first attempted through the ethoxymethylenemalonic ester condensation with *o*-nitroaniline. Although the condensation, cyclization and hydrolysis steps were successful, we were unable to decarboxylate the 3-carboxy-4-hydroxy-8-nitroquinoline. The successful decarboxylation of this substance[4] has since been reported[5] by heating the silver salt of the acid in boiling Dowtherm.

In applying the method of Meisenheimer[6] to various quinoline derivatives, the N-oxide of 5-nitroquinoline (I) was treated with phosphorus oxychloride; 2-chloro-5-nitroquinoline[7] (IV) 35%, 4-chloro-5-nitroquinoline (III) 10%, and 3-chloro-5-nitroquinoline (V) 20% were obtained. The identity of the 2-chloro-5-nitroquinoline was confirmed by its conversion to the known 5-nitrocarbostyril[7]; the structure of the 4-chloro-5-nitroquinoline (III) was proved by demonstrating its identity with one of the products obtained from the nitration of 4-chloroquinoline (II); and the third isomer was assumed to be 3-chloro-5-nitroquinoline (V) by elimination. This assumption has now been verified by comparison of this isomer with an authentic sample[8] whose

(1) Parke, Davis and Company post-doctoral fellow, 1945.

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(3) Jensch, *Angew. Chem.*, **50**, 893–895 (1937)

(4) Riegel, *et al.*, THIS JOURNAL, **68**, 1264–1266 (1946).

(5) Baker, Lappin, Albisetti and Riegel, *ibid.*, **68**, 1267 (1946).

(6) Meisenheimer, *Ber.*, **59**, 1848–1853 (1926); Bachmann and Cooper, *J. Org. Chem.*, **9**, 302–309 (1944).

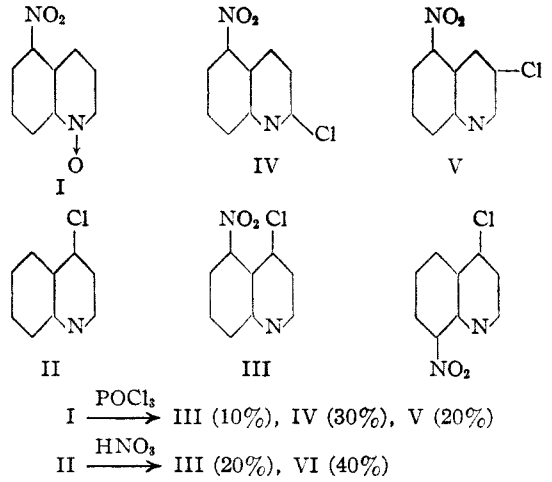
(7) Claus and Setzer, *J. prakt. Chem.*, (2) **53**, 392–396 (1896); Deinet and Lutz, THIS JOURNAL, **68**, 1325–1426 (1946).

(8) We are greatly indebted to Dr. Riegel of Northwestern University for this sample of 3-chloro-5-nitroquinoline.

structure has been proved.[9] Since the N-oxide of 8-nitroquinoline could not be prepared (the starting material was recovered unchanged upon treatment of 8-nitroquinoline with monoperphthalic acid), this method was inapplicable to the synthesis of the desired 4,8-diaminoquinoline. Although the 8-acetylamino-6-methoxyquinoline could readily be converted into the N-oxide, treatment with phosphorus oxychloride gave a finely divided, purple, infusible material.

Direct nitration experiments of 4-substituted quinolines were finally investigated. 4-Hydroxyquinoline was nitrated to give a 91% yield of mixed 4-hydroxynitroquinolines. The resulting mixture was very insoluble in organic solvents and attempts to separate the isomers at this stage were unsuccessful. The mixture was therefore treated with phosphorus oxychloride, and from the resulting 4-chloronitroquinoline mixture, one isomer, m.p. 145°, was obtained in approximately 50% yield. Its melting point was depressed when mixed with 4-chloro-5-nitroquinoline (m.p. 150°), and the melting points of the 8-nitro and 6-nitro[4] isomers vary widely from this value. This compound was probably 4-chloro-3-nitroquinoline as indicated by the melting point, 94°, of the aminoquinoline resulting from reductive cleavage of the halogen substituent. Although both 3-aminoquinoline[10] and 7-aminoquinoline[11] are reported to melt at 94°; it seems unlikely that 4-hydroxy-7-nitroquinoline would be formed in this nitration.

