I. I. Grandberg, A. N. Kost, Yu. A. Naumov

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Abstract

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I. I. Grandberg, A. N. Kost, Yu. A. Naumov

On the Commonality of Rearrangements with Cleavage of N–N or N–O Bonds and Formation of a Nitrile Group

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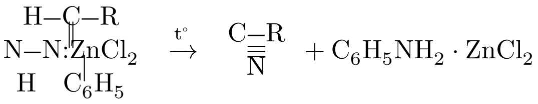
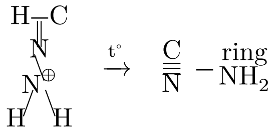
Along with the well-studied Fischer indole rearrangement, the literature contains scattered information on the ability of various compounds of the structure RCH=NNR′R″ to undergo another rearrangement with cleavage of the N—N bond. Thus, according to A. E. Arbuzov, phenylhydrazones of aliphatic aldehydes are capable of splitting into aniline and the corresponding nitrile (^{1}). The reaction catalysts ($ZnCl_2$, Cu_2Cl_2, $PtCl_2$) evidently first add to the more basic nitrogen atom, as a result of which redistribution of electron density occurs, followed by rupture of the N—N bond and migration of the hydrogen atom



$$\begin{matrix} \mathrm{H-C-R} \\ \| \\ \mathrm{N-N:ZnCl_2} \\ \mathrm{H}\quad \mathrm{C_6H_5} \end{matrix} \xrightarrow{t^\circ} \begin{matrix} \mathrm{C-R} \\ \equiv \\ \mathrm{N} \end{matrix} + \mathrm{C_6H_5NH_2 \cdot ZnCl_2}$$

An analogous phenomenon was observed by us on heating the hydrochlorides of pyrazolines (which structurally are cyclic hydrazones). Protonation of the nitrogen atom in position 1 caused the same rearrangement with cleavage of the N—N bond ($^{2-4}$). As in A. E. Arbuzov' s experiments, for the rearrangement it proved necessary that there be a hydrogen atom at the carbon-nitrogen double bond (an unsubstituted third position in the pyrazoline ring).



$$\begin{matrix} \mathrm{H-C} \\ \| \\ \mathrm{N} \\ | \\ \mathrm{N}^{\oplus} \\ \mathrm{H}\quad\mathrm{H} \end{matrix} \xrightarrow{t^\circ} \begin{matrix} \mathrm{C} \\ \equiv \\ \mathrm{N} \end{matrix} - \begin{matrix} \text{ring} \\ \mathrm{NH_2} \end{matrix}$$

Thus, in 5-arylpyrazolines the process is complicated by displacement of the double bond with formation of 3-arylpyrazolines, which are no longer capable of rearrangement (^{5}). We observed an analogous conversion of pyrazolines into aminonitriles under the influence of colloidal platinum (^{4}).

Finally, according to the data of B. V. Ioffe and K. N. Zelenin, cleavage of the N—N bond of the same kind occurs in the splitting of ions of 1,1-dialkylpyrazolinium (^{6})*. In this case, quaternization of the nitrogen atom performs the same function as protonation or complex formation in the examples given above. It causes heterolytic cleavage of the N—N bond, similar to the way in which a bond is broken in the Hofmann cleavage of quaternary ammonium bases.

We pointed out (4) the commonality of this reaction with a Beckmann rearrangement of the second order. However, B. V. Ioffe and K. N. Zelenin reported that the O-methyl ether of acrolein oxime (9) does not rearrange under the experimental conditions they selected. However, as is known (10), the β-cyanoethyl ether of benzaldoxime, under the action of BF_3, undergoes a nitrile rearrangement with cleavage of the N—O bond and formation of benzonitrile and ethylene cyanohydrin. In this case, formation of the borofluoride of an oxonium— causes the corresponding displacement of electrons, leading to rearrangement.

The nitrile (or an analogous) rearrangement of hydrazones or oximes can also be caused by alkaline agents. Thus, isoxazoles that have no substituent in position 3 open the ring, with cleavage of the N–O bond, under the action of sodium amide (11).

