It may be fairly concluded from the preceding experiments that deposits of lead dioxide made in the electrolytic way will be too high unless they have been dried for definite periods at a temperature ranging from 200° to 230° C. Much depends upon the weight of the deposits, but an analytical factor will be necessary.

It is not probable that the excessive weight of the deposits is due to the formation and precipitation of a higher oxide of lead than the dioxide. It is more likely, as is evidenced by Schucht's[1] work also, that the final traces of water, adhering or included, are expelled with difficulty. The fact that the error increases with the density of the deposit might be advanced as an argument in favor of this view.

UNIVERSITY OF PENNSYLVANIA.

[CONTRIBUTION FROM THE HAVEMEYER LABORATORIES OF COLUMBIA UNIVERSITY, NO. 109.]

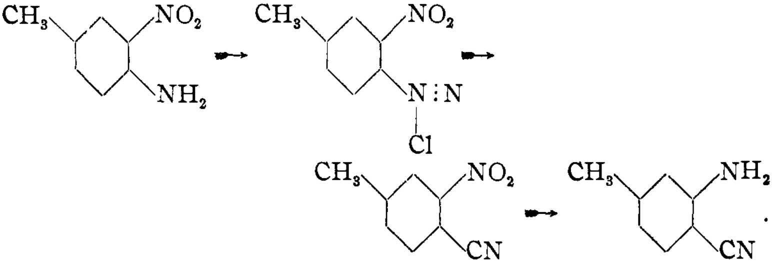
SOME ACYL DERIVATIVES OF HOMOANTHRANILIC NITRILE, AND THE 7-METHYL-4-KETODIHYDROQUINAZOLINES PREPARED THEREFROM.[2]

BY MARSTON TAYLOR BOGERT AND ALFRED HOFFMAN.

Received August 1, 1905.

IN A previous paper, Bogert and Hand[3] have shown that quinazolines can be very easily obtained from anthranilic nitrile. In the present paper, the method is applied to homoanthranilic nitrile with equally successful results.

Homoanthranilic nitrile was prepared from *m*-nitro-*p*-toluidine by converting the latter into *m*-nitro-*p*-tolunitrile by the Sandmeyer reaction, and then reducing the nitro group with stannous chloride and hydrochloric acid:



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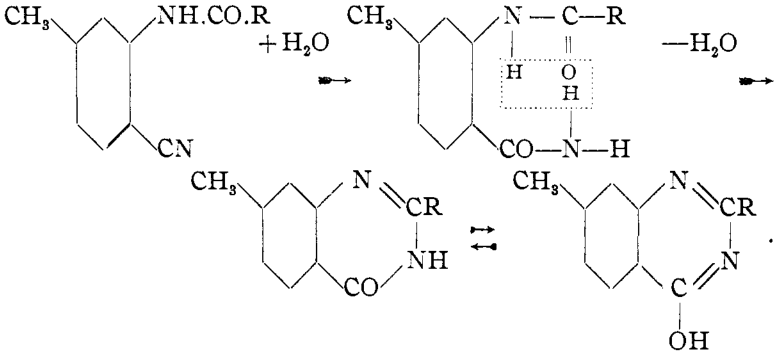
[1] *Z. anal. Chem.*, 19, 4.

[2] Read before the New York Section of the American Chemical Society, May 5, 1905.

[3] This Journal, 24, 1031 (1902).

Various acyl derivatives of homoanthranilic nitrile were prepared, which were then converted into quinazolines by heating them with alkaline hydrogen dioxide solution, as described by Bogert and Hand:[1]

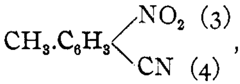


(I.) (II.)

While the free quinazolines may exist in the keto condition (I), their alkaline salts quite certainly possess the enol structure (II).

