Calculated for $C_{19}H_{12}O_3.HCl.C_2H_6O$: Cl, 9.56; C_2H_6O, 12.41.
Found: Cl, 9.37, 9.10, 9.10; C_2H_6O, 11.64.

In substituting nitrobenzene for alcohol as a solvent, we obtained the salt as a voluminous, yellow crystailin precipitate. This was washed with benzene and low boiling petroleum ether, and dried in an atmosphere of hydrochloric acid. The analysis shows that when so prepared it contains a molecule of nitrobenzene of crystallization.

Calculated for $C_{19}H_{12}O_3.HCl.C_6H_5NO_2$: Cl, 7.93. Found: Cl, 8.21, 8.13, 8.22.

The pure salt itself, free from any solvent of crystallization, was obtained by two methods: First, after driving off the alcohol of crystallization at 110°, the salt was treated with dry hydrochloric acid gas until it was a pure yellow color (analysis I); second, a saturated solution of the fluorone in ether, in which it is only slightly soluble, was treated with dry hydrochloric acid. This darkened when heated to 250° but did not melt at 275° (analysis II).

Calculated for $C_{19}H_{12}O_3.HCl$: Cl, 10.93. Found: Cl, (I) 10.99, (II) 10.81.

Phenyl-3-hydroxyfluorone Hydrobromide.—This has been described by Gomberg and Cone[1] as a red compound, prepared by treating the fluorone in dry benzene with dry hydrobromic acid. It may also be prepared by treating an ether or chloroform solution of the fluorone with hydrobromic acid, when it is obtained in small quantities as lemon yellow flakes. From acetone the hydrobromide precipitates as a light brown powder.

Calculated for $C_{19}H_{12}O_3.HBr$: Br, 21.66. Found: Br, 21.30.

It is slightly soluble in acetone, chloroform, nitrobenzene and ethylene bromide. Alcohol decomposes it very quickly, water or dilute alkalies more slowly.

All attempts to make the chloride or bromide take up a second molecule of halogen acid were unsuccessful. Thus, while in the case of phenylfluorone the chloride does form an acid chloride and the bromide does not, in the case of phenyl-3-hydroxyfluorone neither the chloride nor the bromide show any tendency to combine further with halogen acids.

ANN ARBOR, MICHIGAN.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, No. 210.]

THE PREPARATION AND PROPERTIES OF 5-AMINOQUINOLINE-6-CARBOXYLIC ACID AND CERTAIN RELATED COMPOUNDS.

BY MARSTON TAYLOR BOGERT AND HARRY LINN FISHER.

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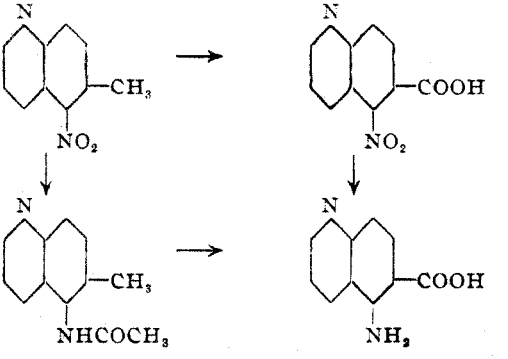
The purpose of this investigation was to prepare an aminoquinoline carboxylic acid of anthranilic type from which, in turn, new heterocyclic systems might be derived and studied.

[1] *Ann.*, 376, 216 (1910).

The point of departure was *p*-toluquinoline, which, on nitration and reduction, yields the *ana*-amino-*p*-toluquinoline (5-amino-6-methylquinoline), as shown by Noelting and Trautmann.[1] It was hoped that the desired acid could be obtained either (*a*) by oxidation of the nitrotoluquinoline to the nitro acid, with subsequent reduction of the nitro group, or (*b*) by direct oxidation of the acetamino toluquinoline:



Unfortunately, attempts to oxidize either the nitro or the acetamino toluquinoline with nitric acid, with potassium permanganate, alone or in presence of magnesium sulfate, or with chromic acid in dilute sulfuric acid solution, all failed. Niementowski[2] found that 7-methyl benzoylene urea was either unattacked by chromic acid in glacial acetic acid solution, or was burned to oxalic acid and carbon dioxide, although he finally succeeded in oxidizing the methyl group to a carboxyl by the use of potassium permanganate in presence of dilute sulfuric acid or, still more readily, in alkalin solution.