Opening of the pyrazole ring with formation of an aminonitrile has recently been observed by A. M. Simonov, B. K. Martsoha, and F. T. Pozharskii under the action of sodium amide on 1-benzylindazole (12). In both cases the primary process is apparently deprotonation in position 3. This same group of reactions may possibly include the amidine rearrangement of arylhydrazones of arylaldehydes, discovered by Robev (13–16), which, under the action of $RMgX$, $NaNH_2$, or C_6H_5Li, proceeds according to a scheme of homolytic reactions, as has already been mentioned (4,20).

Wishing to test the generality of the Arbuzov nitrile rearrangement for the system RCH = NNR′R″, we chose a series of typical objects, namely: phenyl- and diphenylhydrazones of benzaldehyde, for which the Fischer reaction is impossible ($R = R' = C_6H_5,\ R'' = \mathrm{H}$ or C_6H_5); diphenylhydrazones of propionic and isovaleric aldehydes ($R =$ alkyl, $R' = R'' = CH_3$); dimethylhydrazones of isobutyric and benzoic aldehydes ($R =$ alkyl or C_6H_5, $R' = R'' = CH_3$); and benzoylhydrazone of benzaldehyde ($R = C_6H_5,\ R' = \mathrm{H},\ R'' = C_6H_5CO$).

It proved that phenyl- and diphenylhydrazones, under the conditions of A. E.

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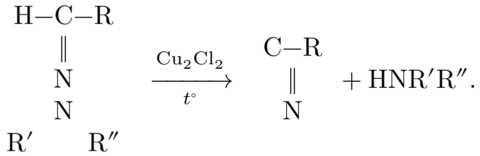
* In 1960 B. V. Ioffe and K. N. Zelenin discovered that dimethyl- and diethylhydrazones of acrolein readily convert into dimethyl- or, respectively, diethylaminopropionitrile (7). As the same authors showed, α, β-unsaturated ketones react with unsymmetrical dialkylhydrazines with formation only of stable dialkylhydrazones (8). In 1962 we published a brief communication (2) on the conversion of 4-ethyl-5-propylpyrazoline hydrochloride into aminonitrile, and subsequently a more complete article (4). Almost simultaneously B. V. Ioffe and K. N. Zelenin published that the rearrangement of dialkylhydrazones of acrolein found by them proceeds through the stage of the 1,1-dialkylpyrazolinium ion and extended it to the cleavage of a series of quaternary bases of 1,1-dialkylpyrazolines (6,9,20).

Arbuzov (200–220°, Cu_2Cl_2), rearrange with self-heating to form aniline (respectively diphenylamine) and a nitrile:



$$\begin{array}{c} H{-}C{-}R \\ \| \\ N \\ N \\ R' \qquad R'' \end{array} \xrightarrow[t^\circ]{Cu_2Cl_2} \begin{array}{c} C{-}R \\ \| \\ N \end{array} + HNR'R''.$$

Benzoylhydrazone of benzaldehyde, which under milder conditions disproportionates under the action of $POCl_3$ with formation of benzalazine and 2,5-diphenyl-1,3,4-oxadiazole (^{17,18}), on heating with Cu_2Cl_2 undergoes the very same nitrile rearrangement, giving benzamide and benzonitrile (yields respectively 38 and 40%):

$$C_6H_5CONHN{=}CHC_6H_5 \rightarrow C_6H_5CONH_2 + N{\equiv}C{-}C_6H_5.$$

For the dimethylhydrazones we also used the quaternization method and carried out cleavage of the quaternary hydrazinium bases (which could not be used in all the cases described above). On quaternization with methyl iodide we isolated trimethylamine and the corresponding nitrile. If the rearrangement was carried out under the conditions of A. E. Arbuzov, dimethylamine was formed.

