(cited in Ref. 7).
47. L. Pauling, "The Nature of the Chemical Bond", Cornell Univ. Press, Ithaca, 1958; Phys. Rev., 54, 899 (1938).
48. F.D. Rossini, D.D. Wagman, W.H. Evans, S. Levine, and I. Jaffe, "Selected Values of Chemical Thermodynamic Properties", U.S. Nat. Bur. Stand., Circ. 500, U.S. Govt. Printing Office, Washington, 1952.
49. B.F. Markov, Yu.K. Delimarskii, and I.D. Panchenko, Zhur. Fiz. Khim., 29, 1987 (1954).
50. M.F. Lantratov and A.F. Alabyshev, Zhur. Prikl. Khim., 26, 353 (1953).
51. B.F. Markov, Zhur. Fiz. Khim., 31, 2288 (1957).
52. M.F. Lantratov and A.F. Alabyshev, Zhur. Prikl. Khim., 26, 263 (1953).
53. M.F. Lantratov and A.F. Alabyshev, Zhur. Prikl. Khim., 27, 722 (1954).
54. I.G. Margulescu and S. Sternberg, Rev. Chim. (Roumania), 2, 251 (1957); 3, 55 (1958).
55. I.G. Margulescu and D.I. Marcidan, Rev. Chim. (Roumania), 3, 47, 69 (1958).
56. S. Sternberg, Rev. Chim. (Roumania), 3, 77 (1958).
57. M.F. Lantratov and T.N. Shevlyakova, Zhur. Neorg. Khim., 3, 1153 (1959); 6, 192 (1961) [Russ. J. Inorg. Chem., 523 (1959); 95 (1961)].
58. K.H. Stern, J. Phys. Chem., 60, 679 (1956); 62, 385 (1958).
59. M.S. Zakhar'evskii and T.V. Permyakova, Zhur. Obshch. Khim., 26, 2947 (1956).
60. M.S. Zakhar'evskii and V.A. Krotova, Uch. Zap. Leningrad. Gos. Univ., No. 272, 57 (1959).
61. N.K. Voskresenskaya, Itogi Nauki, Otd. Khim. Nauk, No. 4, 152 (1959).
62. H. Bloom, Rev. Pure Appl. Chem. (Australia), 9, 139 (1959).
63. J.L. Barton and H. Bloom, Trans. Faraday Soc., 55, 1792 (1959).
64. M.F. Lantratov and O.F. Moiseeva, Zhur. Fiz. Khim., 34, 367 (1960) [Russ. J. Phys. Chem., 171 (1960)].
65. N.M. Tarasova, Zhur. Fiz. Khim., 21, 487 (1947).
66. H. Bloom and E. Heymann, Proc. Roy. Soc., A 188, 392 (1947).
67. N.K. Boardmann, A.R. Palmer, and E. Heymann, Trans. Faraday Soc., 51, 277 (1955).
68. B.S. Harrap and E. Heymann, Trans. Faraday Soc., 51, 259 (1955).
69. R. Lorenz, Z. anorg. Chem., 52, 41 (1907).
70. Yu.V. Baimakov and S.P. Samusenko, Trudy Leningrad. Politekh. Inst., 1, No. 1, 3, 26 (1938).
71. F.R. Duke and R.A. Flemming, J. Electrochem. Soc., 106, 130 (1959).
72. N.K. Boardmann, F.H. Dorman, and E. Heymann, J. Phys. Chem., 53, 375 (1949).
73. H. Flood, T. Förland, and B. Roald, J. Amer. Chem. Soc., 71, 572 (1949).
74. A. Wachter and J.H. Hildebrand, J. Amer. Chem. Soc., 52, 4655 (1930).
75. W.C. Hahn and A. Muan, J. Phys. and Chem. Solids, 19, 338 (1961).
76. J. Lumsden, "Physical Chemistry of Process Metallurgy. Part I" (Edited by G.R. St. Pierre) (AIME Met. Soc. Conf. Vol. VII), Interscience, New York, 1961, p. 165.
77. V.L. Kozheurov, "Termodinamika Metallurgicheskikh Shlakov" (Thermodynamics of Metallurgical Slags), Metallurgizdat, Sverdlovsk, 1955.
78. N.K. Voskresenskaya, Dokl. Akad. Nauk SSSR, 81, 585 (1951).
79. N.K. Voskresenskaya, Izv. Sektora. Fiz.-Khim. Anal., Inst. Obshch. Neorg. Khim., Akad. Nauk SSSR, 23, 155 (1952); 26, 99 (1955).
80. N.K. Voskresenskaya, in Collected Papers "Fizicheskaya Khimiya Solei i Shlakov. Trudy Vsesoyuznogo Soveshchaniya" (Physical Chemistry of Salts and Slags. Proceedings of an All-Union Conference), Moscow, 1962.

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REARRANGEMENTS INVOLVING THE CLEAVAGE OF N–N OR N–O BONDS AND FORMATION OF A NITRILE GROUP

Yu. A. Naumov and I.I. Grandberg

CONTENTS

1. Introduction 9
2. Nitrile fission of N–N or N–O bonds by electrophilic reagents or metal catalysts 9
3. Nitrile rearrangements produced by nucleophilic reagents 12
4. Structural factors determining the possibility of nitrile rearrangements 16

1. INTRODUCTION

There has been much recent work on rearrangements in which an N–N or N–O bond is broken and a nitrile group formed.

Compounds which can undergo this conversion include substituted aldehyde hydrazones, their cyclic analogues, the 3-unsubstituted pyrazolines and indazoles, and their cyclic and acyclic oxygen analogues, that is, aldoximes and 3-unsubstituted isoxazoles.

The nitrile fission of N–N or N–O bonds is observed under diverse experimental conditions: by the action of salts of complex-forming metals or platinum group metals; in the pyrolysis of hydrochlorides or quaternary salts; in the Hofmann degradation of quaternary ammonium bases; and by the action of nucleophilic reagents. The lack of data on the mechanism of the reaction and the variety of conditions, despite the external similarity of the processes, often hinder their comparison and generalisation.

2. NITRILE FISSION OF N–N OR N–O BONDS BY ELECTROPHILIC REAGENTS OR METAL CATALYSTS†

In 1910 Arbuzov observed[1,2] that heating aliphatic aldehyde phenylhydrazones to 180–200° with catalytic

† Metal catalysts are only formally included in this section, in view of the lack of knowledge of the mechanism of their action and the paucity of experimental material.

amounts of Cu_2Cl_2, $PtCl_2$, or $ZnCl_2$ produces the corresponding nitrile and aniline:

$$R-CH=N-NHC_6H_5 \xrightarrow[t^\circ]{Cu_2Cl_2} R-C\equiv N + H_2N-C_6H_5,$$

that is, fission of the aldehyde phenylhydrazone occurs instead of the normal Fischer indole synthesis. The phenylhydrazones of lower aliphatic aldehydes produce mainly the corresponding indoles, but those of higher aldehydes undergo mainly the nitrile fission.

Somewhat earlier a similar fission was observed by Anselmino[3] in the dry distillation of salicylaldehyde phenylhydrazone, which produces salicylonitrile and aniline together with benzene and ammonia.

In 1921 Maihle[4,5] observed nitrile fission when attempting catalytic hydrogenation of various aliphatic aldehyde phenylhydrazones at 180–190° over nickel.

It has recently been shown[6] that aromatic aldehyde phenylhydrazones also rearrange into amine and nitrile under Arbuzov conditions (Cu_2Cl_2, 220°); this is an exothermic reaction. The reaction is in fact general for compounds R–CH=N–NR′R″; thus diphenylamine and the corresponding nitrile are obtained from benzaldehyde phenylhydrazone (R = R′ = R″ = C_6H_5) and the phenylhydrazones of propionaldehyde and isovaleraldehyde (R = = alkyl, R′ = R″ = C_6H_5). Benzaldehyde benzoylhydrazone, which with phosphoryl(V) chloride under milder conditions disproportionates to benzaldehyde azine and 2,5-diphenyl--1,3,4-oxadiazole[7,8], also undergoes the nitrile rearrangement when heated with copper(I) chloride, yielding benzamide and benzonitrile:

$$C_6H_5CONH-N=CHC_6H_5 \xrightarrow[t^\circ]{Cu_2Cl_2} C_6H_5CONH_2 + N\equiv C-C_6H_5.$$

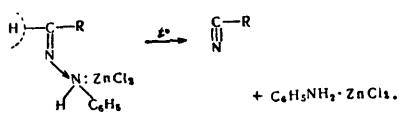
There is only a slight tendency for dialkylhydrazones to decompose with fission of the N–N bond[6]. For example, the decomposition of benzaldehyde dimethylhydrazone (R = C_6H_5, R′ = R″ = CH_3) under Arbuzov conditions (Cu_2Cl_2, 230°) produces benzonitrile in no more than 18% yield, and this falls to 11% if the copper(I) chloride is replaced by anhydrous zinc chloride. Heating heptanol diethylhydrazone at 260° for 4 h in the presence of copper(I) chloride gives only 6% of heptanenitrile and 9% of diethylamine; most of the hydrazone is recovered unchanged[9].

