

solubility near the end of Series C is due to the larger amounts of acid present. The results of C correspond nearly enough with the sums of A and B to show that the effects of the sodium chloride and acid are independent. These facts become even more evident when the results are expressed in the form of curves.

It is clear that the use of a silver dish for sulphur determinations by fusion with sodium dioxide introduces complications. The removal of the dissolved silver is best effected by precipitation with perfectly pure hydrogen sulphide. Dilution to 400 cc., and filtering after cooling, does not suffice to remove all the silver. Dilution to a much larger volume would involve either a tedious evaporation over the alcohol lamp before precipitation with barium chloride or a considerable error, owing to the solubility of barium sulphate in the large volume of solution. It is simpler and more satisfactory to avoid the difficulty by using a nickel crucible or dish.

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[CONTRIBUTIONS FROM THE HAVEMEYER LABORATORIES OF COLUMBIA
UNIVERSITY, No. 124.]

**RESEARCHES ON QUINAZOLINES (SIXTEENTH PAPER).
SYNTHESIS OF 6-NITRO-2-METHYL-4-KETODIHY-
DROQUINAZOLINES FROM 5-NITROACET-
ANTHRANIL AND PRIMARY AMINES.¹**

BY MARSTON TAYLOR BOGERT AND ELLEN PARMELEE COOK.

Received July 13, 1906.

In previous papers² we have reported upon 5- and 7-nitro-4-ketodihydroquinazolines. The following article contains a record of some experiments in the synthesis of derivatives of the 6-nitro isomer.

Dehoff,³ by the direct nitration of 2-methyl-4-ketodihydroquinazoline, obtained a nitro derivative in which the position of the nitro group remained unknown until Thieme⁴ prepared the same substance by heating the ethyl ester of 5-nitro-2-acetamino-

¹ Read at the meeting of the New York Section of the American Chemical Society, May 11, 1906.

² Bogert and Chambers: *This Journal*, **27**, 649 (1905); Bogert and Seil: *Ibid.* **27**, 1305 (1905); **28**, 884 (1906); Bogert and Steiner: *Ibid.* **27**, 1327 (1905).

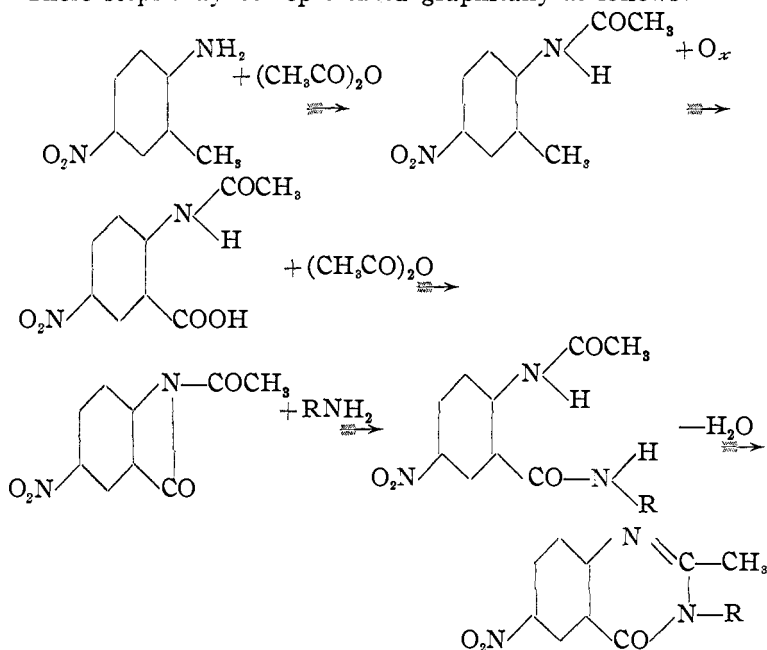
³ *J. pr. Chem.* [2] **42**, 347 (1890).

⁴ *Ibid.* [2] **43**, 473 (1891).

benzoic acid with alcoholic ammonia at 170° , thus fixing the position of the nitro group at 6 in the quinazoline nucleus. Both Dehoff and Thieme prepared also the 2,3-dimethyl-6-nitro-4-ketodihydroquinazoline, and in 1896 Kratz¹ obtained the 3-amino-6-nitro-4-ketodihydroquinazoline.

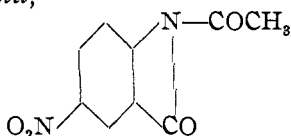
We have prepared a few derivatives of 6-nitro-2-methyl-4-ketodihydroquinazoline by very simple methods, entirely similar to those used in the case of the 5- and 7-nitro isomers. 5-Nitro-2-toluidine was acetylated, the acetyl derivative oxidized to 5-nitroacetanthranilic acid, the latter changed to 5-nitroacetanthranil, which yielded the nitroquinazolines when condensed with primary amines of various kinds.