The synthesis of 4-chloro-8-nitroquinoline was finally accomplished by the nitration of 4-chloroquinoline (II)[12] which gives a mixture of isomers (85% yield) separable into 4-chloro-8-nitroquinoline (VI) m.p. 129–130° (about 40% purified yield), and 4-chloro-5-nitroquinoline (III) m.p. 150° (about 20% yield). The structure of the 5-nitro-4-chloroquinoline isomer was ascertained from the fact that one of the products of the Meisenheimer reaction on 5-nitroquinoline N-oxide melted at 150° and was identical with the product melting at 150° from the nitration of 4-chloroquinoline as shown by mixture melting point studies. Since in the former case there is no doubt as to the position of the nitro group and in the latter case the position of the chloro group is established, the product must be 4-chloro-5-nitroquinoline (III) and the entering position of the chlorine atom in the Meisenheimer reaction and of the nitro group in the nitration is thus proven. The second isomer from the nitration of 4-chloroquinoline, m.p. 129–130°, was proved to be 4-chloro-8-nitroquinoline (VI) by degradative reduction to 8-aminoquinoline which was identical



$$\text{I} \xrightarrow{POCl_3} \text{III (10\%), IV (30\%), V (20\%)}$$

$$\text{II} \xrightarrow{HNO_3} \text{III (20\%), VI (40\%)}$$

to an authentic sample prepared by the reduction of 8-nitroquinoline. 4-Hydroxy-8-nitroquinoline has recently been prepared by Reigel *et al.*[4,5] through the ethoxymethylenemalonic ester synthesis. Our product, m. p. 129–130° (VI), was shown to be identical to a sample of 4-chloro-8-nitroquinoline kindly furnished us by Dr. Riegel

The 4-chloro-8-nitroquinoline thus obtained was converted into 4-hydroxy-8-nitroquinoline, 4-methoxy-8-nitroquinoline, 4-phenoxy-8-nitroquinoline, 4,8-diaminoquinoline, 4-amino-8-nitroquinoline and 8-amino-4-chloroquinoline.

The relative reactivities of the halogens in the isomeric 4-chloro-5-nitro- and 4-chloro-8-nitroquinolines were found very interesting. In the presence of acid, the halogen was replaced with a hydroxyl group twice as rapidly in the case of the 8-nitro isomer. In the amination of 8-nitro-4-chloroquinoline with ammonia in phenol at 175–180°, complete reaction took place in fifteen minutes while two hours are usually required for this type reaction.[13] In addition, refluxing the 4-chloro-8-nitroquinoline in methanol with catalytic amounts of dry hydrogen chloride for short periods of time effected replacement of the chlorine atom with the methoxy group.[14] The greater reactivity of the 8-nitro isomer has been utilized in the method of separation of these two compounds from the nitration mixture.

Acknowledgment.—We wish to thank Dean F. C. Whitmore for his encouragement throughout this work and Parke, Davis and Company whose support made it possible.

Experimental

N-Oxide of 5-Nitroquinoline (I).—A solution of 100 g. (0.57 mole) of 5-nitroquinoline in 50 ml. of dioxane was added to 0.72 mole of monoperphthalic acid in 1300 ml. of ether. The resulting solution, after stirring for two and one-half hours and standing twelve hours, deposited a dark oil which solidified on shaking and cooling. This solid was washed well with ether; 226 g., m. p. 224–230°.

(9) Baker, Albisetti, Dodson, Lappin and Riegel, THIS JOURNAL, **68**, 1535 (1946).

(10) Mills and Watson, *J. Chem. Soc.*, **97**, 746 (1910).

