

Condensation of Nitriles with Thiamides. III. Nitriles with Thioanilides and Thionaphthalides.

By

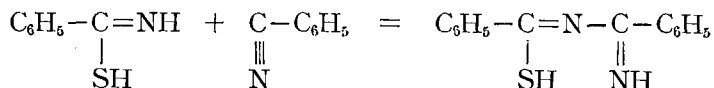
Seiichi Ishikawa.

(Received July 8, 1926)

ABSTRACT.

The condensation of nitriles with thiamides in which the hydrogen atom of the imino-group is replaced by the aryl group was studied with the object of ascertaining whether iminosulphides are obtainable as the condensation-products or not, and if they are really produced, how they are related with imino-isothiamides described in the previous report. It was found that iminosulphides are generally very unstable yellow substances which, when exposed in moist air, quickly change their colour to red and then decompose. In the cases in which no iminosulphide could be isolated either its decomposition-product or another condensation-product deemed to have been produced from the decomposition-product was obtained.

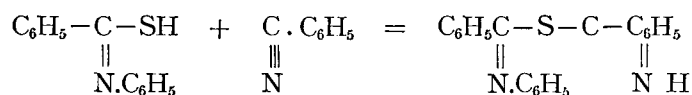
In the First Report⁽¹⁾ on this piece of research, it was stated that benzonitrile and thiobenzamide condense with each other in such a manner that the imino-group of the latter combines with the cyanogen-group of the former, as shown below :



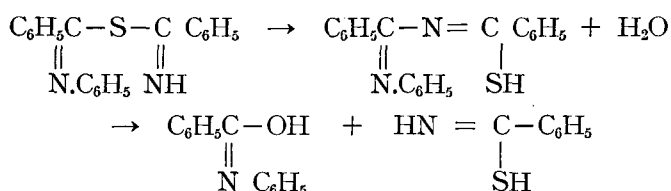
Such condensation is therefore expected with certainty not to take place between nitriles and thioanilides or thionaphthalides, in which the hydrogen atom of the imino-group is replaced by phenyl or naphthyl.

To confirm this experimentally condensation-experiments were conducted by passing dry hydrochloric acid gas into an ethereal solution of benzonitrile and thiobenzamide, when no sign of condensation could be

observed, the solution retaining its original yellow colour even after standing over-night, and no condensation-product crystallizing out. But a yellow substance conceivable as a condensation-product was isolated when the mother-liquor was evaporated under diminished pressure. The action of heat or hydrochloric acid caused the change of its yellow colour to red and decomposed it into thiobenzamide and benzanilide in equimolecular proportion. (Experiment 1). The condensation-product thus obtained may be considered as imino-sulphide, since only one way of condensation is conceivable that in which the sulphhydryl-group of thiobenzamide enters into combination with the cyanogen-group of benzonitrile, thus :



When phenylbenzimosulphide is hydrolysed by acids, its yellow colour always changes to red before decomposition, showing that something like an intermolecular change is taking place before its decomposition. The red intermediate compound being very unstable, its constitutional formula could not be experimentally determined, but inferring from the analogy that an atom-group of C-S-C=N or C-O-C=N rearranges to C-N-C=S or C-N-C=O⁽¹⁾, the mechanism of the decomposition of phenylbenzimosulphide may be explained as shown below :

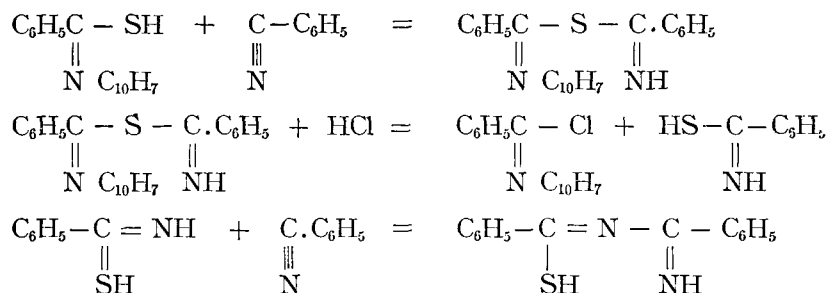


A condensation-product of acetonitrile and thiobenzanilide was also obtained as a yellow unstable substance which turns red by the action of acids and soon decomposes into benzanilide and thioacetamide. (Experiment 2).