These steps may be represented graphically as follows:



EXPERIMENTAL.

5-Nitroacetanthranil,



¹ J. pr. Chem. [2] 53, 224 (1896).

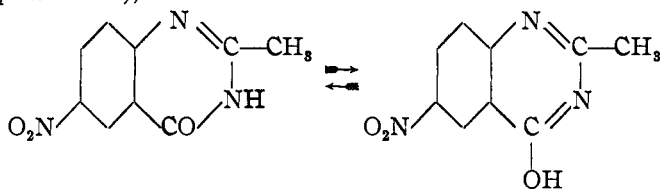
5-Nitro-2-toluidine was acetylated in the usual way, and the acetyl derivative crystallized from alcohol, when it showed a melting-point of 198° . This acetyl derivative was then oxidized by potassium permanganate in presence of magnesium sulphate. The 5-nitroacetanthranilic acid thus obtained melted after several recrystallizations at 221.5° (corr.). This agrees with the melting-point (221°) given by Ullmann,¹ but not with that reported by Seidel (213°).² The yield was about 65 per cent.

The nitroacetanthranilic acid was heated for five minutes with acetic anhydride, and the solution then allowed to cool. Long, colorless needles crystallized out, melting at $161-162^{\circ}$ (corr.). The excess of acetic anhydride was removed by washing with dry ether or with carbon tetrachloride.

Calculated for $C_9H_8O_4N_2$: C, 52.42; H, 2.91. Found: C, 52.24 and 52.14; H, 2.92 and 2.76.

Like the other nitroacetanthranils, this hydrolyzes slowly in moist air, or rapidly when boiled with water, yielding the nitroacetanthranilic acid again.

6-Nitro-2-Methyl-4-Ketodihydroquinazoline (6-Nitro-2-Methyl-4-Oxyquinazoline),



5-Nitroacetanthranil was heated with dilute aqueous ammonia, the mixture then warmed with dilute potassium hydroxide solution to change any intermediate amide to quinazoline, and a current of carbon dioxide passed through the solution. The quinazoline precipitated as an amorphous powder, which was crystallized from hot alcohol.

The same product was obtained by dissolving the nitroacetanthranilic acid in an excess of dilute ammonium hydroxide solution, evaporating to dryness, and heating the residue at 125° in an oil-bath. The yield by this method was very poor.

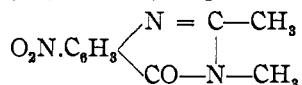
As already stated, this body was first prepared by Dehoff, and later by Thieme. The properties of the substance prepared by

¹ Ber. 36, 1801 (1903).

² Chem. Centr. 1902, II, 554.

us agree entirely with those of the compound obtained by Dehoff and Thieme, both in solubilities and melting-point. They both found that their product darkened between 230° and 280°, while ours begins to darken at about 266°, and melts at 278–281° (corr.).

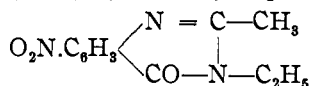
6-Nitro-2,3-Dimethyl-4-Ketodihydroquinazoline,



5-Nitroacetanthranil was warmed for a few minutes with methylamine, and the product recrystallized from alcohol. It then melted at 164–165° (corr.), and was insoluble in alkalis.

Dehoff¹ prepared this substance by heating the potassium salt of the 2-methyl compound with methyl iodide at 120°, and also by the action of fuming nitric acid (sp. gr. 1.5) upon 2,3-dimethyl-4-ketodihydroquinazoline, while Thieme made it from the corresponding silver salt and methyl iodide, and also by heating nitroacetanthranilic acid ethyl ester with methylamine for several hours at 130°. Both authors give the melting-point as 165°.

6-Nitro-2-Methyl-3-Ethyl-4-Ketodihydroquinazoline,

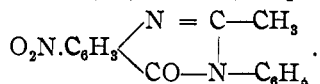


This was prepared in similar fashion from 5-nitroacetanthranil and ethylamine. It crystallizes from alcohol in needles which melt at 166° (corr.).

Calculated for $\text{C}_{11}\text{H}_{11}\text{O}_3\text{N}_3$: N, 18.02. Found: N, 18.07 and 17.95.

The same compound was obtained when the sodium salt of the nitromethylquinazoline was treated with ethyl iodide.