(11) Hamer, *ibid.*, **119**, 1436 (1921).

(12) Since the completion of this work, Halcrow and Kermack, *J. Chem. Soc.*, 415–417 (1945), have published on the analogous nitration of 4-chloroquinaldine, and Baker, *et al.*, ref. 9, have published on the nitration of 4-chloroquinoline.

(13) Backeberg and Marais, *J. Chem. Soc.*, 381–383 (1942).

(14) For analogous reaction in other heterocyclic ring nuclei, see: Tomisek and Christensen, THIS JOURNAL, **67**, 2112–2115 (1945), and Banks, *ibid.*, **66**, 1127–1130 (1944).

It was powdered and stirred for thirty minutes with 1 liter of 5% ammonium hydroxide; yield 86 g. (79%), m. p. 155–157°.

The Treatment of 5-Nitroquinoline N-Oxide with Phosphorus Oxychloride.—The above N-oxide, 86 g., was added in small portions to 430 ml. of phosphorus oxychloride which was precooled to 5°. The reaction was vigorous and required cooling in an ice-bath. After the addition was complete, the mixture was refluxed gently for thirty minutes, cooled and decomposed with crushed ice. The precipitate was suspended in water and ammonium hydroxide added until the *p*H of the solution was approximately 6.0. The precipitate was separated and the wet cake dissolved in 1 liter of boiling ethanol and allowed to crystallized. The long needles which separated (wt. 33.5 g.) were recrystallized from ethanol, m. p. 135°.

Anal. Calcd. for $C_9H_5O_2N_2Cl$: N, 13.42. Found: N, 13.12.

This material was identified as 2-chloro-5-nitroquinoline by converting to the known 5-nitrocarbostyril[7] by refluxing with concentrated hydrochloric acid for fifteen minutes and recrystallizing the product from absolute ethanol, m. p. 303–305°.

The aqueous filtrate containing the other isomers was adjusted to a *p*H of 8.0 with ammonium hydroxide and the voluminous precipitate collected and dried, 19 g. of crude material m. p. 120°; recrystallized from ethanol, m. p. 129–130°. This melting point was lowered when mixed with either of the other two isomers obtained from this reaction, but was undepressed when mixed with an authentic sample of 3-chloro-5-nitroquinoline (m. p. 126–127).[8,9] To the remaining filtrate was added excess ammonium hydroxide and the light green precipitate of crude 4-chloro-5-nitroquinoline, 10 g., recrystallized from ethanol, long needles, m. p. 146°; repeatedly recrystallized, melting point 150°; mixture melting point with the isomer from the nitration of 4-chloroquinoline was undepressed.

N-Oxide of 6-Methoxy-8-acetylaminoquinoline.—To 400 ml. of a 0.58 molar solution of monoperphthalic acid in ether was added 35 g. of 6-methoxy-8-acetylaminoquinoline dissolved in 120 ml. of warm dioxane over a period of thirty minutes. The reaction mixture was cooled in a water-bath and stirred during the addition and for five hours thereafter. The oil, 20 g., which separated on standing, was stirred with 200 ml. of 5% ammonium hydroxide, the precipitate filtered, washed with water, and air dried; 10 g., m. p. 118–120°, mixture melting point with starting material (m. p. 126°) was about 98°.

Reaction of Phosphorus Oxychloride with 8-Acetylamino-6-methoxyquinoline N-Oxide.—The above N-oxide, 11 g., was added slowly to 55 ml. of phosphorus oxychloride which was cooled to 5° in an ice-bath. After the addition, the reaction mixture was refluxed gently for fifteen minutes, cooled and decomposed with crushed ice. Upon the addition of ammonium hydroxide, 10 g. of material, soluble in dilute hydrochloric acid and chloroform, and slightly soluble in ether and benzene, was obtained. The deep purple coloration was not removed by treatment with decolorizing carbon in either organic or aqueous solution and all other attempts to purify the product were unsuccessful.