Success was finally attained by boiling the nitrotoluquinoline with alcoholic caustic alkali, the methyl group being thereby oxidized and the nitro group compensatingly reduced, thus giving directly the amino acid sought, a method which has been successfully employed for the production of anthranilic acid from *o*-nitrotoluene.[3]

Experimental.

5-Nitro-6-methylquinoline (ana-nitro-p-toluquinoline).—Noelting and Trautmann[4] have prepared this both by the direct nitration of *p*-toluquinoline and by the application of the Skraup reaction to 2-nitro-4-aminotoluene.

We have tried both methods, and find the former much the more satisfactory. According to our experience, the following procedure gives the best results: 20 grams *p*-toluquinoline are dissolved in 54 cc. con-

[1] *Ber.*, **23**, 3655 (1890).
[2] *Ibid.*, **29**, 1357 (1896).
[3] D. R. P., 114,839; *Winther*, **1**, 562.
[4] *Loc. cit.*

centrated sulfuric acid, the solution cooled and added very slowly with constant stirring to a mixture of 10 cc. concentrated nitric and 16 cc. concentrated sulfuric acid, taking about 20 minutes for the operation, and keeping the nitrating mixture surrounded by ice. The whole solution is left for 24 hours at laboratory temperature, then poured into about 2 liters of ice water (or cracked ice), and the turbid aqueous solution carefully neutralized with solid sodium carbonate. The yellow voluminous precipitate is filtered out, washed with cold water, and crystallized from boiling water, giving light yellow needles, melting at 116–117° (uncor.). Yield, nearly theoretical. On long boiling with water, the compound seems to resinify somewhat. If the nitrating mixture is heated, there is apt to be some charring, with consequent reduction in the yield of pure product.

Numerous attempts were made to oxidize this nitromethylquinoline to the corresponding nitroquinoline acid, by long boiling with dilute nitric acid, or by heating with it under pressure, by the use of potassium permanganate alone or in the presence of magnesium sulfate, but all proved fruitless. The compound either remained unattacked or was completely burned, and our efforts to regulate the reaction so as to yield the desired acid were unsuccessful. When the substance was heated with chromic acid and dilute sulfuric acid for 27 hours at 100°, it was practically unaffected. With a similar oxidizing mixture in a sealed tube for 18 hours at 160°, it was completely burned. Boiled with sodium hydroxide, in alcoholic solution, it gave the desired aminoquinoline carboxylic acid, as described beyond.

5-Amino-6-methylquinoline (*ana-amino-p-toluquinoline*) was prepared from the nitro compound by reduction with iron and acetic acid, as described by Noelting and Trautmann.[1] Yield, 92%. These investigators give its melting point as 145°. Our product melted at 135° (cor.), and this melting point was not altered by further recrystallization. The same melting point was obtained when the substance was prepared by the hydrolysis of its carefully purified acetyl derivative. The latter crystallizes from water in colorless needles, m. p. 160°, as stated by Noelting and Trautmann; it is but slowly saponified by hot aqueous solutions of the caustic alkalies, but is easily hydrolyzed by mineral acids.

Experiments were conducted with the object of oxidizing the methyl group of this acetamino toluquinoline to carboxyl, but all failed to give the desired acid. The oxidations were carried out with potassium permanganate, alone and in presence of magnesium sulfate, and with chromic acid in dilute sulfuric acid solution. As in the case of the attempts to oxidize the nitrotoluquinoline, the original substance was either un-

[1] *Ber.*, **23**, 3657 (1890).

attacked (except for the hydrolysis of the acetyl group), or it was totally destroyed; there seemed no intermediate halting point.