The condensation-reaction between benzonitrile and α -thiobenzanaphthalide or β -thiobenzanaphthalide turned out a little different ; in neither case was iminosulphide isolated, thiobenzamide and benziminoisothiobenzonide

1 Hoffmann Ber. deut. chem. Ges., **19**, 2061 (1886); Billeter, *Ibid.*, **26**, 1681 (1893); Knorr, **30**, 922 (1897); Wislicenus and Goldschmidt, *Ibid.*, **35**, 1470 (1900); Wislicenus and Körber, *Ibid.*, **35**, 164 (1902); Lander, *Journ. Chem. Soc.*, **83**, 406 (1903); Wheeler and Johnson, *Amer. Chem. Journ.*, **30**, 24 (1903); Wheeler, Johnson & McFarland, *Journ. Amer. Chem. Soc.*, **25**, 787 (1903); Jamieson, *Ibid.*, **26**, 177 (1904); Rivier and Schneider, *Chem. Ztrbl.*, **1**, 643 (1920); Dixon and Taylor, *Journ. Chem. Soc.*, **101**, 2512 (1912); **117**, 720 (1920); etc. Dixon and Kennedy, *Ibid.*, **117**, 81 (1920).

being obtained in the former case and β -benznaphthalide in the latter. (Experiments 3 and 4). The results of these experiments, however, are not at all contradictory to those of the First and the Second Experiments. The production of thiobenzamide and benznaphthalide as well as that of benziminoisothiobenzamide may well be explained by assuming the primary formation of iminosulphide, as is clear from the following scheme :



All other condensations between many different thioanilides or thio-naphthalides and nitriles were found to take place in such a manner that the mechanism of the reaction could well be explained from the same point of view. It will probably be interesting to note that the reaction between thiobenznaphthalide and benzonitrile proceeds only to a small extent, while that between thiobenzanilide and benzonitrile takes place far better. A similar influence of a naphthyl radical on condensation was also observed in the case of thioacetophthalides.

The condensation of benzonitrile with thioacetanilide, α -thioacetophthalide and β -thioacetophthalide took place in an analogous way as in the cases of Experiments 3 and 4, giving thiobenzamide and benziminoisothiobenzamide as the reaction-products (Experiments 5, 6, 7). The amounts of thiobenzamide thus formed were calculated to correspond to 64, 10 and 10% of benzonitrile respectively. The condensation-reaction between acetonitrile and thioacetanilide was also examined, and thioacetamide was separated as the reaction-product, the amount of which corresponded to only 4% of the acetonitrile used. (Experiment 8).

Though acetonitrile thus condenses with thioacetanilide with great difficulty, it reacts with thioformanilide very smoothly giving nearly the theoretical yield of thioacetamide (Experiments 9 and 10). It may therefore be concluded that the degree of condensation between nitriles and thioanilides is governed by the mutual relation of both the substances which partake in the condensation, but not by the property of either one of them.

Experimental part.

The thioanilides and thionaphthalides used in this investigation were prepared by the action of phosphorus pentasulphide upon anilides and naphthalides according to the method of Jacobson⁽¹⁾ and Wallach.⁽²⁾

1. Benzonitrile with Thiobenzanilide.

4.12 grams of benzonitrile and 8.53 grams of thiobenzanilide (molecular proportion) were dissolved together in absolute ether; and this solution, kept cool with a freezing-mixture, was saturated with dry hydrochloric acid gas, whereupon yellow crystals began to deposit gradually on the wall of the vessel, but no change of colour was observed in the solution even after a day. The crystalline substance was first deemed to be a condensation-product, but when it was taken out of the mother-liquor into the moist air, it immediately changed into a red mass which once again turned yellow quickly. The crystals separated from the mother-liquor were therefore washed with dry ether as quickly as possible and the last trace of hydrogen chloride and ether was removed in a vacuum, great care being taken to avoid moisture. They melted at 98° without decomposition and were proved to be nothing but thiobenzanilide. The colour change in the moist air was found, by the next experiment, to be due to a condensation-product adhering to thiobenzanilide.