Nitration of 4-Hydroxyquinoline.—A cooled mixture of 10 ml. of concentrated sulfuric acid and 10 ml. of fuming nitric acid was added slowly during forty-five minutes to a sulfuric acid solution of 10 g. of 4-hydroxyquinoline (prepared by the ethoxymethylenemalonic ester synthesis in an over-all yield of 60% according to the method outlined by Price and Roberts[15] for 4-hydroxy-6-methoxyquinoline). The reaction mixture was maintained at 0 to 5° during the addition and for one and one-half hours thereafter. The product was obtained by decomposing with 500 g. of crushed ice, treating with ammonium hydroxide, and filtering the white precipitate which was dried at 100°; 12 g. (91.7%), m. p. 290–301°. Previous experiments had indicated the difficulty of purifying this mixture as such; therefore, the crude product was converted to the mixture of 4-chloronitroquinolines directly.

Reaction of Phosphorus Oxychloride with the Mixed 4-Hydroxynitroquinolines.—A solution of the above 12 g. of crude 4-hydroxynitroquinolines in 120 ml. of phosphorus oxychloride was refluxed for two hours, cooled, poured onto crushed ice, and the resulting solution made faintly alkaline with ammonium hydroxide. Ether extracts of this solution upon evaporation to dryness gave 12 g. of a yellow solid melting at 120–130° which on crystallization from ligroin after treatment with Norit gave 6 g., m. p. 138°. Two recrystallizations from methanol raised the melting point to 145°.

Anal. Calcd. for $C_9H_5O_2N_2Cl$: C, 51.82; H, 2.42. Found: C, 51.74; H, 2.67.

A mixture melting point determination with 4-chloro-5-nitroquinoline (m. p. 150°) showed a depression of 35°. This compound is probably 4-chloro-3-nitroquinoline which has not been previously reported. The above evidence does not eliminate the possibility of the unreported 4-chloro-7-nitroquinoline or 4-chloro-6-nitroquinoline[5] (m. p. 141.0–141.5°); the following degradation studies were therefore carried out.

4-Chloro-3-aminoquinoline.—To 175 ml. of a 60% acetic acid solution of 3.75 g. of 4-chloro-3-nitroquinoline from the above nitration of 4-hydroxyquinoline was added 2.8 g. of iron powder over a forty-five minute period at a temperature of 60°. The reaction mixture was poured into water, the unreacted iron filtered, and the solution concentrated to dryness under vacuum. The residue was treated with ammonium hydroxide, extracted with ether, and the ether extracts decolorized with Norit and evaporated to dryness. The light yellow solid (3-amino-4-chloroquinoline) was recrystallized from dilute methanol; 0.25 g., m. p. 170° dec. (depends upon rate of heating). Solutions of this substance showed a purple fluorescence.

Anal. Calcd. for $C_9H_7N_2Cl$: C, 60.56; H, 4.28. Found: C, 60.12; H, 3.94.

3-Aminoquinoline.—The above 3-amino-4-chloroquinoline, 0.20 g., was subjected to catalytic reduction over Raney nickel in ethanol solvent. Upon filtering the catalyst and evaporating the solution to dryness under vacuum, there was obtained a red oil which solidified. This was taken up in ether, treated with dilute sodium hydroxide, water, treated with Norit and crystallized from ligroin; m. p. 94°. Both 3-aminoquinoline[9] and 7-aminoquinoline[10] are reported to melt at 94°. 6-Aminoquinoline melts at 107° and this possibility is therefore eliminated.

Nitration of 4-Chloroquinoline.[9]—4-Chloroquinoline (II), 90 g. (prepared in 91% yield by the action of phosphorus oxychloride on 4-hydroxyquinoline), was added to 400 ml. of concentrated sulfuric acid with cooling and stirring at such a rate that the temperature did not rise above 15°. This solution was cooled and maintained at −5° while a mixture of 80 ml. of concentrated sulfuric acid and 80 ml. of fuming nitric acid (sp. gr. 1.50) was added dropwise over a period of 1.3 hours. The mixture was allowed to reach room temperature with stirring over a three-hour period and was then poured into a mixture of crushed ice and ammonium hydroxide. The precipitate when washed and dried gave 96.5 g. (85%) of tan powder, m. p. 94–105°. The crude mixture was dissolved in two liters of hot methanol, filtered from a trace of dark tarry material, treated with Norit and allowed to crystallize at 0°. The first crop consisted of almost pure 4-chloro-8-nitroquinoline; 46 g., m. p. 128–129°. Recrystallization from 1200 ml. of methanol gave 42 g., m. p. 129–130°.