5-Aminoquinoline-6-carboxylic Acid.—The method finally worked out for the preparation of this acid is as follows: 50 grams of the nitrotoluquinoline are dissolved in 125 cc. 95% alcohol in a liter flask provided with a reflux condenser and heated at 100°; 35 grams powdered potassium hydroxide are added gradually to this boiling solution during 4 hours, and the boiling is then continued for 4 hours longer. The mixture is distilled with steam, to remove alcohol and a small amount of volatil basic substances formed in the reaction, and is then filtered. The brownish solid remaining on the filter contains a certain amount of the material mentioned below as obtained from the filtrate. The deep red filtrate is brought nearly to the neutral point with strong acetic acid and then treated carefully, drop by drop, with dilute acetic acid. At first, there comes down a brown, flocculent precipitate, apparently identical with the minor constituent of the first residue referred to above.[1] When all this brown flocculent material has been precipitated and removed, further acidification brings down the amino acid as an orange or reddish brown precipitate, either granular or amorphous. The amorphous form, on standing for half an hour, generally becomes granular. Yield, 30%.

It takes some practice to tell just when the brown flocculent material is all precipitated and the amino acid is beginning to come down. If hydrochloric is used instead of acetic acid, the process is further complicated by the precipitation of a mixture of the amino acid and its hydrochloride. These mixtures give sharp and definit melting points, running all the way from that of the acid itself (218.5°) to that of the pure hydrochloride (264.7°), depending upon the proportion of each present. The hydrochloride is quite difficultly soluble in hydrochloric acid, and, after acetic acid has thrown down as much of the amino acid as it will, addition of excess of concentrated hydrochloric acid to the filtrate may be used to precipitate the rest of the amino acid as hydrochloride.

The crude amino acid was purified by repeated solution in caustic alkali and precipitation with acetic acid. It crystallizes slowly from dilute acetic acid, and melts with decomposition at 218.5° (cor.). From concentrated solutions it separates as a bright yellow mass, but from dilute solutions it comes down slowly as a reddish brown solid, darkening on drying. From water it crystallizes in red nodules. It dissolves easily in alkalies, pyridine, quinoline, glycerol, mineral acids, formic or acetic acid, or in acetic anhydride; less readily in water, methyl or ethyl alcohols, or in acetone; very slightly in benzene or toluene; and is apparently insoluble in ether, petroleum ether, chloroform, carbon tetrachloride, carbon bisulfide or turpentine. Most of these solutions are reddish.

[1] The composition of these residues has not yet been satisfactorily worked out.

For analysis, the acid was purified as stated, dried to constant weight, and proven to be ash-free.

Calculated for $C_{10}H_8O_2N_2$: C, 63.75; H, 4.28; N, 14.89. Found: C, 63.98; H, 4.78; N, 14.96, 15.01.

A neutral aqueous solution of the acid gave amorphous precipitates with aqueous solutions of the following salts: barium chloride, light brown, moderately soluble; calcium chloride, light brown, moderately soluble; cadmium iodide, light brown, abundant; copper sulfate, brown; nickel chloride, light green; indium chloride, light brown, moderately soluble; mercuric chloride, light brown, abundant; silver nitrate, yellowish green.

Heated with soda lime, the acid yields 5-aminoquinoline. When used as a coupler for benzidine diazonium salts, a deep magenta solution resulted; and with diazosulfanilic acid, in alkalin solution, a similar color.

Hydrochloride.—Red needles, or an orange powder, melting at 264.7° (cor.) with decomposition, difficultly soluble in hydrochloric acid, but dissolving easily in water to a beautiful red solution.

Calculated for $C_{10}H_8O_2N_2.HCl$: N, 12.48. Found: N, 12.75.

On standing, it very slowly loses its hydrochloric acid, and the melting point recedes towards that of the free amino acid. Thus, after two months' standing, it melted at 245° and contained 54.05% carbon, the carbon percentage in the pure hydrochloride being 53.46.

In our first experiments for the preparation of the amino acid, the boiling of the nitrotoluquinoline with alcoholic sodium hydroxide was invariably followed by a treatment with ammonia and hydrogen sulfide, but, as a careful study of the reaction showed that this treatment did not increase the yield of amino acid, it was omitted in all subsequent preparations.