Several of the quinazolines described in this paper have been previously reported by Niementowski,[2] who obtained them by heating either homoanthranilic acid with an amide, or homoanthranilamide with an acid. Both homoanthranilic acid and its amide he prepared from the nitrile. Our process permits of the preparation of the quinazolines directly from the acylated nitriles, without the isolation of the amides; and, further, as we have elsewhere shown,[3] thioquinazolines may be obtained from these aminonitriles with equal facility.[4]

EXPERIMENTAL.

m-Nitro-p-Tolunitrile, (1)  $CH_3.C_6H_3\left<\begin{array}{l}NO_2\ (3)\\CN\ (4)\end{array}\right.$, was prepared from *m*-nitro-*p*-toluidine, by the Sandmeyer reaction, in exactly the same way as *o*-nitrobenzonitrile was prepared by Bogert and Hand[1] from *o*-nitraniline. The addition of a few drops of ether from time to time during the diazotizing materially assisted the reaction, by causing the solution of the diazonium body. The

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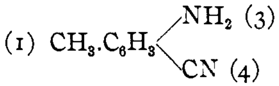
[1] *Loc. cit.*

[2] *J. prakt. Ch.* [2], **40**, 12 (1889); **51**, 566 (1895); *Ber.*, **27**, 516 (1894).

[3] This Journal, **25**, 372, 935 (1903).

[4] A paper will appear later upon the thioquinazolines derived from homoanthranilic nitrile.

diazotizing was carried out at 33°, and was complete in three to four hours. When ether was used, there resulted a perfectly clear purple solution, while, in absence of ether, the solution was dark brown, and considerable of the diazonium body remained undissolved as a flocculent precipitate. The yield of pure nitronitrile was 80 per cent. of the theoretical. The pure substance crystallizes from water in nearly colorless needles, of a slight greenish cast, and melts at 99.8° (corr.).



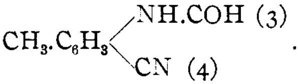
Homoanthranilic Nitrile, $(1)\ CH_3.C_6H_3{<}^{NH_2\ (3)}_{CN\ (4)}$.—*m*-Nitro-*p*-tolunitrile was reduced to the corresponding aminonitrile, by stannous chloride and hydrochloric acid, as follows:

Five hundred grams stannous chloride were dissolved in 425 cc. concentrated hydrochloric acid, and 75 cc. water added. The solution was heated to 50°, and stirred vigorously with a turbine. 108.9 grams of the nitronitrile were added gradually, at such a rate that the temperature remained at 50–55°. When the reduction was complete, a clear solution resulted. An equal volume of alcohol was then added, a concentrated solution of 340 grams sodium hydroxide slowly stirred in, and the mixture finally made alkaline with ammonium hydroxide. A large amount of alcohol was then poured in, and the mixture left several hours to settle. The clear alcoholic solution of the nitrile was decanted through a filter, and the precipitated metastannic acid washed several times with alcohol, the washings being added to the first filtrate. The alcoholic solution was distilled down until it turned a deep red, and the nitrile was then precipitated by the addition of a large volume of water. The precipitate, after being washed with water (to remove ammonium chloride), was quite pure. It was further purified by crystallization from carbon disulphide in presence of bone-black. Small amounts of homoanthranilic acid and its amide are frequently formed in the reduction, but do not interfere, and are found in the mother-liquors from the nitrile crystals. The yield of aminonitrile was 80 per cent. of the theoretical.

The pure aminonitrile crystallizes from carbon disulphide in beautiful, large, yellowish crystals, melting at 94° (corr.).

The Preparation of Acyl Derivatives of Homoanthranilic Nitrile.—With the exception of the formyl compound, the aliphatic acyl derivatives were all prepared by heating the aminonitrile with the acid anhydride, and crystallizing the product from a suitable solvent. In the case of the aromatic acids, the acid chloride and the aminonitrile were dissolved in separate portions of pyridine, the solutions carefully mixed, and the acyl derivative then precipitated by adding water.