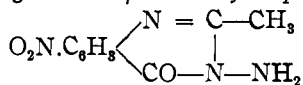
6-Nitro-2-Methyl-3-Phenyl-4-Ketodihydroquinazoline,



This was made by heating the nitroacetanthranil with aniline. It is difficultly soluble in alcohol, and crystallizes from glacial acetic acid in small, compact, light-yellow crystals, which melt at 219–220° (corr.).

Calculated for $\text{C}_{15}\text{H}_{11}\text{O}_3\text{N}_3$: N, 14.95. Found: N, 14.80.

¹ Loc. cit.

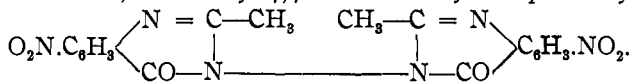
6-Nitro-2-Methyl-3-Amino-4-Ketodihydroquinazoline,

When the nitroacetanthranil was heated with a 50 per cent. aqueous solution of hydrazine hydrate, there resulted a deep-red solid, soluble in hot water. Colorless needles crystallized from the aqueous solution on cooling, which melted at 208–209° (corr.).

Calculated for $\text{C}_9\text{H}_8\text{O}_3\text{N}_4$: C, 49.09; H, 3.64; N, 25.45. Found: C, 49.00; H, 3.81; N, 25.56.

The compound is readily soluble in dilute alcohol, from which it crystallizes in long, colorless needles. It dissolves in solutions of the caustic alkalies with a deep red color.

When it was crystallized from glacial acetic acid and the crystals allowed to dry in the air, the compound showed a nitrogen content of 23.31 per cent. When this air-dried material was heated at 135° until the weight became constant, it lost 9.27 per cent. of acetic acid. This would make the nitrogen percentage in the substance dried at 135°, 25.68 per cent. On analysis, it was found to be 25.65 per cent. This appears to indicate the presence of acetic acid of crystallization in the proportion of two molecules of the acid to five of the quinazoline. This may not, however, represent the actual proportion between acid and quinazoline in the crystals as they first separate, as it is not unlikely that the crystals analyzed had already lost some of their acetic acid on standing in the air.

6,6'-Dinitro-2,2'-Dimethyl-4,4'-Diketotetrahydrodiquinazolyl,

One molecule of hydrazine (using a 50 per cent. aqueous solution of the hydrate) was added to two of the nitroacetanthranil, and the mixture heated for twenty minutes at 160–180° in an oil-bath. The cooled melt was pulverized and heated with alcohol, to remove aminoquinazoline, unchanged anthranil, and other impurities. The residual diquinazolyl was crystallized from glacial acetic acid. Small, compact crystals resulted, which melted with darkening at 281–286° (corr.). The yield was very poor.

Calculated for $\text{C}_{18}\text{H}_{12}\text{O}_6\text{N}_6$: N, 20.59. Found: N, 17.71 and 18.00.

These analytical results made it quite clear that we did not have the free diquinazolyl in hand. The air-dried substance was, therefore, dried to constant weight at 145°. In this drying at 145° it lost 12.1 per cent. of acetic acid, which would make the nitrogen percentage in the acetic acid-free substance, 20.3. The crystals analyzed apparently contained one molecule of the diquinazolyl to one of acetic acid.

Calculated for $C_{18}H_{12}O_6N_6 \cdot CH_3COOH$: N, 17.95.

HAVEMEYER LABORATORIES, COLUMBIA UNIVERSITY,
July, 1906.

[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON THIOCYANATES AND ISOTHIOCYANATES.

(SIXTH PAPER.)

BY TREAT B. JOHNSON.

Received July 19, 1906.

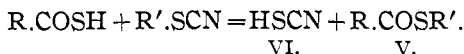
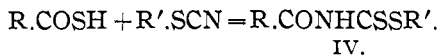
THE object of the work¹ described in this paper was to prepare some new thiol acids, I, and examine their behavior towards thiocyanates, II, and isothiocyanates, III.

R.COSH,
I.

R.SCN,
II.

R.NCS.
III.

It has been shown in several papers from this laboratory² that thiocyanates and isothiocyanates can be sharply distinguished by their behavior towards thiol acids, I. Thiocyanates, II, react with thiol acids in two ways. The most commonly observed reaction is a direct addition to the acid to give a dithiourethane, IV. Certain ones, on the other hand, react in a complicated manner to give thiol esters, V, and thiocyanic acid, VI.



Alkyl isothiocyanates, VII, and acyl isothiocyanates, VIII, react

¹ All the experimental work described in this paper was accomplished by advanced Senior students (1906), who had completed the required laboratory course in practical organic chemistry.—T. B. JOHNSON.

² Wheeler and Merriam: This Journal, 23, 283; 24, 439; Wheeler and Johnson: Ibid. 24, 680; 26, 185; Wheeler and Jamieson: Ibid. 24, 744.