It has not proved possible to obtain an amine and nitrile from aldehyde monoalkylhydrazones, because of their decomposition with evolution of nitrogen[6]; thus when benzaldehyde isopropylhydrazone is heated with copper(I) chloride the double bond is probably displaced and the resulting azo-compound then decomposes, isobutylbenzene and stilbene being obtained:

$$(CH_3)_2CH-NH-N=CHC_6H_5 \longrightarrow (CH_3)_2CH\{N=N\}CH_2C_6H_5 \longrightarrow$$
$$\longrightarrow (CH_3)_2CH\cdot + N_2 + \cdot CH_2C_6H_5 \longrightarrow (CH_3)_2CHCH_2C_6H_5.$$

The conversion of ketone benzylhydrazones proceeds similarly, but in more complex fashion[10].

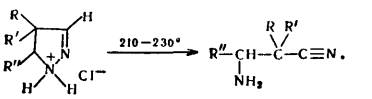
In the fission of aldehyde phenylhydrazones the catalyst ($ZnCl_2$, Cu_2Cl_2, $PtCl_2$) apparently first attaches itself to the more basic nitrogen atom, causing a redistribution of electron density and then cleavage of the N–N bond and displacement of a hydrogen atom:



The amine is often obtained in higher yield than the nitrile, probably because of the formation of the intermediate zwitter-ion $R-\bar{C}=\overset{+}{N}$, which can polymerise. This, and the influence of the solvent on the reaction when copper(I) chloride is used, indicate that the reaction occurs with heterolytic cleavage of the N–N bond. Benzaldehyde phenylhydrazone produces benzonitrile by the action of copper(I) chloride in very much greater yield in polar solvents than in non-polar; in protic (for example, diethyleneglycol) and aprotic polar solvents (for example, dibutyl phthalate, benzyl benzoate, or diphenyl oxide) the yield is about the same (50–60%), but in non-polar solvents such as 2-methylnaphthalene or liquid paraffin the benzonitrile is obtained in ~ 10% yield[11].

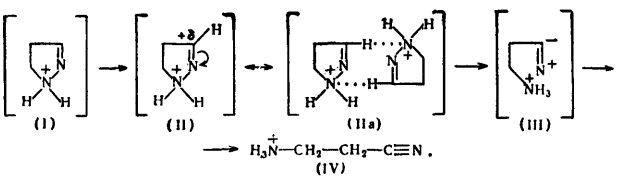
The analogous fission of the N–N bond with formation of a nitrile group is also known in the cyclic analogues of aldehyde hydrazones, the pyrazolines.

In 1962 Grandberg and Potapova found[12] that when heated to 230° 4-ethyl-5-propylpyrazolinium chloride decomposes to yield 3-amino-2-ethylhexanenitrile. This reaction has also been observed[13] with a number of other pyrazolines containing a hydrogen atom in position 3:.



Protonation of the 1-nitrogen atom therefore produces the same rearrangement, with cleavage of the N–N bond, as complex-formation with copper(I) chloride in Arbuzov's experiments. The reaction is highly exothermic, and with large amounts of material can get out of control.

The pyrazolinium cation (I) formed by the acid is considered[13] to undergo a redistribution of electron density:

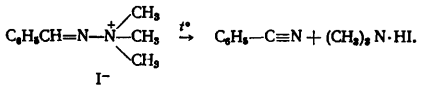


$$\longrightarrow H_3\overset{+}{N}-CH_2-CH_2-C\equiv N.$$
(IV)

Because of the positive charge on the 1-nitrogen atom (for this is the salt-forming atom)[14], the electron pair forming the nitrogen–nitrogen σ bond is attracted towards the 1-nitrogen atom, and this causes a displacement of the electrons of the carbon–nitrogen double bond towards the nitrogen atom, leaving a residual positive charge on the 3-carbon atom; thus in the pre-rearrangement state, (II) or (IIa), the bond between the 3-carbon atom and the hydrogen atom is weakened, the the hydrogen is readily lost as a proton. The nitrogen–nitrogen bond is also weakened, because of the strong attraction of the electron pair towards the first nitrogen atom. In the rearrangement step the proton migrates from position 3 to the electron pair associated with the 1-nitrogen atom, and the nitrogen–nitrogen bond finally breaks to form the intermediate (III), which immediately rearranges to the β-aminonitrile cation (IV).

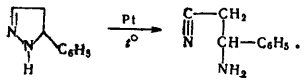
Under the very severe reaction conditions, the resulting β-aminonitriles partially lose ammonia to form αβ-unsaturated nitriles which polymerise during the reaction. These side-reactions greatly reduce the yield of β-aminonitrile, which does not exceed 25%. With 4,4-dimethyl--5-isopropylpyrazoline, where ammonia cannot be lost in this way, the yield reaches 36%.

A reaction similar to the nitrile fission of pyrazolinium chlorides is also possible with aldehyde dialkylhydrazones (when protonation or quaternation occurs on the farther nitrogen atom)[6]; thus pyrolysis of benzaldehyde dimethylhydrazonium chloride at 140° produces an exothermic reaction (the temperature rising to 230°) with the formation of benzonitrile (22%) and dimethylamine (48%), and pyrolysis of benzaldehyde dimethylhydrazone methiodide at 230° yields benzonitrile (21%) and trimethylamine (49%):

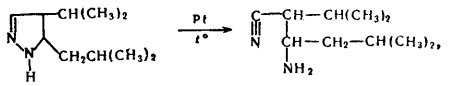


1,1-Dimethylpyrazolinium iodide also produces an aminonitrile when heated at 150° to 180° for a short time, but in low yield[15].

Colloidal platinum also causes rearrangement of 3-unsubstituted pyrazolines into aminonitriles[16]; thus heating 5-phenylpyrazoline to 140° with platinum black gave 3-amino-3-phenylpropanenitrile in 65% yield, instead of the expected mixture of pyrazole and pyrazolidine:



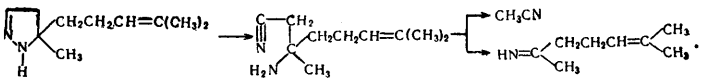
Similarly at 120–140° platinum produced 3-amino-2-isopropyl-6-methylhexanenitrile from 5-isobutyl-4-isopropylpyrazoline:



but the greater part of the material was converted into high-boiling condensation products. With 4-ethyl-5-propylpyrazoline the reaction is exothermic, with evolution of much ammonia, and the main reaction products are resinous materials, probably from polymerisation of the unsaturated nitrile formed.

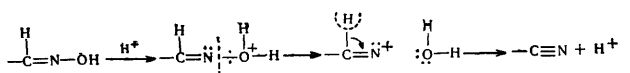
Attempts to carry out the rearrangement using a Raney nickel catalyst have been unsuccessful.

Kizhner has noted[17] that heating 5-isohexenyl-5-methylpyrazoline with platinised alkali gives acetonitrile and a methylheptenone imine in addition to the corresponding cyclopropane hydrocarbon. Apparently this anomalous reaction also passes through the β-aminonitrile stage, and under the severe reaction conditions this decomposes in the way that is known, for example, for Mannich bases[18]:



In addition to the substituted aldehyde hydrazones and pyrazolines, their oxygen analogues the aldoximes also produce nitriles under the action of acidic reagents.

Primarily this is a dehydration of aldoximes to nitriles by means of acids. The mechanism of the reaction is essentially analogous to that considered above for the nitrile fission of substituted aldehyde hydrazones and pyrazolinium chlorides, and may be represented[19]:

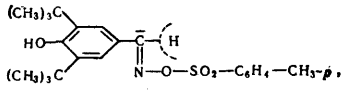


Unlike aldoximes themselves, their *O*-ethers are very stable; they are unaffected by aqueous or alcoholic hydrogen chloride or bromide or by 60% sulphuric acid[20], and like ketoxime *O*-ethers they do not undergo the Beckmann rearrangement[21], which is explained by their inability to form salts[22,23]. However, in the presence of a complex-forming reagent such as boron trifluoride, which can form an oxonium fluoroborate, it has been possible to decompose benzaldehyde oxime *O*-2-cyanoethyl ether into benzonitrile and 2-cyanoethanol[24]:

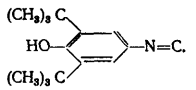
The addition products of aldoximes with methylketen diethyl acetal $CH_3CH_2C(OC_2H_5)_2$–O–N=CH–R decompose to form R–C≡N and R–N=C when boiled in ether with boron trifluoride and mercury(II) oxide[25].