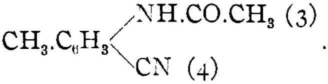
Formyl Homoanthranilic Nitrile,



$$(1)\ CH_3.C_6H_3\begin{cases}NH.COH\ (3)\\ CN\ (4)\end{cases}.$$

—All attempts to prepare this derivative failed, the product in every case being the quinazoline. Apparently the formyl derivative is so unstable that it rearranges spontaneously to the quinazoline. Niementowski[1] experienced the same difficulty in the preparation of the formyl derivative of homoanthranilamide, which invariably passed over into the quinazoline by loss of water.

Acetyl Homoanthranilic Nitrile,

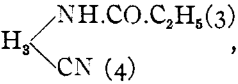


$$(1)\ CH_3.C_6H_3\begin{cases}NH.CO.CH_3\ (3)\\ CN\ (4)\end{cases}.$$

—Four grams of homoanthranilic nitrile were dissolved in 5 cc. of acetic anhydride, the solution boiled gently for two hours, poured into water, the precipitate crystallized from dilute acetic acid, and then from alcohol. It then appeared in colorless needles, m. p. 136° (corr.), identical with the product described by Niementowski.[2] It is easily soluble in alcohol, acetone, or chloroform; moderately soluble in benzene or ether; difficultly soluble in carbon disulphide, amyl alcohol, or gasoline.

	Calculated for $C_{10}H_{10}ON_2$.	Found.
Nitrogen	15.96	16.3

Propionyl Homoanthranilic Nitrile,



$$(1)CH_3.C_6H_3\begin{cases}NH.CO.C_2H_5(3)\\ CN\ (4)\end{cases},$$

prepared from homoanthranilic nitrile and propionic anhydride, was crystallized from dilute propionic acid and then from alcohol. It forms colorless needles, m. p. 138° (corr.), showing approximately the same solubilities as the acetyl derivative in acetic acid, ethyl or amyl alcohols, acetone, chloroform, benzene, ether, carbon disulphide, or gasoline.

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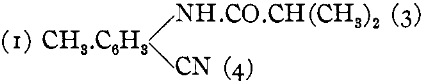
[1] *J. prakt. Chem.* [2], **51**, 566 (1895).

[2] *Ibid.*, [2], **40**, 8 (1889).

	Calculated for $C_{11}H_{12}ON_2$.	Found.	
Carbon	70.2	69.9	70.08
Hydrogen	6.4	6.3	6.26
Nitrogen	14.9	15.3	15.5

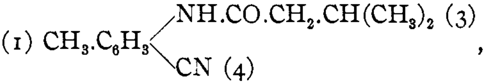
Isobutyryl Homoanthranilic Nitrile,


$$(1)\ CH_3.C_6H_3\left\langle\begin{array}{l}NH.CO.CH(CH_3)_2\ (3)\\ CN\ (4)\end{array}\right.$$

, from homoanthranilic nitrile and isobutyric anhydride, crystallizes from alcohol in colorless needles, m. p. 144° (corr.); easily soluble in benzene, acetic acid, acetone, chloroform, or hot alcohol; moderately soluble in cold alcohol, hot carbon disulphide or amyl alcohol; difficultly soluble in cold carbon disulphide, cold amyl alcohol, or gasoline.

	Calculated for $C_{12}H_{14}ON_2$.	Found.
Nitrogen	13.9	13.7

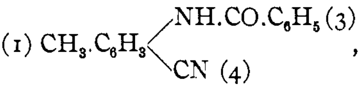
Isovaleryl Homoanthranilic Nitrile,


$$(1)\ CH_3.C_6H_3\left\langle\begin{array}{l}NH.CO.CH_2.CH(CH_3)_2\ (3)\\ CN\ (4)\end{array}\right.$$

, from homoanthranilic nitrile and isovaleric anhydride, crystallizes from alcohol in small colorless needles, m. p. 139° (corr.); easily soluble in benzene, carbon disulphide, acetone, acetic acid, ether, ethyl or amyl alcohols, chloroform, or hot gasoline; moderately soluble in cold gasoline.