An examination of the distillate obtained by blowing steam through the mixture, after boiling the nitrotoluquinoline with alcoholic sodium hydroxide, disclosed the presence of small amounts of ammonium carbonate and of *acetaldehyde*, together with a trace of a pleasant smelling basic substance not isolated in sufficient amount to be identified.

Methyl Ester.—An attempt to prepare this ester by suspending the amino acid in *methyl alcohol* and saturating the solution with hydrochloric acid gas gave only the hydrochloride of the acid.

The amino acid was then treated with the calculated amounts of sodium bicarbonate and dimethyl sulfate, in presence of sufficient water, the mixture stirred for several minutes, and then left over night at room temperature. The deep red liquid gradually deposited red needles, which crystallized from water in beautiful, lustrous, bright red needles, carrying water of crystallization.

The amount of water present in these crystals was determined by drying them to constant weight at 110–115°.

Calculated for $C_{11}H_{10}O_2N_2.2H_2O$: H_2O, 15.12. Found: H_2O, 13.97, 14.59.

The first of the above analyses was run on a sample which had been standing for several days in a desiccator, while the second sample had merely been drying in the open for about 12 hours. The hydrated ester loses some of its water very easily and, on the other hand, the anhydrous ester is quite hygroscopic.

The anhydrous ester forms an amorphous scarlet powder, melting with decomposition at 245° (cor.). Yield, 35%.

Calculated for $C_{11}H_{10}O_2N_2$: N, 13.87. Found: N, 13.93.

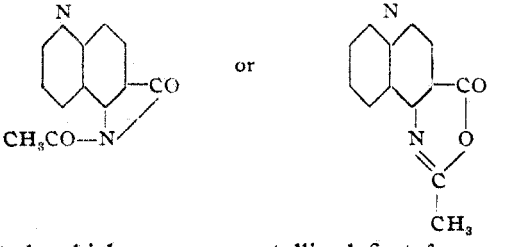
The ester is more or less soluble in water, methyl or ethyl alcohols, acetic or hydrochloric acids; insoluble in sodium carbonate solution, and is readily saponified by warm dilute sodium hydroxide solution.

5-Acetaminoquinoline-6-carboxylic Acid.—The amino acid dissolved in hot acetic anhydride to a red solution, from which on cooling there separated yellowish needles of the lactam of the acetamino acid. When these needles were warmed with dilute sodium hydroxide solution and the solution then carefully acidified with dilute acetic acid and allowed to stand, the turbidity, which formed at first, gradually cleared and fine yellow needles of the acetamino acid separated, often united in rosets. These were filtered out, washed with water, dried to constant weight at 110°, and analyzed.

Calculated for $C_{12}H_{10}O_3N_2$: N, 12.17. Found: N, 12.18.

The compound is soluble in alcohol, dilute acetic acid or in the mineral acids, and melts with decomposition at 237° (cor.).

5-Acetaminoquinoline-6-carboxylic Acid Lactam.—5-Aminoquinoline-6-carboxylic acid was added slowly to boiling acetic anhydride and the clear red solution concentrated one-third. On cooling, long, yellowish brown



needles separated, which were recrystallized first from acetic anhydride and then from ligroin, giving nearly colorless branched needles, melting at 190° (uncor.), which tend to become slightly yellow on standing, but show no great tendency to absorb moisture from the air and pass into the acetamino acid again. The compound is more or less soluble in benzene, toluene, acetic anhydride, ligroin, chloroform, or carbon tetrachloride.

Calculated for $C_{12}H_8O_2N_2$: N, 13.21. Found: N, 13.48.

With primary amines it yields naphthoisotriazines, as will be described in a subsequent paper.

5-Benzalaminoquinoline-6-carboxylic Acid, $C_6H_5.CH : N.C_9H_5N.COOH$. —When the amino acid was boiled with excess of benzaldehyde, it rapidly dissolved and water was driven off. On cooling, rosets of needles separated, which were filtered out, washed with ether, then with petroleum ether, dried at 110° to constant weight, and analyzed.

Calculated for $C_{17}H_{12}O_2N_2$: N, 10.15. Found: N, 10.14.