In the course of their comparison of the nitrile rearrangements of oximes and hydrazones, Grandberg and coworkers[6] obtained benzonitrile from benzaldehyde oxime *O*-benzyl ether under Arbuzov reaction conditions (210°, Cu_2Cl_2).

Müller and Narr[26] observed a new type of Beckmann rearrangement from aldoxime *p*-tolylsulphonates such as



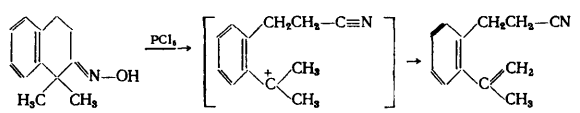
which when prepared in absolute alcohol at -30° gave *p*-toluenesulphonic acid and a 72% yield of the isonitrile



Depending on the mesomeric, inductive, and steric effects of the substituents on the benzene ring, the tolylsulphonates *syn*-Ar–CH=N–OT either ionise at the N–O bond with subsequent rearrangement, leading to formation of the isocyanide ArNC, or lose the proton from the CH-group, giving the nitrile ArCN, or undergo both conversions.

Many investigators have indicated the similarity of the nitrile rearrangements of substituted aldehyde hydrazones[6,16,27] and 3-unsubstituted pyrazolines[6,16] to the Beckmann rearrangement of the second type. This rearrangement is particularly characteristic of α-hydroxyketone oximes, monoximes of certain aliphatic-aromatic α-diketones, aromatic ketoximes containing a tertiary carbon atom in the α-position to the oxime group, and some oximes of cyclic ketones. Information on this rearrangement, which also involves cleavage of an N–O bond and formation of a nitrile, may be found in reviews[28,29].

Conley and Lange[30] recently demonstrated the intermediate formation of carbonium ions in this reaction, using the rearrangement of cyclic ketoximes under the influence of phosphorus pentachloride:

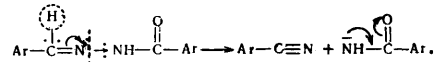


The carbon–carbon bond splits heterolytically, with formation of a carbanion at the carbon atom of the C=N double bond and a carbonium ion at the quaternary carbon atom, the latter being stabilised by elimination of a proton. The overall process is thus similar to a fragmentation reaction[31].

3. NITRILE REARRANGEMENTS PRODUCED BY NUCLEOPHILIC REAGENTS

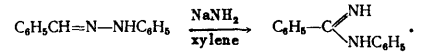
Naumov and coworkers[11] have established that substituted aldehyde hydrazones also decompose into nitrile and amine when heated to 260–290° with a catalytic amount of solid potassium hydroxide or sodium amide, thus benzaldehyde phenylhydrazone produces benzonitrile and aniline‡. Similarly benzaldehyde diphenyl-, acetyl-, and benzoyl-hydrazones decompose to give benzonitrile with diphenylamine, acetamide, and benzamide respectively. Fission produced by solid alkalis proceeds more smoothly than with copper(I) chloride, but yields are about the same.

The reaction apparently proceeds by β-elimination: the hydroxyl or amido-group attacks the "aldehydic" hydrogen atom, and the deprotonisation increases the polarisation of the nitrogen–nitrogen bond, which when heated splits anionically. The reaction is thus apparently heterolytic:



Nitrile fission produced by alkalis is not characteristic of aldehyde mono- or di-alkylhydrazones; as Todd[33] showed, monoalkylhydrazones decompose when heated with solid potassium hydroxide with evolution of nitrogen (as in the Kizhner reaction). On the other hand, benzaldehyde dimethyl- and diethyl-hydrazones are stable to solid alkalis[6,11,33].

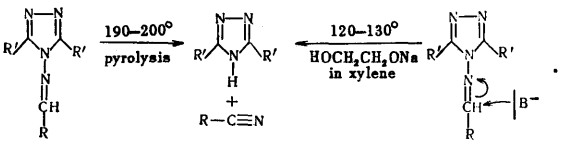
A particular conversion of aldehyde phenylhydrazones involving cleavage of the nitrogen–nitrogen bond is the Robev amidine rearrangement. In 1954 Robev found[34,35] that phenylhydrazones of aromatic aldehydes rearrange to amidines when heated to 140–145° with sodium amide in xylene:



Under the reaction conditions the amidine is partially decomposed into aniline and the nitrile, and this reaction goes to completion at a more elevated temperature[36]. Since aromatic amines and nitriles are known to produce *N*-phenylamidines by the action of sodium amide in xylene[37], the amidine rearrangement might have been thought to proceed by initial decomposition of the hydrazone into amine and nitrile followed by reaction between the latter[36,38]; however, it has recently been decisively established[39–43] that the reaction involves homolytic cleavage of the N–N bond, and is not a nitrile fission of the type under review.

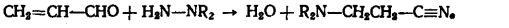
Hodgkins and King[44] observed the formation of benzonitrile in the photochemical decomposition of benzaldehyde azine in the presence of benzophenone, and thought it to involve a radical mechanism, the intermediate azine being reduced to benzaldehyde phenylhydrazone which then undergoes the nitrile fission.

Becker and Timpe have recently found[45] that the azomethines formed from aromatic or heterocyclic aldehydes and 4-amino-1,2,4-triazole decompose into 1,2,4-triazole and the corresponding nitrile when heated to 190–200°. Kinetic studies showed the reaction to be catalysed by bases, and in accordance with this the decomposition temperature in the presence of a base ($HOCH_2CH_2ONa$) is somewhat lower (120–130°) than in pure pyrolysis:

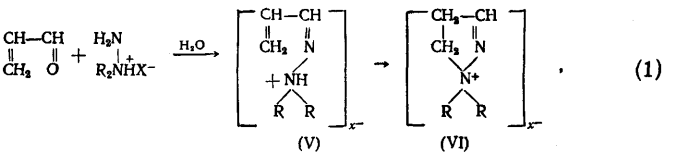


This was proposed as a preparative reaction for various nitriles (other than-aliphatic§), giving yields of up to 85%.

In 1960 Ioffe and Zelenin found[46] that the condensation of acrolein with unsymmetrical dimethyl- or diethyl-hydrazine in the cold in a weakly acid medium gives not the expected unsaturated *NN*-dialkylhydrazones, but β-dialkylaminopropionitriles:



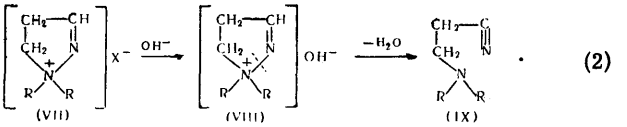
Under the same conditions αβ-unsaturated ketones produce only the stable dialkylhydrazones[47]. In 1962 these workers showed[15,38,48–50] that their formation of β-dialkylaminopropionitriles proceeds by cyclisation of the acrolein and unsymmetrical dialkylhydrazine to produce a pyrazolinium salt:



(1)

(V) (VI)

followed by decomposition of the quaternary pyrazolinium base (by addition of alkali at room temperature):



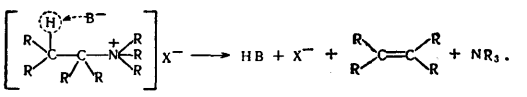
(2)

(VII) (VIII) (IX)

The structure of the quaternary pyrazolinium salt (VII; R = CH_3) was proved by cross-synthesis from methylhydrazine and acrolein. Addition of 50% NaOH to a concentrated aqueous solution of 1,1-dimethylpyrazolinium iodide causes immediate separation of β-dimethylaminopropionitrile, scheme (2) with R = CH_3, X = I. Several other 1-methylpyrazolinium iodides substituted in positions 1, 4, and 5 decompose analogously[38].

Ioffe and Zelenin concluded that the aminonitrile rearrangement of quaternary pyrazolinium salts proceeds analogously to the Hofmann degradation of quaternary ammonium bases.