	Calculated for $C_{13}H_{16}ON_2$.	Found.
Nitrogen	13.00	13.28

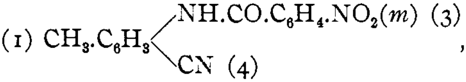
Benzoyl Homoanthranilic Nitrile,


$$(1)\ CH_3.C_6H_3\left\langle\begin{array}{l}NH.CO.C_6H_5\ (3)\\ CN\ (4)\end{array}\right.$$

, from homoanthranilic nitrile and benzoyl chloride, in pyridine solution, crystallizes from benzene in fine white needles, m. p. 145° (corr.); easily soluble in cold chloroform, or hot benzene, in carbon disulphide, ethyl or amyl alcohols, acetone, or acetic acid; difficultly soluble in ether or gasoline.

	Calculated for $C_{15}H_{12}ON_2$.	Found.
Nitrogen	11.8	11.9

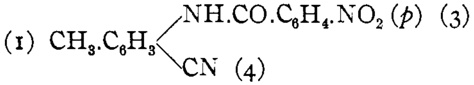
m-Nitrobenzoyl Homoanthranilic Nitrile,


$$(1)\ CH_3.C_6H_3\left\langle\begin{array}{l}NH.CO.C_6H_4.NO_2(m)\ (3)\\ CN\ (4)\end{array}\right.$$

, from *m*-nitrobenzoyl chloride and homoanthranilic nitrile, in pyridine solution, crystallizes in a finely felted mass of colorless needles, m. p. 218° (corr.); easily soluble in cold acetone, or hot benzene, in chloroform, ethyl or amyl alcohols, or acetic acid; difficultly soluble in ether, carbon disulphide, or gasoline.

	Calculated for $C_{15}H_{11}O_3N_3$.	Found.
Nitrogen	14.9	14.98

p-Nitrobenzoyl Homoanthranilic Nitrile,



$$(1)\ CH_3.C_6H_3\left\langle\begin{array}{l}NH.CO.C_6H_4.NO_2\ (p)\ (3)\\ CN\ (4)\end{array}\right.$$

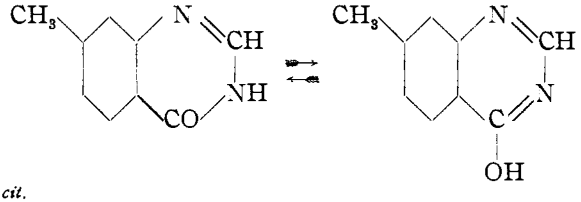
, from homoanthranilic nitrile and *p*-nitrobenzoyl chloride, in pyridine solution, melts at 223° (corr.), and resembles the meta isomer in appearance. It is easily soluble in hot alcohol, acetic acid, amyl alcohol, or acetone; moderately soluble in hot benzene, or chloroform; difficultly soluble in carbon disulphide, ether, or gasoline.

	Calculated for $C_{15}H_{11}O_3N_3$.	Found.
Nitrogen	14.9	15.04

The Preparation of Quinazolines from Acyl Homoanthranilic Nitriles.

The acyl homoanthranilic nitriles were heated with a mixture of equal parts 10 per cent. aqueous potassium hydroxide solution and commercial (approximately 3 per cent.) hydrogen dioxide solution. The yield of quinazoline was excellent in most cases. These quinazolines dissolve in caustic alkalies, or in strong mineral acids, the former solution being precipitated by carbon dioxide, the latter by ammonia. Of the quinazolines described, the isobutyl, phenyl, *m*- and *p*-nitrophenyl derivatives are new; the others have been prepared by Niementowski[1] from homoanthranilic acid or its amide.