It turned out that the nitrile rearrangement of substituted hydrazones takes place in the presence of various substituents. Under the action of acidic agents (including Lewis acids), a positive charge is created on the amino nitrogen atom. As a result, the σ-pair of electrons of the nitrogen–nitrogen bond is drawn toward this atom, and a cationoid character appears at the carbon atom. This is followed by deprotonation and cleavage of the N–N bond. If the process proceeds heterolytically, one may expect the intermediate formation of a binary ion

$$R\overset{\ominus}{C} = \overset{\oplus}{N},$$

which may polymerize (therefore the yield of amine is always higher than that of nitrile). There are, however, data indicating that the reaction may also proceed by a homolytic path. Indeed, according to our data, the rate and yields of the rearrangement depend little on the nature of the substituent bonded to the nitrogen atom. The conversion of benzoylbenzaldehyde hydrazone into benzalazine makes probable the intermediate formation of the free radical $C_6H_5CH \equiv N$. The experiments of Robev (^{16}) speak for the homolytic character of the amidine rearrangement. We still have too few data for final conclusions.

Comparing the nitrile rearrangements of oximes and hydrazones, under our conditions (210°, Cu Cl) we subjected *O*-benzylbenzaldoxime to cleavage and isolated benzonitrile, which confirms the relatedness of these reactions. In attempts to extend the reaction to monoalkylhydrazones, we encountered the competing reaction of decomposition of these substances with evolution of nitrogen. Thus, in the isopropylhydrazone of benzaldehyde, on heating with Cu Cl , migration of the double bond occurs. The azo compound formed decomposes, and we succeeded in isolating stilbene and isobutylbenzene:

$$(CH_3)_2CHNHN = CHC_6H_5 \to (CH_3)_2CHN = NCH_2C_6H_5 \to$$
$$\to (CH_3)_2CH \cdot + N_2 + \cdot CH_2C_6H_5 \to (CH_3)_2CHCH_2C_6H_5.$$

The reaction is not specific to alkylhydrazones of aldehydes. Thus, from the benzylhydrazone of acetone, on heating with various acidic agents (ZnCl , HCl, polyphosphoric acid), the following were isolated: toluene, 1,2-diphenylethane, isobutylbenzene, and various condensation products of the pyrazoline and pyrazole series. Similar results were obtained with several other hydrazones (19).

Experimental Part

Dimethylhydrazone of benzaldehyde. In a flask fitted with a reflux condenser, 14.8 g of dimethylhydrazone of benzaldehyde was mixed with 12 ml of methyl iodide, and the mixture was heated on a water bath for half an hour. From the crystalline mass of methiodide that formed, the excess methyl iodide was distilled off under the vacuum of a water-jet pump. To the flask were added 50 ml of a 20% sodium hydroxide solution, and the benzonitrile formed was distilled off with steam. Obtained: 5.8 g (56%) of benzonitrile, b.p. 189-191°/754 mm, n_D^{20} 1.5284 (on saponification, benzoic acid was obtained). In an analogous experiment with quantities reduced by a factor of 10, the yield of trimethylamine (determined by Kjeldahl analysis) was 81%. When the pyrolysis of the methiodide of dimethylhydrazone of benzaldehyde was carried out in a metal bath at 230°, the yield of benzonitrile was 21%, and that of trimethylamine 49%. On decomposition of dimethylhydrazone of benzaldehyde by catalytic traces of cuprous chloride (at 230°), the yield of benzonitrile was 18%, and that of dimethylamine 52%. On decomposition by catalytic traces of anhydrous zinc chloride at 230°, the yield of dimethylamine was 44%, and that of benzonitrile 11%.

On decomposition of the same hydrazone by catalytic traces of sodium amide at 230°, dimethylamine is evolved, but most of the hydrazone is recovered unchanged (b.p. 240°/747 mm, 124°/16 mm, n_D^{20} 1.5986). Benzonitrile was not isolated.

On pyrolysis of the dry hydrochloride of dimethylhydrazone of benzaldehyde at 140°, an exothermic reaction occurs, and the temperature rises to 230°. The yield of benzonitrile was 22%, and of dimethylamine 48%.

Dimethylhydrazone of isobutyraldehyde. From 0.1 mole of the methiodide of the hydrazone, alkaline cleavage gave isobutyronitrile, b.p. 104-105°/751 mm,

n_D^{20} 1.3791 (saponified to isobutyric acid), in 38% yield, and trimethylamine in 74% yield. On direct pyrolysis of the methiodide, the yield of nitrile was 9%, and of trimethylamine 47%.