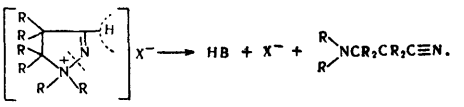
The structural feature characteristic of compounds which undergo this type of rearrangement is the presence of a quaternary nitrogen atom and a hydrogen atom in position 3, that is, in the β-position relative to the quaternary atom. Quaternary ammonium compounds are known to decompose under the action of bases:



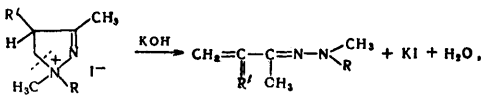
‡ Wolf[32] heated benzaldehyde phenylhydrazone with alcoholic sodium ethoxide at 165° for 20 h and obtained aniline (57%) and benzoic acid (89%). Benzonitrile may have been produced initially.

§ Aliphatic aldehydes give alkylidenebisamines with 4-amino-1,2,4-triazole, and not azomethine derivatives[45].

With quaternary pyrazolinium salts there is an initial abstraction of the proton at the C=N double bond produced by the action of the base (alkali), and then formation of the C≡N bond:

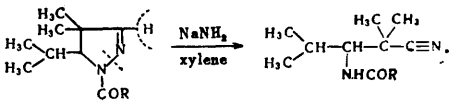


3-Substituted quaternary pyrazolinium salts, for which the aminonitrile rearrangement is impossible, invariably decompose by opening of the ring at the nitrogen–carbon bond, with formation of unsaturated *NN*-dialkylhydrazones[51]:

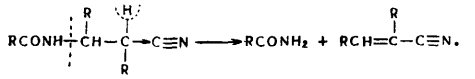


where (R = CH_3 or C_2H_5; R′ = H or CH_3). The reaction is carried out by heating with the solid potassium hydroxide to 130–160°, that is, to a considerably high temperature than is required by the aminonitrile rearrangement. However, these conditions are the same as for the Hofmann degradation of other hydrogenated nitrogen-containing heterocyclic compounds (pyrrolidine, piperidine, etc.)[52,53].

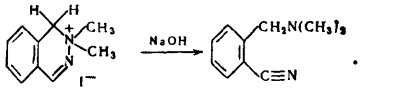
Naumov and coworkers have found[11] that 3-unsubstituted 1-acyl- (including 1-benzoyl- and 1-benzenesulphonyl-) pyrazolines can also produce the corresponding acylaminonitriles when heated with sodium amide in xylene:



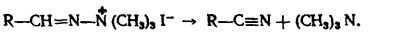
If position 4 of the pyrazoline ring carries a hydrogen atom a further degradation becomes possible:



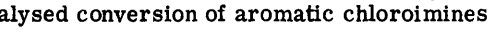
In 1962 Smith and Otremba observed[54] that 2,2-dimethyl-1,2-dihydrophthalazinium iodide is converted into *o*-dimethylaminomethylbenzonitrile by treatment with an aqueous solution of sodium hydroxide:



On the assumption that this is a general reaction for *NNN*-trimethylhydrazinium salts obtained from aldehydes, Smith and Walker studied it in some detail[55], and showed that the quaternary salts derived from the dimethylhydrazones of various aldehydes (aliphatic, aromatic, and unsaturated) are smoothly converted into the corresponding nitriles by treatment with a methanol solution of sodium methoxide



Smith considered his reaction to have an affinity with the base-catalysed conversion of aromatic chloroimines into nitriles:



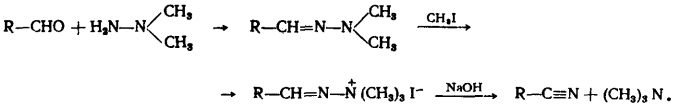
described in 1930 by Hauser and Gillaspie[56], that is, β-elimination occurs, and it differs from the chloroimine reaction only in the group which is eliminated.

Smith and Walker studied the behaviour of quaternary aldehyde hydrazonium salts in aqueous solution. The salts derived from aromatic aldehydes with electron-accepting substituents underwent slow β-elimination when the solutions were boiled for 6–8 h; the trimethylhydrazonium iodides obtained from *o*-nitro-, *m*-nitro-, and *o*-chlorobenzaldehyde gave the corresponding nitriles in yields of 75, 45, and 82% respectively. On the other hand, analogous treatment of benzaldehyde derivatives led to a recovery of 47% of the starting material, together with a mixture of benzaldehyde and benzonitrile. The quaternary *p*-dimethylaminobenzaldehyde hydrazonium iodide also underwent simultaneous elimination and hydrolysis when boiled in aqueous solution. Treatment of benzaldehyde derivatives with 1 *N* NaOH at room temperature caused rapid separation of an oil, which was also a mixture of benzonitrile and benzaldehyde.

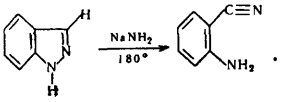
Hauser and coworkers[57] showed the conversion of aromatic chloroimines to nitriles to be of the second order kinetically.

Smith and Walker consider that the elimination reaction shown by the quaternary hydrazonium salts in water alone also proceeds by an E_2 mechanism, the water acting as the base. Under these conditions the elimination can be considered as proceeding by a mechanism similar to that of the decomposition of the trimethyl-2-(*p*-nitrophenyl)-ethylammonium ion to *p*-nitrostyrene in aqueous solution[58]; here electron-withdrawing substituents increase the acidity of the β-hydrogen atom and so facilitate the elimination. With the quaternary hydrazonium salts obtained from unsubstituted benzaldehyde or *p*-dimethylaminobenzaldehyde, the reduced acidity of the β-hydrogen atom enables hydrolysis to complete successfully with the β-elimination reaction. Smith and Walker find these results to be in accordance with those of Hauser and coworkers[57], who obtained relative rates of reaction of 1 : 7.7 : 540 for the sodium hydroxide-catalysed decomposition of chloroimines derived from benzaldehyde, *o*-chlorobenzaldehyde, and *o*-nitrobenzaldehyde.

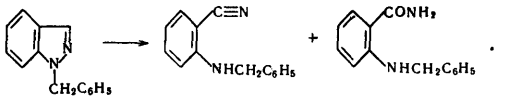
The alkaline fission of quaternary aldehyde hydrazonium salts was described almost simultaneously by other workers also[6,59-61]. It has also been proposed to use this reaction for the preparation of nitriles from aldehydes in yields of 40–80%[59]



Huisgen and coworkers observed[62] the formation of *o*-aminobenzonitrile when indazole is heated to 180° with sodium amide:

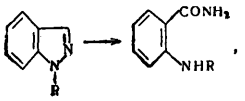


When attempting the amination of certain indazoles with alkali metal amides, Simonov and coworkers found[63] that the action of sodium amide and sodium hydroxide on 1-benzylindazole in xylene causes expansion of the pyrazole ring to a pyrimidine ring, and also ring opening with formation of the amide and nitrile of *N*-benzylanthranilic acid:



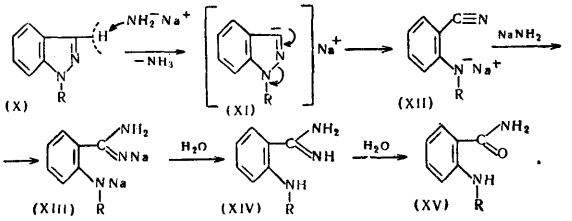
The same result is obtained in a current of ammonia and when thoroughly dry air is passed through the reaction mixture. 1-Benzylindazole reacts very readily with potassium amide in liquid ammonia[65], the main product being the nitrile of *N*-benzylanthranilic acid (67% yield).

The pyrazole ring is also opened when 1-alkylindazoles are heated with sodium amide in xylene in the presence of sodium hydroxide, with the formation of amides of *N*-alkylanthranilic acids in 40–50% yields[66]:



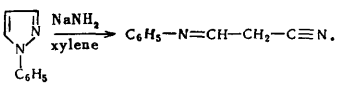
where R = CH_3, C_2H_5, n-C_3H_7 or iso-C_3H_7. Under the same conditions 1-butylindazole yields the nitrile of *N*-butylanthranilic acid in addition to the amide.

The ring is also opened when 1-arylindazoles react with sodium amide in xylene, producing nitriles, amides, or amidines of *N*-phenylanthranilic acid, depending on the structure of the aryl moiety[65]. Apparently[65] there is first a direct nucleophilic attack by the sodium or potassium amide on the hydrogen in position 3 of the pyrazole ring (X) (3-substituted indazoles do not react with sodium amide) with abstraction of a proton, liberation of ammonia and formation of the unstable sodium derivative (XI). After this, or at the same time, there is a redistribution of electron density around the ring, leading to weakening and then cleavage of the N–N bond with formation of the nitrile (XII):

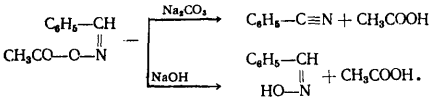


The nitrile (XII) adds on sodium amide at the nitrile group to give the sodium salt of the corresponding amidine (XIII) which, when water is added to the reaction mixture after the reaction, is readily hydrolysed to the amide of the corresponding *N*-substituted anthranilic acid (XV).