7-Methyl-4-ketodihydroquinazoline (7-methyl-4-hydroxyquinazoline),



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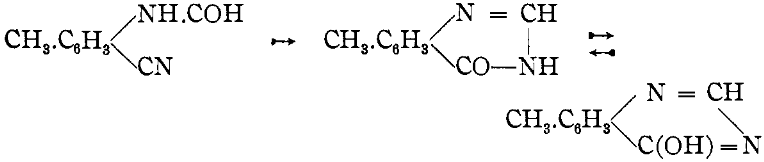
[1] *Loc. cit.*

—As already stated, all efforts to prepare formyl homoanthranilic nitrile resulted in the formation of the quinazoline by rearrangement:



When glacial formic acid and homoanthranilic nitrile reacted, even at low temperature, the product was the quinazoline. It was purified by solution in boiling hydrochloric acid, reprecipitating with ammonia, washing the precipitate thoroughly with water, and subliming. A mass of fluffy crystals resulted, melting at 239° (corr.), and similar to the compound described by Niementowski.[1]

To make certain of the identity of our product with Niementowski's, we prepared some of the quinazoline by the latter's method. Homoanthranilamide was obtained by boiling 4 grams of the nitrile with 80 cc. of water and 2 grams of potassium hydroxide until a clear solution resulted. On cooling, the amide separated in crystals. It was filtered out, washed with water, and recrystallized from alcohol, when it melted sharply at 146°. To make the quinazoline, 2 grams of the amide were boiled with 0.5 cc. of formic acid for half an hour, when the mass suddenly solidified. The product, washed with water and sublimed, proved to be identical in all respects with the quinazoline obtained from the nitrile. Niementowski[1] also obtained this quinazoline by the action of formamide upon homoanthranilic acid.

The sublimed quinazoline forms colorless needles, m. p. 239° (corr.); apparently insoluble in water, carbon disulphide, ether, chloroform, or mixtures of these; slightly soluble in benzene, glacial acetic acid, or amyl alcohol; easily soluble in aniline or phenol. It forms a crystalline hydrochloride, which is quite easily dissociated by water, and a crystalline chlorplatinate.

2,7-Dimethyl-4-ketodihydroquinazoline (*2,7-Dimethyl-4-hydroxyquinazoline*),

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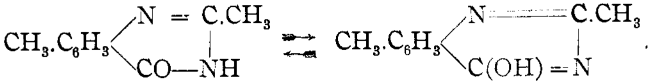
[1] *Loc. cit.*

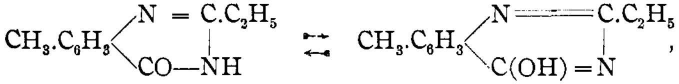


$$CH_3.C_6H_3\left\langle\begin{array}{l}N = C.CH_3\\ \qquad\;\; |\\ CO—NH\end{array}\right. \rightleftarrows CH_3.C_6H_3\left\langle\begin{array}{l}N \!=\!=\!=\!= C.CH_3\\ \qquad\qquad\;\; |\\ C(OH) = N\end{array}\right. .$$

—1.5 grams of acetyl homoanthranilic nitrile were warmed at 40–50° for two hours with 50 cc. 10 per cent. potassium hydroxide solution and 50 cc. commercial 3 per cent. hydrogen dioxide solution, when a clear solution of the potassium salt of the quinazoline resulted. This solution was acidified with hydrochloric acid, and ammonium hydroxide then added in excess. The precipitated quinazoline was crystallized from alcohol, giving fine fluffy needles, m. p. 255° (corr.); easily soluble in acetone, ethyl or amyl alcohols, acetic acid, or hot chloroform; difficultly soluble in benzene, gasoline, ether, or carbon disulphide. It is identical with the product obtained by Niementowski[1] from homoanthranilic acid and acetamide.