The compound melts with decomposition at 221.4° (cor.). It dissolves in alcohol or chloroform; only slightly in ether; and is practically insoluble in water, petroleum ether, or benzene. It is easily soluble in aqueous caustic alkalies, and is reprecipitated in white flocs on acidification with dilute acetic acid.

An attempt was made to prepare a metoxazine compound from this, by the method recently described by Ekeley and Dean,[1] but it was unsuccessful.

5-Hydroxyquinoline-6-carboxylic Acid.—The hydrochloride of the amino acid was dissolved in the calculated amount of warm dilute hydrochloric acid, and an aqueous solution of the calculated amount of sodium nitrite added slowly with stirring. Nitrogen was evolved vigorously. At the close of the reaction, the heating was continued for a few minutes, the solution allowed to cool, and then acidified with dilute acetic acid. A dark greenish granular precipitate separated, of pleasant odor, melting with decomposition at 211.7° (cor.), which dissolved in alkalies to a dark greenish solution and in acids to a reddish green one. Yield, nearly theoretical. This crude product was dissolved in sodium hydroxide solution, and this solution treated with boneblack twice. On acidifying the final filtrate from the boneblack, rosets of brown needles gradually separated, of the same melting point as before (211.7°) and dissolving in alkalies or in acids to a light yellowish green solution.

The compound dissolves in concentrated or in dilute hydrochloric acid, in glacial acetic acid, in alkalin hydroxides or carbonates, pyridine, quinoline or glycerol; less readily in methyl, ethyl or amyl alcohol, benzene, toluene or carbon bisulfide; and is apparently insoluble in ether, chloroform, carbon tetrachloride or acetone.

Calculated for $C_{10}H_7O_3N$: N, 7.40. Found: N, 7.57.

It gives amorphous precipitates with aqueous solutions of the following salts: barium chloride, brownish green, moderately soluble; zinc chloride, dark green; cadmium iodide, dark green; copper sulfate, brownish green; mercuric chloride, brownish green; silver nitrate, olive green.

Efforts to esterify this acid with dry hydrochloric acid gas in absolute

[1] THIS JOURNAL, 34, 161 (1912).

ethyl alcohol solution, or with dimethyl sulfate, proved unavailing, while the action of nitrous acid upon the corresponding ester of the amino acid gave chiefly the free hydroxy acid.

The free acid, used as a coupler for diazotized benzidine, gave a dark purple solution, and with diazo sulfanilic acid, in alkalin solution, a red solution.

NEW YORK CITY.

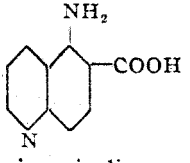
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, NO. 211.]

THE SYNTHESIS OF 1,3,7-NAPHTHOISOTRIAZINES: DERIVATIVES OF A NEW HETEROCYCLIC SYSTEM.

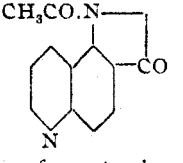
BY MARSTON TAYLOR BOGERT AND HARRY LINN FISHER.

Received September 11, 1912.

In the foregoing paper, the authors have described the preparation and properties of 5-aminoquinoline-6-carboxylic acid, its acetyl derivative, and the lactam of the latter:

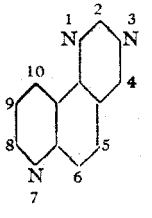


5-Aminoquinoline-6-carboxylic acid.



Lactam of 5-acetaminoquinoline-6-carboxylic acid.

From these substances, by reactions entirely analogous to those used by us in the synthesis of quinazolines,[1] we have prepared compounds containing the nucleus which, in conformity with the system of nomenclature adopted in Richter's Lexikon, we have designated the 1,3,7-naphthoisotriazine nucleus. So far as we have been able to discover, by a careful



search of the literature, these are the first compounds to be described containing this nucleus, although, as all organic chemists will appreciate, it is an exceedingly difficult task to look up all possible derivatives, and we may be wrong in this assumption.

[1] THIS JOURNAL, 32, 784 (1910), and later papers in same from this laboratory.