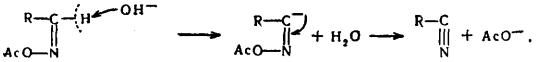
Recently Bobrova achieved the opening of the pyrazole ring itself[67]; when 1-phenylpyrazole and certain other 3-unsubstituted pyrazoles are heated with sodium amide in xylene the N–N bond opens to form the corresponding β-iminonitriles:



Aldoximes and their derivatives can also undergo nitrile fission of the N–O bond by the action of alkaline substances. Hantsch showed[68] that in addition to alkaline hydrolysis, acetyl β-benzaldehyde oxime can undergo fission of the N–O bond under the action of sodium carbonate in the cold:

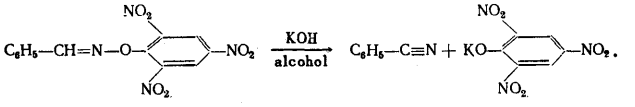


Benger and Brady.[69] studied this reaction with many acetylated aromatic β-aldoximes and showed that the nitrile may be formed as follows:



They consider that the deprotonisation under the action of the nucleophilic reagent leads to a redistribution of electron density and rupture of the N–O bond.

Unlike the acetylated oximes, the alkyl *O*-ethers are very stable, and even withstand boiling with 2 *N* NaOH.[20] However, benzaldehyde oxime *O*-2,4-dinitrophenyl ether[70] and benzaldehyde oxime *O*-2,4,6-trinitrophenyl ether[71] decompose to produce benzonitrile when boiled with alcoholic alkali:



In the 1930's it was suggested independently by several workers that when a molecule HX (where X is halogen, acetoxy, etc.) is split off from certain organic compounds by the action of bases a proton is first abstracted, followed by liberation of X with a full octet of electrons. This mechanism was suggested by Drake and McElvain[72] for the removal of hydrogen bromide from ethyl β-bromopropionate in the presence of piperidine, and by Mills[73] for the removal of acetic acid from β-aldoxime acetates in the presence of alkali.

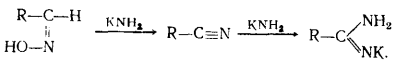
According to Hauser and coworkers[57,74], the removal of hydrogen chloride from aldochlorimines by various bases, and the splitting of benzaldehyde oxime di- and tri-nitrophenyl ethers observed by Brady[70,71], also proceed by the same mechanism.

O-Alkyl ethers of aldoxomes are converted into nitriles by the action of potassium amide in liquid ammonia[75]. The *O*-benzyl ether of α-benzaldehyde oxime decomposes into benzonitrile (some benzamide is also formed) and benzyl alcohol when heated with fused potassium hydroxide[76].

Jordan and Hauser had earlier found[77] that certain *anti*-aldoximes in solution in 2 *N* NaOH at 97–100° are slowly converted into a mixture of the corresponding carboxylic acids and the isomeric *syn*-aldoximes; the latter are also slowly converted into carboxylic acids. It was suggested that the carboxylic acids are formed by hydrolysis of the nitriles produced as intermediates in the dehydration of the *anti*-aldoximes.

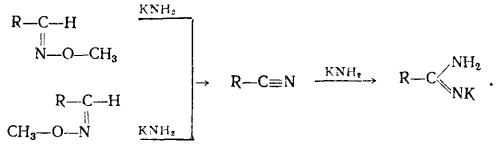
Vermillion and Hauser investigated the action of potassium amide on certain *syn*- and *anti*-aldoximes and their *O*-methyl ethers and acetyl derivatives[75].

After 9 d in a sealed tube with potassium amide in liquid ammonia at room temperature, *anti*-4-methoxybenzaldehyde oxime produces 4-methoxybenzamidine (48%) and 4-methoxybenzamide (15%). Under the same conditions the corresponding *syn*-aldoxime is apparently partly decomposed, but no products were isolated. The formation of the amidine from the *anti*-aldoxime is apparently due to the loss of water with formation of the nitrile, which then reacts with the potassium amide:



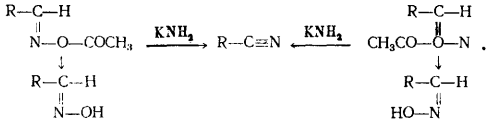
In fact, the nitriles are rapidly converted into amidines in the presence of potassium amide in liquid ammonia. The amides are probably produced by hydrolysis of the amidines, and possibly also directly from the nitriles by reaction with the potassium hydroxide produced by the action of potassium amide with the water split off from the *anti*-aldoximes.

Vermillion and Hauser also found that in the presence of potassium amide in liquid ammonia the *O*-methyl ethers of both *syn*- and *anti*-4-methoxybenzaldehyde oximes split off the elements of methanol to form 4-methoxybenzonitrile, which under the reaction conditions is completely or partially converted into the corresponding amidine:



With reaction for 2 h in the presence of 1.28 equiv. potassium amide, the *anti*-ether is fully decomposed, but the *syn*-ether only partially; the removal of the elements of methanol proceeds more readily from the *anti*-form than from the *syn*-form of the ether, as would be expected. The elimination from the *anti*-ether may be substantially complete within a few minutes. With 3 equiv. of potassium amide, the *syn*-ether is fully decomposed in 4 h, giving the amidine in a yield of ~ 90%.

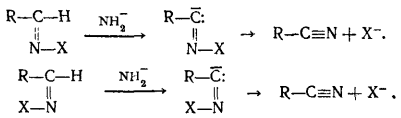
The acetyl derivatives of *syn*- and *anti*-benzaldehyde oximes react with potassium amide in liquid ammonia to form a mixture of the nitrile with the corresponding benzaldehyde oxime:



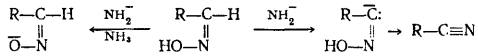
With reaction for 10 min at -33° *anti*-4-methoxybenzaldehyde oxime acetate gave yields of nitrile and aldoxime of 87% and 4% respectively; the corresponding *syn*-compound gave nitrile and aldoxime yields of 25% and 61% respectively. As would be expected, the yields of nitrile from the *anti*-acetates are higher, and the yields of aldoximes lower, than from the isomeric *syn*-acetates. It is of interest that the *syn*-acetates are not isomerised into the *anti*-forms by the action of potassium amide in liquid ammonia, and consequently the formation of nitriles from the *syn*-acetates is the result of direct removal of the elements of acetic acid, without preliminary isomerisation into the *anti*-acetates.

As compared with sodium hydroxide, which reacts with most *syn*-acetates to form substantially only the *syn*-aldoximes, potassium amide allows more of the β-elimination and less of the hydrolysis, giving a considerable amount of nitrile with *syn*-acetates also.

Vermillion and Hauser consider that the loss of HX from *syn*- and *anti*-aldoximes and their *O*-methyl ethers and acetyl derivatives by means of potassium amide is caused by attack by the base on the aldehydic hydrogen, which comes off as a proton; this is followed by the elimination of X as the anion with formation of the nitrile:

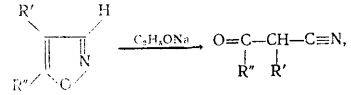


The elimination of water from an *anti*-aldoxime in the presence of potassium amide may be represented as follows:



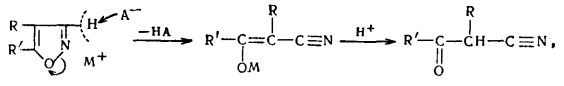
Here the base undoubtedly reacts with the hydroxyl hydrogen to give the aldoxime salt, but this salt is in equilibrium with unchanged aldoxime. This dehydration by means of bases is of particular interest since it proceeds by abstraction of the proton attached to carbon, although this proton is less active than that attached to the oxygen.

The cyclic analogues of the aldoximes — the 3-unsubstituted isoxazoles — can undergo ring-opening to form ketonitriles by the action of nucleophilic reagents, under conditions very similar to those of the aminonitrile rearrangement of quaternary pyrazolinium and aldehyde hydrazonium salts:



where R', R" = H, alkyl, aryl, etc.

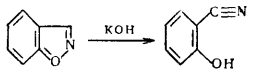
The nucleophilic opening of the isoxazole ring has been much studied[78-80]. Its mechanism involves initial abstraction of a proton from the 3-carbon atom followed by the substantially irreversible isomerisation of the resulting ion into the enolate ion of the end-product[78,80]:



where M = Na, K; A = OH^-, OR^-, NH_2^-.

Pino and coworkers showed that this reaction goes to completion, and is of the first order[81].