	Calculated for $C_{10}H_{10}ON_2$.	Found.
Nitrogen........................	15.96	16.12

2-*Ethyl*-7-*methyl*-4-*ketodihydroquinazoline* (2-*Ethyl*-7-*methyl*-4-*hydroxyquinazoline*),



$$CH_3.C_6H_3\left\langle\begin{array}{l}N = C.C_2H_5\\ \qquad\;\; |\\ CO—NH\end{array}\right. \rightleftarrows CH_3.C_6H_3\left\langle\begin{array}{l}N \!=\!=\!=\!= C.C_2H_5\\ \qquad\qquad\;\; |\\ C(OH) = N\end{array}\right. ,$$

from propionyl homoanthranilic nitrile and alkaline hydrogen dioxide solution, crystallizes in felted needles, m. p. 240° (corr.); easily soluble in alcohol, chloroform, acetic acid, hot benzene, hot acetone, or hot amyl alcohol; difficultly soluble in gasoline, ether, or carbon disulphide.

	Calculated for $C_{11}H_{12}ON_2$.	Found.	
Carbon.......................	70.2	70.7	69.3
Hydrogen..................	6.4	6.4	6.4
Nitrogen.........	14.9	14.81	.....

The compound was first described by Niementowski.[1]

2-*Isopropyl*-7-*methyl*-4-*ketodihydroquinazoline* (2-*Isopropyl*-7-*methyl*-4-*hydroxyquinazoline*), from isobutyryl homoanthranilic nitrile and alkaline hydrogen dioxide solution, crystallizes in felted needles, m. p. 228° (corr.); easily soluble in alcohol, acetic acid, hot benzene, acetone, or amyl alcohol; moderately soluble in gasoline, ether, or chloroform; difficultly soluble in carbon disulphide.

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[1] *Loc. cit.*

	Calculated for $C_{12}H_{14}ON_2$.	Found.
Nitrogen........................	13.9	13.97

This quinazoline also has been previously described by Niementowski.[1]

The following quinazolines were prepared from the corresponding acyl homoanthranilic nitriles and alkaline hydrogen dioxide solution, as just described.

2-*Isobutyl*-7-*methyl*-4-*ketodihydroquinazoline* (2-*Isobutyl*-7-*methyl*-4-*hydroxyquinazoline*). — Felted needles, m. p. 219° (corr.); easily soluble in acetone, acetic acid, hot benzene, carbon disulphide, chloroform, ethyl or amyl alcohols; difficultly soluble in gasoline.

	Calculated for $C_{13}H_{16}ON_2$.	Found.
Nitrogen........................	13.00	13.3

2-*Phenyl*-7-*methyl*-4-*ketodihydroquinazoline* (2-*Phenyl*-7-*methyl*-4-*hydroxyquinazoline*) crystallizes either in needles or plates, both of which forms melt at 243° (corr.). It is easily soluble in chloroform, hot benzene, ethyl or amyl alcohols, or acetic acid; difficultly soluble in carbon disulphide, acetone, gasoline, or ether.

	Calculated for $C_{15}H_{12}ON_2$.	Found.
Nitrogen........................	11.8	11.95

2-*m*-*Nitrophenyl*-7-*methyl*-4-*ketodihydroquinazoline* (2-*m*-*Nitrophenyl*-7-*methyl*-4-*hydroxyquinazoline*). — Microcrystalline powder, melting sharply above 370°; easily soluble in acetone, chloroform, hot amyl alcohol, acetic acid, or ethyl alcohol; difficultly soluble in benzene, carbon disulphide, gasoline, or ether. In contradistinction to the foregoing quinazolines, it is not easily soluble either in mineral acids or caustic alkalies.

	Calculated for $C_{15}H_{11}O_3N_3$.	Found.
Nitrogen........................	14.9	15.03

2-*p*-*Nitrophenyl*-7-*methyl*-4-*ketodihydroquinazoline* (2-*p*-*Nitrophenyl*-7-*methyl*-4-*hydroxyquinazoline*) melts sharply above 370°, and in general appearance and properties closely resembles the above meta isomer.

	Calculated for $C_{15}H_{11}O_3N_3$.	Found.
Nitrogen........................	14.9	14.6

HAVEMEYER LABORATORIES, COLUMBIA UNIVERSITY,
April, 1905.

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[1] *Loc. cit.*