Anal. Calcd. for $C_9H_5O_2Cl$: C, 51.82; H, 2.42. Found: C, 52.17; H, 2.95.

When this was mixed with an authentic sample of 4-chloro-8-nitroquinoline (m. p. 126.5–128°) prepared by the ethoxymethylenemalonic ester method,[4,5] the mixture melted at 128.5–129.5°.

When the mother liquors from the above 4-chloro-8-nitroquinoline were concentrated, a constant melting material, 32.5 g., 105–120°, was obtained; this melting point

(15) Price and Roberts, THIS JOURNAL, **68**, 1204–1208 (1946).

was not altered appreciably by further recrystallization. It was primarily a mixture of 4-chloro-8-nitroquinoline and 4-chloro-5-nitroquinoline which could not be purified by crystallization, but from which the 4-chloro-5-nitroquinoline was obtained by taking advantage of the much greater reactivity of the halogen in the 8-nitro isomer.

A 7-g. portion of the material melting at 105–120° was boiled for ten minutes with a mixture of 90 ml. of water and 10 ml. of concentrated hydrochloric acid. After standing for twelve hours a solid had separated which was filtered and extracted with 100 ml. of 5% sodium hydroxide. The alkali insoluble portion was washed well with water and crystallized from methanol, 4.0 g., m. p. 144–148°. Repeated recrystallizations from methanol raised the melting point to 150°. This material proved to be identical (mixture melting point 150°) with the compound melting at 150° obtained by the action of phosphorus oxychloride on the N-oxide of 5-nitroquinoline.

Anal. Calcd. for $C_9H_5O_2N_2Cl$: C, 51.82; H, 2.42. Found: C, 52.13; H, 2.90.

4-Hydroxy-5-nitroquinoline.—A mixture of 0.5 g. of 4-chloro-5-nitroquinoline and 15 ml. of 10% hydrochloric acid was boiled for five minutes, cooled and treated with 25 ml. of 30% sodium hydroxide solution. This solution was filtered and the filtrate just neutralized with hydrochloric acid to precipitate the 4-hydroxy-5-nitroquinoline, 0.09 g., (20%), dec. 340.°

Anal. Calcd. for $C_9H_6N_2O_3$: C, 56.84; H, 3.18. Found: C, 56.71; H, 3.22.

4-Hydroxy-8-nitroquinoline.—The above experiment was duplicated using 0.5 g. of 4-chloro-8-nitroquinoline; 0.19 g. (42%) of 4-hydroxy-8-nitroquinoline, m. p. 201–202° was obtained.

Anal. Calcd. for $C_9H_6N_2O_3$: C, 56.84; H, 3.18. Found: C, 56.56; H, 3.36.

Apparently the relative rate of hydrolysis of the 4-chloro-8-nitroquinoline is at least twice that of the 4-chloro-5-nitro isomer.

Proof of Structure of 4-Chloro-8-nitroquinoline.—The isomer melting at 129–130° obtained by the nitration of 4-chloroquinoline was subjected to catalytic reduction in ethanol solvent using Raney nickel catalyst and pressures of approximately three atmospheres. After the theoretical hydrogen absorption for the nitro group had been observed, fresh catalyst and a solution of one equivalent of potassium hydroxide in 95% ethanol were added and the reduction continued. A further equivalent of hydrogen was absorbed; the catalyst was separated and the solution evaporated to dryness under vacuum. The residual oil was taken up in ether, washed with water, dried with potassium carbonate and the solvent removed. The crystalline residue was recrystallized three times from ligroin, m. p. 65°, mixture melting point with an authentic sample of 8-aminoquinoline, 65°. The acetate was prepared; m. p. 102–103°, mixture melting point with an authentic sample 102–103°.