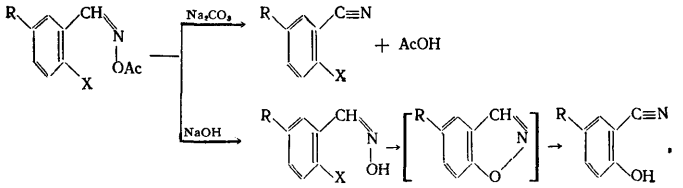
4,5-Benzoisoxazole is particularly unstable towards alkalis; when dissolved in potassium hydroxide it decomposes to salicylonitrile[82]:



The same product is obtained when 4,5-benzoisoxazole is heated[83].

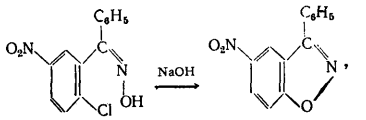
Treatment of the acetyl derivative of 2-chloro-5-nitro-β-benzaldehyde oxime with sodium carbonate eliminates acetic acid, with formation of the corresponding nitrile[84]. The action of sodium hydroxide on this oxime (and on 2-chloro-, 2-bromo- and 2-iodo-β-benzaldehyde oxime[85])

converts it into the nitrile, the halogen atom being replaced by the OH group. The reaction proceeds through the intermediate formation of the 3-unsubstituted nitrobenzoisoxazole, which here is unstable and cannot be isolated:



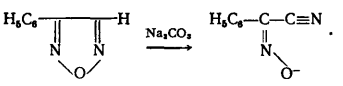
where R = H, NO_2; X = Cl, Br, I.

The action of sodium hydroxide on 2-chloro-5-nitrobenzophenone oxime produces 5-nitro-3-phenylbenzoisoxazole[86]:

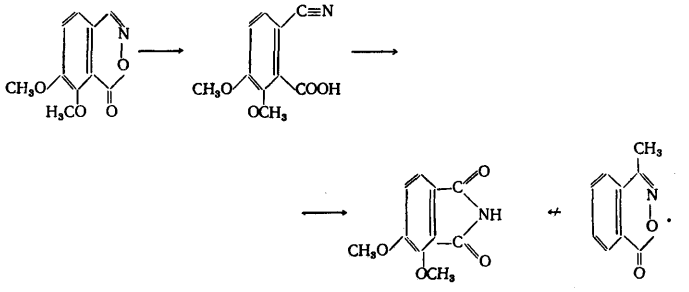


but this does not undergo further rearrangement, since the hydrogen atom in position 3 has been replaced by the phenyl group.

Furazans decompose analogously to the isoxazoles[87], cyanoketoximes being obtained even by the action of sodium carbonate solution:



Brady and coworkers have observed similar reactions in the benzo[*d*]oxazine ring[88]; the anhydride of the oxime of opianic acid forms the nitrile on gentle heating and the imide 3,4-dimethoxyphthalic acid on further heating:

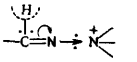


Under comparable conditions 4-methylbenzo[*d*]oxazin-1-one does not give the phthalimide, since the methyl group occupies the position of the hydrogen atom on the C=N double bond, and the formation of the nitrile is impossible.

4. STRUCTURAL FACTORS DETERMINING THE POSSIBILITY OF NITRILE REARRANGEMENTS

As is seen from the material above, the nitrile fission of N–N, N–O, and N–Cl bonds has been observed under very diverse experimental conditions. Most frequently the rearrangement requires the action of a strong nucleophilic reagent, and the part played by such a reagent is clear: it causes deprotonation of the aldehydic carbon atom and so facilitates or induces the reaction.

The nitrile rearrangement occurs only in compounds in which the N–N (or N–O) bond is strongly polarised[11,76]. This polarisation is strongest in compounds containing a quaternary nitrogen atom, such as quaternary pyrazolinium[15,38,48-50], dihydrophthalazinium[54] and hydrazonium salts[6,55,59-61], which are typically ionic compounds carrying a full positive charge on the terminal nitrogen atom of the grouping $-CH=N-\overset{+}{N}<$. This charge attracts towards itself the pair of σ electrons forming the N–N bond, that is, it induces polarisation of the nitrogen–nitrogen bond, which in its turn produces a considerable shift of the π electrons of the C=N double bond, which leads to increased lability of the proton on the carbon atom:



The deprotonation proceeds readily in aqueous alkaline solution, by the action of the hydroxide ions. As a result of this twofold action (polarisation of the N–N bond and the action of the nucleophilic reagent) nitrile fission proceeds very readily, usually at room temperature.

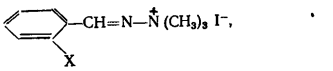
It is of interest to note here that where there is a single action (thermal fission of quaternary hydrazonium or pyrazolinium salts or pyrazolinium chlorides) the reaction requires much more severe conditions[6,12,13,15].

In other instances the necessary polarisation of the N–N bond is produced by including some cationoid activity on the terminal nitrogen atom, by substituting it with electron-withdrawing groups (phenyl, acetyl, benzoyl, etc.) or by increasing this cationoid activity by means of complex-forming agents, or by protonisation.

In particular, for nitrile fission of substituted aldehyde hydrazones of structure RCH=N–NR′R″, the substituents R′ and R″ may be groups which facilitate polarisation and cleavage of the N–N bond under the experimental conditions; however, if R′ = R″ = CH_3, the +*I*-effect of the methyl groups prevents this polarisation (hence benzaldehyde dimethylhydrazone is stable to boiling with solid potassium hydroxide or sodium amide[6,11,33]).

Activation of the $-CH=N-N<$ (or $-CH=N-O-$) grouping may generally be accomplished in two ways, since the ease with which it dissociates increases (*i*) with the strength of polarisation of the N–N (or N–O) bond, and (*ii*) with the ease of deprotonation of the carbon atom in the β position to the sp^3 nitrogen atom. The former is best achieved by creating the maximum positive charge on the sp^3 nitrogen atom; the influence of this charge is then transmitted through the C=N double bond and facilitates deprotonation of the carbon atom.

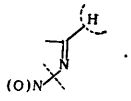
The deprotonation is also facilitated by the introduction of electron-accepting groups near this carbon atom, as in shown, in particular, by the data of Smith and Walker[55] who, as mentioned above, established that quaternary hydrazonium salts of the formula



containing an electron-accepting substituent in the benzene ring (X = NO_2 or Cl), this substituent increasing the acidity of the β-hydrogen atom, form the corresponding benzonitrile even when boiled in aqueous solution. However, the unsubstituted compound, or one containing an electron-donating group such as *p*-dimethylamino, undergo hydrolysis as well as β-elimination, to give a mixture of nitrile and aldehyde.

We have already remarked that the presence of electron-accepting substituents in the benzene ring of aromatic chloroimines also increases the rate of their nitrile fission[57] and, finally, it is known that the introduction of electron-accepting substituents (for example, the nitro-group) into position 4 of the isoxazole ring greatly increases its reactivity towards alkaline reagents[89,90].

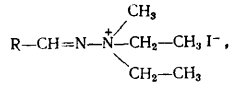
In considering the nitrile fission of oximes and their *O*-substituted derivatives, it must be borne in mind that trans-elimination is the more easily achieved, that is, the *anti*-isomers are the more reactive. We note that in the fission of the pyrazoline, pyrazole, or isoxazole ring, the structure of the heterocycles is such that it is trans-elimination which occurs here also:



The similarity between the nitrile rearrangement of quaternary pyrazolinium and aldehyde hydrazonium salts and the Hofmann degradation of quaternary ammonium bases has been repeatedly remarked[6,11,38,54,61].

Ioffe and coworkers have noted[51,61] that although the aldehyde hydrazonium salts which they investigated contained two ethyl groups (they used diethylhydrazones), which are the most readily removed in the Hofmann degradation, they never observed the formation of ethylene; consequently, the nitrile formation proceeds much more readily than the Hofmann decomposition with elimination of the β-hydrogen atom in the structure $CH_3-CH_2-\overset{+}{N}\!\!<$.

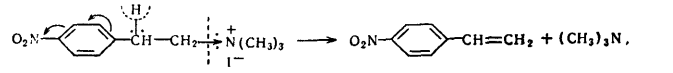
In compounds of the structure



the positive charge on the quaternary nitrogen atom causes strong polarisation of the C–$\overset{+}{N}$ bonds and the N–$\overset{+}{N}$ bond. Naturally, insofar as the molecule is potentially able to undergo either nitrile formation or Hofmann degradation, the β-elimination will occur in the direction in which the β-hydrogen atom is most readily removed. Clearly, the effect of the positive charge on the nitrogen atom is much more readily transmitted across the C=N double bond to the aldehydic hydrogen atom than to the β-hydrogen atoms of the ethyl groups, and this is why the nitrile rearrangement is the reaction that occurs here, and, for the same reasons, why quaternary pyrazolinium salts carrying β-hydrogen atoms in both position 3 and position 4 undergo nitrile formation and not Hofmann degradation.

