

Condensation of Nitriles with Thiamides

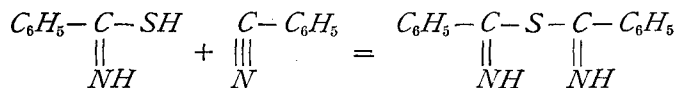
I. Benzonitrile and Thiobenzamide

By

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About 10 years ago M. Matsui¹ isolated a condensation-product from thiobenzamide and benzonitrile by passing dry hydrochloric acid gas into their ethereal solution cooled with a freezing mixture, and named it benzimino-sulphide based on the assumption that the condensation takes place according to the following equation :



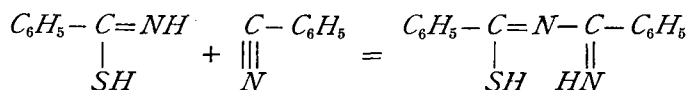
In the condensation-reactions of this kind, benzimino-chloride is generally considered to be produced as an intermediate product, which further reacts so as to form the final condensation-product. If, therefore, the condensation-product is really benziminosulphide as above assumed, it may be expected that the same substance will be produced by the interaction of benzimino-chloride and thiamide. So Matsui² made many trials to prepare the similar substances by using imono-chlorides; but he never could succeed, the only substances he could isolate were found similar to those obtained by S. Jamieson³ under similar treatment. Thus suspicion naturally arose as to the constitution

¹ Mem. Coll. Sci. Eng., Kyoto **2**, 401 (1910).

² Hitherto not published.

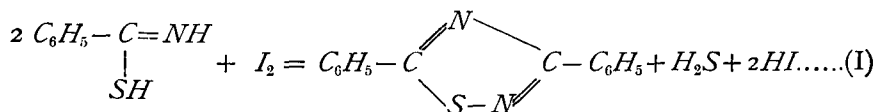
³ Am. Chem. Soc. **26**, 179 (1904).

of the condensation-product, for which the benzimino isothio-benzamide formula is also assignable, assuming the condensation-reaction to proceed as follows :

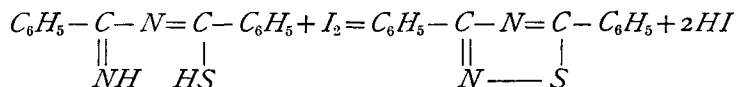


The present investigation undertaken at the suggestion of Prof. M. Matsui with the object of making this ambiguous point clear, chiefly deals with the oxidation, reduction and alkylation of the condensation-product.

As Matsui¹ has already pointed out, the condensation-product is very oxidable and gives dibenzylazosulphime as the oxidation-product. Now the formation of dibenzylazosulphime from the condensation-product by oxidation can not be explained by the iminosulphide formula, unless we consider that the condensation-product is first decomposed into benzonitrile and thiobenzamide, and this latter undergoes oxidation thus :



If this assumption be correct two molecules of the condensation-product must give rise to one molecule of dibenzylazosulphime, that is, 0.496 grams of oxidation-product must be produced from every 1 gram of original substance. The result of the experiment, however, was found not to agree. As is seen in the experimental part of this report 0.24 grams of the condensation product gave 0.234 grams of dibenzylazosulphime, when oxidised in an alcoholic solution with $\frac{1}{10}$ normal iodine solution, 19.4 c.c. of which was used up for complete oxidation. Since the relation of these quantities is nearly in the molecular proportion, the oxidation reaction must be such as is expressed in the following equation :



¹ loc. cit.

but not such as is represented by the equation (I), that is, the theory that decomposition precedes oxidation, and thiamide, one of the decomposition-products undergoes oxidation so as to form dibenzylazosulphime must be abandoned. Evidently this fact is sufficient to confirm the conclusion that the iminosulphide formula proposed beforehand is incorrect, and for that the benziminoisothiobenzamide formula must be adopted. Furthermore, the results of reduction and alkylation were both found in accord with that of oxidation to point out the correctness of the latter formula.

Reduction was conducted by warming the alcoholic hydrochloric acid solution with zinc on a water-bath till the evolution of hydrogen sulphide ceased, and as the chief reduction product benzylbenzamidine was obtained. Now the production of benzylbenzamidine and the evolution of hydrogen sulphide as the consequence of reduction may be conceived to occur, only when the condensation-product has the constitution represented by benziminoisothiobenzamide, in which the atomic linking $-C-N=C$ combined with the *SH* group exists. In



benzimosulphide as sulphur is linked to two carbon atoms, we can but expect benzylamine as the reduction-product, which may be formed with the elimination of sulphur.

Alkylation of the condensation-product with ethyl iodide readily takes place and gives rise to a product in which the ethyl radical is evidently combined with sulphur, as it is very unstable in the free state and instantly decomposes into ethyl mercaptane and cyaphenine exactly similar to the alkylation-product of thiobenzamide¹, thus affirming the presence of the *SH* group in the condensation-product.

From these results the author has come to the conclusion that the iminosulphide formula once given by Matsui to the condensation-product of benzonitrile and thiobenzamide must now be rejected, and for it the benziminoisothiobenzamide formula should be adopted.

Experimental Part

1. Oxidation of the Condensation-product with Iodine

The condensation-product of benzonitrile and thiobenzamide was

¹ A. Bernthsen: *Ann. d. Chem.*, **197**, 348 (1879).