If the reduction was stopped when the theoretical absorption of hydrogen for the nitro group was observed and before any potassium hydroxide was added, the ethanol solution gave on concentration a cream-colored crystalline solid, m. p. 100–101°, which was undoubtedly 8-amino-4-chloroquinoline.[16]

4-Amino-8-nitroquinoline.—Ammonia, dried over calcium oxide, was bubbled for fifteen minutes into a mixture of 15 g. of 4-chloro-8-nitroquinoline in 150 g. of phenol at a temperature of 175–180°. The reaction mixture was diluted with water and steam distilled to remove most of the phenol. The residue was treated with Norit while hot, filtered, and the hot filtrate made basic with dilute sodium hydroxide. If the neutralization was done in the cold, the precipitate was very finely divided and difficult to filter, but when made basic while still hot, the product came down as golden yellow needles, m. p. 230–231 dec., 10.7 g. (79%). Recrystallization from absolute ethanol raised the melting point to 232° dec.

Anal. Calcd. for $C_9H_7O_2N_3$: C, 57.14; H, 3.73. Found: C, 57.05; H, 3.68.

The conditions of temperature and time in this reaction were critical. If lower temperatures were used, a good yield of 4-phenoxy-8-nitroquinoline was obtained, m. p. 105–106°, and if the time of reaction were extended, the yields dropped off rapidly due to the formation of tars. Thus when the reaction was conducted for one hour on the steam-bath an 11% yield of the 4-amino-8-nitroquinoline and an 80% yield of the 4-phenoxy-8-nitroquinoline was obtained. On the other hand, a temperature of 180° for one hour resulted in only 25% yield of the product. In trial runs yields as high as 94% were obtained using the conditions described above. The fact that good yields were obtained in such a short time in this amination illustrates the enhanced activity of the halogen in 4-chloro-8-nitroquinoline.

4,8-Diaminoquinoline.—A mixture of 10 g. of 4-amino-8-nitroquinoline in 600 ml. of methanol was shaken at 40° in the presence of Adams catalyst under three atmospheres of hydrogen. As the reduction proceeded, the nitro compound went into solution. The hydrogenation was complete in eight minutes; the catalyst was removed and the alcohol distilled under vacuum to incipient crystallization. On cooling 7.65 g. (91%) of light tan crystals, m. p. 185° dec. was obtained. Recrystallization gave colorless crystals but failed to raise the melting point. The crystals darkened on standing in air.

Anal. Calcd. for $C_9H_9N_3$: C, 67.44; H, 5.61. Found: C, 67.74; H, 5.57.

4-Methoxy-8-nitroquinoline.—4-Chloro-8-nitroquinoline, 1.00 g., was refluxed for two hours with 100 ml. of methanol into which had been bubbled a small amount of dry hydrogen chloride. On evaporating the solution, diluting with water, and making basic with ammonium hydroxide, 0.920 g. of light yellow product was obtained; m. p. 179–180°. This gave long needles from methanol, m. p. 181–182°.

Anal. Calcd. for $C_{10}H_8O_3N_2$: N, 13.72. Found: N, 13.52.

An authentic sample of 4-methoxy-8-nitroquinoline was kindly furnished us by Dr. Riegel of Northwestern University, m. p. 181–182°, mixture melting point with the above sample, 181–182°.

Summary

1. The nitration of 4-chloroquinoline, the nitration of 4-hydroxyquinoline and the action of phosphorus oxychloride on 5-nitroquinoline N-oxide have been studied and the structures of the products proven.

2. Suitable intermediates for the preparation of possible antimalarial derivatives of 4,8-diaminoquinoline have been prepared.

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(16) Elderfield, Kupchan, Williamson and Birstein, THIS JOURNAL, **16**, 1528 (1946), report m. p. of 99–100° for this compound.