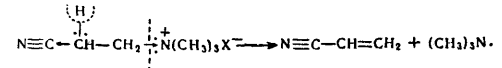
Even electron-accepting groups (nitrile or phenyl) in the β position of the ethyl radical in quaternary *N*-ethylpyrazolinium salts do not facilitate the Hofmann degradation of the C–N bond; here also the pyrazoline ring opens, with formation of β-dialkylaminopropionitriles[91].

Nevertheless, instances are known where the Hofmann degradation of quaternary ammonium bases proceeds as readily as the aminonitrile rearrangement, when the structure of the compounds is such that elimination of the β-hydrogen atom is facilitated. Thus salts of quaternary ammonium bases containing the phenylethyl group decompose when heated with aqueous alkali[92-94]. Moreover, according to von Braun[95], steam distillation of trimethyl-(2-phenylethyl)ammonium hydroxide causes it to decompose almost quantitatively to give styrene. However, aqueous solutions of trimethyl-(3-phenylpropyl)ammonium and other ammonium hydroxides in which the phenyl radical is further removed from the β-hydrogen atom can be evaporated on a water-bath with no sign of decomposition. Finally, trimethyl-2-(*p*-nitrophenyl)ethylammonium iodide readily decomposes to produce *p*-nitrostyrene even in aqueous solution[58]:

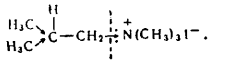


This is because of the influence of the *p*-nitrophenyl group adjacent to the β-carbon atom; the inductive and electromeric effects of this group both act in the same sense, greatly facilitating elimination of the β-hydrogen atom.

In quaternary ammonium salts derived from β-dialkylaminopropionitriles, removal of the β-hydrogen atom is facilitated by the inductive effect of the nitrile group; these salts readily undergo Hofmann degradation (in the presence of alkali at 100°):[96]



On the other hand, if the β-carbon atom carries alkyl groups, the rate of this reaction decreases[97], since the $+I$-effect of such groups compensates for the inductive effect of the positively charged nitrogen atom, and hinders elimination of the hydrogen atom:



Here, hydrolysis competes successfully with the β-elimination in an aqueous alkaline medium, so that the Hofmann degradation of such quaternary ammonium salts is usually carried out by heating with silver oxide or solid alkali.

The influence of inductive and electromeric factors on elimination reactions has been investigated by Hughes and Ingold[58,98]. An analogous analysis of the influence of structural factors provides an understanding of the possibility and varying ease of accomplishment of nitrile rearrangements.

1. A.E.Arbuzov, Ber., 43, 2296 (1910).
2. A.E.Arbuzov, Zhur.Russ.Fiz.-Khim.Obshch., 45, 74 (1913).
3. O.Anselmino, Ber., 36, 580 (1903).
4. A.Maihle, Compt.rend., 172, 1108 (1921).
5. A.Maihle, Bull.Soc.chim.France, [4], 29, 418 (1921).
6. I.I.Grandberg, A.N.Kost, and Yu.A.Naumov, Dokl.Akad. Nauk SSSR, 149, 838 (1963).
7. N.K.Kochetkov and L.A.Vorotnikova, Zhur.Obshch.Khim., 26, 1143 (1956).
8. R.S.Sagitullin and A.N.Kost, Vestnik Moskov.Gos.Univ., Ser.Khim., No.4, 187 (1959).
9. K.M.Dervinskaite, Diploma Work, Leningrad State University, 1963; referred to in the Candidate's Thesis of K.N.Zelenin, Leningrad State University, 1963.
10. R.S.Sagitullin, Candidate's Thesis, Moscow State University, Moscow, 1962.
11. Yu.A.Naumov, A.N.Kost, and I.I.Grandberg, Vestnik Moskov.Gos.Univ., Ser.Khim., No.1, 46 (1965).
12. I.I.Grandberg and A.V.Potapova, Zhur.Obshch.Khim., 32, 651 (1962).