The mother-liquor was evaporated under reduced pressure, great care being taken to avoid any trace of moisture by attaching an apparatus containing phosphorus pentoxide to the evaporating vessel. When a small portion of the yellow residue obtained on evaporation was taken out of a vacuum desiccator into the moist air, it turned red immediately and finally changed into a yellow mass as was observed above. The yellow substance was found to contain no trace of thiobenzanilide and was separated into thiobenzamide and benzanilide by treating it with ether. The amounts of thiobenzamide and benzanilide separated from a portion of the yellow mass were 0.5374 gram and 0.7280 gram respectively, corresponding to 1 mol of the former and 0.94 mol of the latter. From this result it is clear that the residue which was obtained by the evaporation of the mother-liquor is really a condensation-product. It melted at about 60° to a red liquid and was easily hydrolysed by hydrochloric acid, first changing its colour to red. Without further purifying, it was analysed with the following results :

1 Jacobson, Ber., **19**, 171 (1886); **20**, 1897 (1887); **21**, 2627 (1888).

2 Wallach, Ibid., **16**, 145 (1883).

1. 0.2408 gram of the sample gave 0.1844 gram of BaSO₄
2. 0.2826 gram of the sample gave 0.1973 gram of BaSO₄

Found		Cal. C ₂₀ H ₁₆ N ₂ S
(1)	(2)	
S	10.51	9.58
		10.14

The molecular weight of the substance was determined by the cryoscopic method, its benzene solution being used.

Benzene 19.5696 grams, the substance 0.1227 gram, depression of the freezing point 0.095°.

Found	Cal. C ₂₀ H ₁₆ N ₂ S
Mol. weight	323
	316

2. Acetonitrile with Thiobenzanilide.

1.64 grams of acetonitrile and 8.53 grams of thiobenzanilide (molecular proportion) were dissolved in 200 c.c. of ether, and into this solution dry hydrochloric acid gas was conducted, when the solution acquired a reddish tint which soon became yellow, a considerable amount of yellow crystals being deposited. No colour change was observed in the solution even after standing 12 hours. When the crystals separated out from the mother-liquor were taken out in the moist air, they became instantly red and gradually decomposed leaving a yellow substance. This decomposition-product dissolved completely in ether, leaving no trace of the benzanilide which was anticipated to be present in it. It was washed with water, and about 6.0 grams of thiobenzanilide melting at 98° were obtained. A small amount of thioacetamide was also detected in the aqueous washings from which it was extracted with ether. The residue obtained by the evaporation of the mother-liquor was a yellow resinous substance which became red at once in the moist air and gradually decomposed into a yellow mass. The decomposition-product was washed with water and then with a dilute caustic soda solution to remove thioacetamide and thiobenzanilide, and the white mass obtained thus was crystallized from a mixture of benzene and petroleum ether. The crystals melted at 159° and were found to be benzanilide from the result of the following analysis:

0.3145 gram of the sample produced 19.1 c.c. of nitrogen gas at 29.3° and 772.3 mm.

	Found	Calc. C ₁₃ H ₁₁ NO
N	6.97	7.11

The amount of benzanilide was about 0.6 gram, and this corresponds to about 8% of the thiobenzanilide used. From the aqueous washings a

small quantity of thioacetamide and from the caustic soda solution about 1.5 grams of thiobenzanilide were isolated. The total amount of recovered thiobenzanilide was 7.5 grams (about 96% of the thiobenzanilide used). An attempt to isolate a condensation-product was not successful, owing to the poorness of the yield and its instability. From the quantities of thiobenzanilide and benzanilide obtained above, it is roughly calculated that about 9% of the acetonitrile had reacted upon the thiobenzanilide.

3. Benzonitrile with α -Thiobenznaphthalide.

2.06 grams of benzonitrile and 5.26 grams of α -thiobenznaphthalide (molecular proportion) were dissolved together in 150 c.c. of ether, and the solution was treated with hydrochloric acid gas, whereupon the colour of the solution changed to red, and a large amount of yellow crystals separated out. The crystals were α -thiobenznaphthalide hydrochloride, mixed with a small quantity of a condensation-product. The latter crystallized in red needles from a mixture of benzene and petroleum ether. It melted at 70° and produced dibenzylazosulphime when oxidized with iodine. From these properties and others it is clear that this substance is benziminoisothiobenzamide. On evaporating the mother-liquor a minute quantity of thiobenzamide was isolated.

4. Benzonitrile with β -Thiobenznaphthalide.

150 c.c. of ether in which 2.06 grams of benzonitrile and 5.26 grams of β -thiobenznaphthalide (molecular proportion) were dissolved, was saturated with hydrogen chloride in the usual way, whereupon the colour of the solution was gradually converted red. On standing over-night, a large amount of β -thiobenznaphthalide hydrochloride mixed with some condensation-products separated out. The latter consists of red needles, melting at 72° and was easily oxidized to dibenzylazosulphime with an alcoholic iodine solution. It is therefore evident that this substance is benziminoisothiobenzamide. The same substance was also found in a residue obtained by evaporating the mother-liquor. About 0.3 gram of white needle crystals melting at 155° was also isolated from the residue. They were analysed with the following result and confirmed to be β -benznaphthalide.