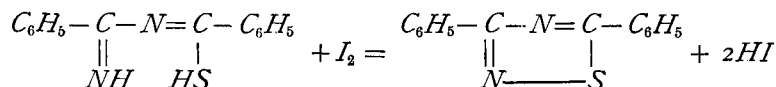
M. Matsui: *Mem. Coll. Sci. Eng. Kyoto*, **2**, 40 (1909).

prepared according to Matsui's description,¹ that is by saturating dry hydrochloric acid gas in an ethereal solution of benzonitrile and thiobenzamide taken equimolecularly. The hydrochloride crystallized out after having been washed with ether, was decomposed by a soda solution, and the free condensation-product thus separated was extracted with ether and recrystallized from benzene. It is a very oxidable substance and easily changes into dibenzylazosulphime as was described in Matsui's previous report. As this behaviour is very analogous to that of thiobenzamide one may naturally doubt, whether it is not possible that the condensation-product is first decomposed into its components, and thiamide thus liberated undergoes oxidation and yields dibenzylazosulphime.

In order to decide this doubtful point clearly the oxidation reaction was studied quantitatively using iodine as the oxidizing agent as follows: 0.240 grams of the condensation-product dissolved in 20 c.c. of alcohol was added with 25 c.c. of $\frac{1}{10}$ normal iodine solution, and after shaking the mixture for a few minutes the excess of iodine was titrated with $\frac{1}{10}$ normal sodium thiosulphate. After the titration was over the solution was neutralized with sodium hydroxide, diluted with an excess of water, and the dibenzylazosulphime which crystallized out was filtered, washed well, dried and weighed. The results obtained are shown below:

$\frac{1}{10}$ N-Iodine (c.c.)	$\frac{1}{10}$ N-Na ₂ S ₂ O ₃ (c.c.)	Dibenzylazosulphime		Found
		Calc. from Iodine	Calc. from original Substance	
25	5.6	0.231	0.238	0.234

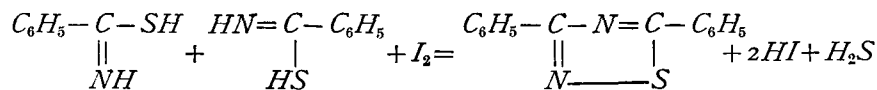
The calculated value of dibenzylazosulphime in the above table, obtained on the assumption that the oxidation takes place according to the equation given below agrees fairly well with the value actually found experimentally,



This decidedly confirms the view that the substance which undergoes oxidation is the condensation-product itself and not the thiamide, one of its decomposition-products. Moreover, if the formation of diben-

¹ loc. cit.

zenylazosulphime comes from the oxidation of thiobenzamide, its formation must always be accompanied by the evolution of hydrogen sulphide as is seen in the equation:



In our experiment, however, no trace of hydrogen sulphide could be detected.

2. Reduction of the Condensation-product

In a flask containing an alcoholic solution of the condensation-product and zinc powder, a concentrated hydrochloric acid was added and the flask well shaken, whereupon reduction took place, and hydrogen sulphide was evolved. When the evolution of hydrogen sulphide stopped, hydrochloric acid was again added and the mixture shaken, and this process was repeated several times till the evolution of hydrogen sulphide became nearly imperceptible. The contents of the flask were now heated on a water bath under a reflux condenser to make the reduction complete. The solution after having been separated from zinc powder by filtration was treated with a concentrated sodium hydroxide solution to dissolve zinc hydroxide completely, when a yellowish oil separated out. The oily substance was extracted with ether, and into this ethereal solution an ethereal hydrochloric acid solution was added, and the mixture was evaporated to drive off the ether. By this treatment a small quantity of a yellow viscous substance first separated out and a larger quantity (about 1.5 grams from 4 grams of the condensation-product) of a white crystalline substance crystallized out on further evaporation. This white reduction product was recrystallized from water and was found to melt at 211-215°. Its platinum double salt obtained as yellow prismatic crystals melting at 148° was used for analysis, the result having been found to be as follows:

0.1250 gram of the double salt gave 0.0295 gram platinum on ignition

	Found	Calc. (C ₁₄ H ₁₅ N ₂ Cl) ₂ Pt Cl ₄
Pt	23.60	23.50%

From the result of this analysis there is no doubt that the white crystalline substance above obtained as the reduction-product is

benzylbenzamidine hydrochloride. The yellow viscous substance produced as the bye-product was not further examined.

3. Alkylation of the Condensation-product

About 3 grams of the condensation-product were mixed with 4 grams of ethyl iodide and the mixture was heated on a water bath for a few minutes. Reaction similar to the alkylation of thiobenzamide readily took place and gave the product which solidifies on cooling. The product was well washed with ether to remove the original substance and ethyl iodide left unchanged and was obtained as yellow monoclinic crystals. It is insoluble in ether, and when heated it darkens in colour at about 170° , melts at 181° and decomposes on a further heating, evolving iodine. The result of analysis was found to be as follows:

0.2049 gram of the substance gave 0.1211 gram silver iodide.

	Found	Calc. (C ₁₆ H ₁₇ N ₂ SI)
I	32.01	32.03%

Free S-ethyl benziminoisothiobenzamide was isolated as an oily substance by treating the hydroiodide with caustic soda. It is a very unstable substance and spontaneously decomposes into mercaptane and cyaphenine as ethyl thiobenzamide does.

The author desires to express his sincere thanks to Prof. M. Matsui for the interest he has taken throughout the work.