Benzoylhydrazone of benzaldehyde. A mixture of 11.2 g of benzoylhydrazone of benzaldehyde and 0.2 g of Cu Cl was heated in a bath with Wood’ s alloy. At a temperature of about 270°, evolution of bubbles began, and at about 295° vigorous boiling began. The temperature rose spontaneously to 304°, then again fell slightly. A liquid with the odor of benzonitrile distilled into the receiver. Heating was continued for about 1 hour. From the distillate and the residue in the flask were isolated 1.8 g (38%) of benzonitrile and 2.4 g (40%) of benzamide.

Diphenylhydrazone of propionaldehyde. A mixture of 6.7 g of diphenylhydrazone of propionaldehyde (b.p. 172-174°/12-13 mm, n_D^{20} 1.6138) and 0.1 g of Cu Cl was heated. At 210° decomposition began; the temperature rapidly rose to 260°, and a small amount of liquid distilled into the receiver. To the resin remaining in the flask, with indol-

···with odor, ether was added, the mixture was stirred, and the ethereal solution was filtered off. After removal of the ether, the residue was distilled in vacuo. At a pressure of 12-13 mm and a temperature of 143-153°, 3.5 g (69%) of diphenylamine, m.p. 53-54°, distilled over.

Diphenylhydrazone of isovaleraldehyde. A mixture of 11 g of diphenylhydrazone of isovaleraldehyde (b.p. 167-175° at 12-15 mm; n_D^{20} 1.5888) and 0.2 g of Cu_2Cl_2 was heated. Decomposition began at about 210°, and the temperature spontaneously rose to 238°. A dark-brown liquid with an indole odor remained in the flask. Vacuum distillation gave 6.6 g (97%) of diphenylamine.

Diphenylhydrazone of benzaldehyde. On heating 17.8 g of diphenylhydrazone of benzaldehyde with 0.2 g of Cu_2Cl_2 to 220°, evolution of ammonia and vigorous boiling of the liquid began; the temperature spontaneously rose to 265°. The resinified reaction product was steam-distilled. The distillate was extracted with ether. After drying with potassium carbonate and distillation, 2.5 g (37%) of benzonitrile, b.p. 184-190°, n_D^{20} 1.5292, was isolated. The solidified resin remaining in the flask after steam distillation was dissolved in ether and, on distillation, yielded 4.7 g (43%) of diphenylamine.

Phenylhydrazone of benzaldehyde. A mixture of 19.6 g of phenylhydrazone of benzaldehyde and 0.1 g of Cu_2Cl_2 was heated. At 180° in the melt, evolution of ammonia and vigorous boiling began. The temperature spontaneously rises to 240°, and a light-yellow liquid begins to distill. At a temperature of about 255°, when distillation had ceased, heating was stopped. Into the receiver distilled 10.2 g of liquid. The resinified residue in the reaction flask was subjected to steam distillation. The distillate was extracted with ether. The ethereal extract was combined with the product obtained from the reaction and shaken several times with $2N$ HCl, then washed with water and dried with potassium carbonate. After distillation, 6.2 g (60%) of benzonitrile was obtained. The hydrochloric acid solution was alkalized, extracted with ether, and, by distillation, 5.1 g (55%) of aniline was isolated.

O-Benzylbenzaldoxime. A mixture of 4.3 g of O-benzyloxime of benzaldehyde and 0.1 g of Cu_2Cl_2 was heated to 210° for 2 h. Then steam distillation yielded 0.52 g (25%) of benzonitrile, b.p. 187–189° at 751 mm, n_D^{20} 1.5291.

Isopropylhydrazone of benzaldehyde. A mixture of 16.2 g of isopropylhydrazone of benzaldehyde and 0.1 g of Cu_2Cl_2 was heated while distilling off the products formed. At 200° an energetic reaction begins in the mixture, with evolution of gas (nitrogen) and low-boiling products. After half an hour the distillate that had boiled out of the reaction mixture up to 300° was fractionated. 2.6 g (19%) of isobutylbenzene, b.p. 170–172°, n_D^{20} 1.4877, and 0.8 g (9%) of trans-stilbene, m.p. 123°, were obtained.

Moscow State University
named after M. V. Lomonosov

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Note: Figure translations are in progress. See original paper for figures.