0.2533 gram of the sample gave 12.1 c.c. of nitrogen gas at 17.8° and 766.5 mm.

	Found	Calc. $C_{17}H_{13}NO$
N	5.66	5.67

Beside these, about 0.2 gram of thiobenzamide was also isolated.

5. Benzonitrile with Thioacetanilide.

3.09 grams of benzonitrile and 4.54 grams of thioacetanilide (molecular proportion) were dissolved in 150 c.c. of ether, and this solution was treated with hydrogen chloride in the usual way, whereupon a yellow crystalline substance immediately began to deposit and frequently stopped up the delivery tube, making the passage of the gas impossible. The solution remained nearly unchanged till the solution saturated with hydrochloric acid gas was left to stand over-night when it became vividly coloured red. From the yellow crystals separated from the mother-liquor thioacetanilide was isolated.

A residue obtained by evaporation of the mother-liquor was treated with an aqueous solution of sodium bicarbonate and extracted with ether. The ethereal extract thus obtained was evaporated, and the residue, after having been washed with warm water to remove the admixed substances, was recrystallized from a mixture of benzene and petroleum ether. About 0.2 gram benziminoisothiobenzamide was obtained. Besides this about 2.5 grams of thiobenzamide and some acetanilide were also found in the residue left on evaporation of the mother-liquor.

In the above experiments about 22% of thioacetanilide was recovered unchanged and about 64% of benzonitrile was converted into thiobenzamide, showing that about 71% of each of the substances taken had entered into condensation.

6. Benzonitrile and α -Thioacetophthalide.

2.06 grams of benzonitrile and 4.02 grams of α -thioacetophthalide (molecular proportion) were dissolved in 150 c.c. of ether, and the solution was treated with hydrochloric acid gas. The colour of the solution changed gradually to red. After standing over-night, the mother-liquor was poured out and evaporated under reduced pressure, and the residue was neutralized with an aqueous solution of sodium bicarbonate and washed with hot water until the washings became colourless. A mixture of white needles with a red substance was obtained, from which 0.25 gram of α -acetophthalide, 0.06 gram of benziminoisothiobenzamide and 0.27 gram of thiobenzamide were separated.

From the yields of thiobenzamide and benziminoisothiobenzamide it was calculated that about 11% of the benzonitrile had thus been converted into thiobenzamide.

7. Benzonitrile with β -Thioacetophthalide.

An ethereal solution containing 3.09 grams of benzonitrile and 6.3 grams

of β -thioacetophthalide (molecular proportion) was treated with hydrochloric acid gas, and a result analogous to that of Experiment 6 was obtained. The amount of benzonitrile converted into thiobenzamide was a little less, being 9%.

8. Acetonitrile and Thioacetanilide.

In the condensation-experiment conducted in a similar manner by passing hydrogen chloride into an ethereal solution of acetonitrile and thioacetanilide, no special product was obtained, except a small quantity of thioacetamide which was confirmed by analysing its platinum double salt according to the method of Ray:¹

0.1308 gram of the double salt gave 0.0560 gram of platinum on ignition.

	Found	Calc. $(\text{CH}_3 \cdot \text{CSNH})_3\text{PtCl}_2\text{HCl}$
Pt	42.81	43.20

9. Benzonitrile with Thioformanilide.

4.12 grams of benzonitrile and 5.48 grams of thioformanilide (molecular proportion) were dissolved in 120 c.c. of ether, and the solution was saturated with hydrochloric acid gas. The solution became red in a few minutes, but no crystals were observed to deposit even after 12 hours. From the crude crystalline residue obtained by evaporating the red solution in a vacuum a small quantity of benziminoisothiobenzamide, aniline and about 5.0 grams of thiobenzamide were separated. The percentage of benzonitrile which was converted into thiobenzamide was about 91%.

10. Acetonitrile and Thioformanilide.

1.23 grams of acetonitrile and 4.11 grams of thioformanilide (molecular proportion) were dissolved in 120 c.c. of ether, and the solution was saturated with hydrochloric acid gas. The solution became orange-yellow, but no precipitate separated out even after 12 hours. The residue obtained by the evaporation of the solution under reduced pressure was found to contain aniline hydrochloride (4.5 gram) and thioacetamide

The author wishes to express his sincere thanks to Prof. M. Matsui for the interest he has taken throughout this investigation and also to Prof. O. Kubota of The Seventh Higher School for his valuable advice.

¹ Ray, Journ. Chem. Soc., 115, 871 (1919).