13. I.I.Grandberg and G.A.Golubeva, Zhur.Obshch.Khim., 33, 244 (1963).
14. G.Duffin and I.Kendall, J.Chem.Soc., 408 (1954).
15. B.V.Ioffe and K.N.Zelenin, Dokl.Akad.Nauk SSSR, 144, 1303 (1962).
16. A.N.Kost, G.A.Golubeva, A.P.Terent'ev, and I.I.Grandberg, Dokl.Akad.Nauk SSSR, 144, 359 (1962).
17. N.M.Kizhner, Zhur.Russ.Fiz.-Khim.Obshch., 50, 1 (1918).
18. H.Hellmann and G.Optiz, "α-Aminoalkylierung: Darstellung und Eigenschaften der Kondensationsprodukte H-acider Stoffe mit Carbonylverbindungen und Aminen", Verlag Chemie, Weinheim, 1960, p.12.
19. J.Mathieu and A.Allais, "Cahiers de Synthèse Organique" (Translated into Russian), Inostr.Lit., Moscow, 1962, p.287.
20. O.L.Brady and L.Klein, J.Chem.Soc., 877 (1927).
21. O.L.Brady and F.P.Dunn, J.Chem.Soc., 2416 (1926).
22. L.Semper and L.Lichtenstadt, Ber., 51, 928 (1918).
23. M.Kuhara, N.Agatsuma, and K.Araki, Mem.Coll.Sci., Kyoto Univ., 3, 1 (1917); Chem.Abs., 13, 119 (1919).
24. T.Mukaiyama and T.Hata, Bull.Chem.Soc.Japan, 33, 1712 (1960); Ref.Zhur.Khim., 22Zh96 (1961).
25. T.Mukaiyama, K.Tonooka, and K.Inoue, J.Org.Chem., 26, 2202 (1961); Ref.Zhur.Khim., 6Zh147 (1962).
26. E.Müller and B.Narr, Z.Naturforsch., 16b, 845 (1961); Ref.Zhur.Khim., 19Zh100 (1962).
27. W.Theilacker and O.Leichtle, Annalen, 572, 121 (1951).
28. I.L.Knunyants and B.P.Fabrichnyi, "Reaktsii i Metody Issledovaniya Organicheskikh Soedinenii" (Reactions and Methods of Investigation of Organic Compounds), Vol.3, Goskhimizdat, Moscow, 1954, p.141.
29. L.G.Donaruma and W.Z.Heldt, Org.Reactions, 11, 1 (1960).
30. R.T.Conley and R.J.Lange, J.Org.Chem., 28, 210 (1963).
31. C.A.Grob, in "Theoretical Organic Chemistry", Papers presented to the Kekulé Symposium, London, 1958, Butterworths, London, 1959 (Translated into Russian), Inostr. Lit., Moscow, 1963, p.114.
32. L.Wolf, Annalen, 394, 106 (1912).
33. D.Todd, J.Amer.Chem.Soc., 71, 1353 (1949).
34. S.Robev, Compt.rend.Acad.bulg.Sci., 7, No.3, 37 (1954).
35. S.Robev, Dokl.Akad.Nauk SSSR, 101, 277 (1955).
36. S.Robev, Izv.Khim.Inst., Bulgar.Akad.Nauk, 3, 495 (1955).
37. F.Cooper and M.Partridge, J.Chem.Soc., 257 (1953).
38. B.V.Ioffe and K.N.Zelenin, Zhur.Obshch.Khim., 33, 3231 (1963).
39. S.Robev, Compt.rend.Acad.bulg.Sci., 13, No.2, 159 (1960).
40. S.Robev and D.D.Tsitovich, Compt.rend.Acad.bulg.Sci., 17, 737 (1964).
41. I.I.Grandberg, Yu.A.Naumov, and A.N.Kost, Zhur.Vses. Khim.Obshch.im.Mendeleeva, 9, 707 (1964).
42. I.I.Grandberg, Yu.A.Naumov, and A.N.Kost, Compt.rend. Acad.bulg.Sci., 17, 1025 (1964).
43. I.I.Grandberg, Yu.A.Naumov, and A.N.Kost, Zhur.Org. Khim., 1, 805 (1965).
44. I.E.Hodgkins and J.A.King, J.Amer.Chem.Soc., 85, 2679 (1963).
45. H.G.O.Becker and H.I.Timpe, Z.Chem., 4, 304 (1964); Ref.Zhur.Khim., 14Zh297 (1965).
46. B.V.Ioffe and K.N.Zelenin, Dokl.Akad.Nauk SSSR, 134, 1094 (1960).
47. B.V.Ioffe and K.N.Zelenin, Dokl.Akad.Nauk SSSR, 141, 1369 (1961).
48. B.V.Ioffe and K.N.Zelenin, Zhur.Obshch.Khim., 32, 1708 (1962).
49. B.V.Ioffe and K.N.Zelenin, Tetrahedron Letters, 11, 481 (1962).
50. B.V.Ioffe and K.N.Zelenin, "Tezisy Dokladov na Konferentsiyu po Pyatichlennym Azotistym Geterotsiklam, Rostov-na-Donu" (Abstracts of Papers Presented at the Conference on Five-Membered Nitrogen-Containing Heterocycles, Rostov-on-Don), 1962.
51. B.V.Ioffe and K.N.Zelenin, Dokl.Akad.Nauk SSSR, 154, 864 (1964).
52. A.C.Cope and E.R.Trumbull, Org.Reactions, 11, 317 (1960).
53. J.McKennan, Chem.and Ind., 406 (1954).
54. R.F.Smith and E.D.Otremba, J.Org.Chem., 27, 879 (1962).
55. R.F.Smith and L.E.Walker, J.Org.Chem., 27, 4372 (1962).
56. C.R.Hauser and A.G.Gillaspie, J.Amer.Chem.Soc., 52, 4517 (1930).
57. C.R.Hauser, J.W.Le Maistre, and A.E.Rainsford, J.Amer. Chem.Soc., 57, 1056 (1935).
58. E.D.Hughes and C.K.Ingold, Trans.Faraday Soc., 37, 659 (1941).
59. I.I.Grandberg, USSR P. 159508 (1962).
60. I.I.Grandberg, Zhur.Obshch.Khim., 34, 569 (1964).
61. B.V.Ioffe, Z.I.Sergeeva, and K.M.Dervinskaite, Zhur. Obshch.Khim., 33, 2794 (1963).
62. R.Huisgen, F.Wimmer, and K.Bast, cited in a review by R.Huisgen, Angew.Chem., 72, 371 (1960).
63. A.M.Simonov, B.K.Martsokha, and F.G.Pozharskii, Zhur. Obshch.Khim., 32, 2388 (1962).
64. A.M.Simonov, B.K.Martsokha, and F.G.Pozharskii, Zhur. Obshch.Khim., 33, 1001 (1963).
65. B.K.Martsokha, Candidate's Thesis, Rostov-on-Don State University, Rostov-on-Don, 1963.
66. B.K.Martsokha and A.M.Simonov, Zhur.Obshch.Khim., 33, 3777 (1963).
67. N.I.Bobrova, Diploma Work, Moscow State University, Moscow, 1964.
68. A.Hantsch, Ber., 24, 36 (1891).
69. M.Benger and O.L.Brady, J.Chem.Soc., 1221 (1950).
70. O.L.Brady and R.Truszkowski, J.Chem.Soc., 125, 1087 (1924).
71. O.L.Brady and L.Klein, J.Chem.Soc., 127, 844 (1925).
72. W.V.Drake and S.M.McElvain, J.Amer.Chem.Soc., 56, 699, 1810 (1934).
73. W.H.Mills, J.Soc.Chem.Ind., 51, 750 (1932).
74. C.R.Hauser and E.Moore, J.Amer.Chem.Soc., 55, 4526 (1933).
75. G.Vermillion and C.R.Hauser, J.Org.Chem., 6, 507 (1941).
76. Yu.A.Naumov, Candidate's Thesis, Moscow State University, Moscow, 1964.
77. E.Jordan and C.R.Hauser, J.Amer.Chem.Soc., 58, 1304 (1936).
78. A.Quilico, Atti Accad.naz.Lincei, Rend.Classe Sci.fis.mat. nat., 15, 357 (1953).
79. R.A.Barnes, "Isoxazoles", in "Heterocyclic Compounds. Vol.V. Five-Membered Heterocycles with Two Hetero Atoms and Their Benzo Derivatives" (Edited by R.C.Elderfield) (Translated into Russian), Inostr.Lit., Moscow, 1961, p.377.
80. N.K.Kochetkov and S.D.Sokolov, in "Advances in Heterocyclic Chemistry, Vol.2" (Edited by A.R.Katritzky and J.M.Lagowski), Academic Press, New York, 1963, p.398.
81. P.Pino, A.Scartabelli, and E.Lombardi, Rend.Inst.Lombardo Sci., Pt.I, Classe Sci.mat.nat., 87, 229 (1954); Chem.Abs., 49, 15397 (1955).
82. A.Conduche, Ann.Chim.Phys., [8], 13, 48 (1908).
83. H.Lindemann and H.Thiele, Annalen, 449, 67 (1926).
84. O.L.Brady and G.Bishop, J Chem.Soc., 127, 1357 (1925).
85. O.L.Brady, A.N.Kosson, and A.I.Roper, J.Chem.Soc., 127, 2427 (1925).
86. J.Meisenheimer, P.Zimmermann, and U.Kummer, Annalen, 446, 205 (1925).
87. A.Bussanow, Ber., 24, 3497 (1891).

88. O.L.Brady, L.C.Baker, R.F.Goldstein, and S.Harris, J.Chem.Soc., 529 (1928).
89. H.S.Hill and W.J.Hale, J.Amer.Chem.Soc., 29, 253 (1903).
90. A.Quilico and C.Musante, Gazzetta, 72, 399 (1942); Chem. Abs., 36, 771 (1942).
91. I.I.Grandberg and Yu.A.Naumov, "Khimiya Geterotsiklicheskikh Soedinenii" (Chemistry of Heterocyclic Compounds), Vol.2, 1965, p.307.
92. M.Freund, Ber., 32, 168 (1899).
93. R.Pschorr and C.Massacin, Ber., 37, 2780 (1904).
94. R.Pschorr and H.Einbeck, Ber., 38, 2067 (1905).
95. I.von Braun, Annalen, 382, 45 (1911).
96. A.P.Terent'ev, A.N.Kost, and S.M.Gurvich, Zhur.Obshch. Khim., 23, 615 (1953).
97. E.Müller, "Neuere Anschauungen der organischen Chemie" ["Organischen Chemie" (Edited by H.Bredereck and E.Müller), Vol.I] (Translated into Russian), Inostr.Lit., Moscow, 1960, p.548.
98. C.K.Ingold, "Structure and Mechanism in Organic Chemistry" (Translated into Russian), Inostr.Lit., Moscow, 1959, p.347.

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SELECTIVE REDUCTION OF ALIPHATIC NITRO-COMPOUNDS WITH OTHER FUNCTIONAL GROUPS

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CONTENTS

I. Introduction 19

II. Selective reduction of the nitro-group in aliphatic nitro-compounds with other functional groups 19
1. Reduction of nitro-alcohols to amino-alcohols 19
2. Reduction of alkyl ethers of nitro-alcohols to alkyl ethers of amino-alcohols 20
3. Reduction of nitro-ketones and nitro-aldehydes to amino-ketones and amino-aldehydes 21
4. Reduction of nitro-acids and their derivatives to amino-acids and derivatives 21
5. Reduction of nitro-nitriles to amino-nitriles 22
6. Reduction of nitro-amines to polyamines 23
7. Reduction of halogeno-nitro-compounds to halogeno-alkylamines 23
8. Selective reduction of nitro-groups in aliphatic sulphur-containing compounds 23
9. Reduction of nitro-alkynes to amino-alkynes 24
10. Reduction of nitro-alkenes to amino-alkenes 24
11. Reduction of nitro-groups in compounds with other functional groups 25

III. Selective reduction of functional groups in nitro-compounds 26
1. Catalytic reduction of functional groups in nitro-compounds 27
2. Chemical reduction of functional groups in nitro-compounds 27
3. Electrochemical reduction of functional groups in nitro-compounds 29

I. INTRODUCTION

In recent years there has been a great development of the chemistry of aliphatic nitro-compounds. The improvement of old and the discovery of new methods of synthesis has led to a sharp increase in the number of nitro-products that have become readily available; some of these are already produced on the industrial scale.

The nitroalkanes, which are now manufactured in tens of thousands of tons a year, are used as starting materials in the production of many aliphatic nitro-compounds.

In this connection, the attention of chemists has been increasingly attracted to the possibility of using nitro-derivatives of the aliphatic series for the needs of industry and agriculture, both directly and as a relatively cheap chemical material for the synthesis of various products with important applications.

Reduction occupies a special position in the chemical transformations of nitro-compounds. There is no need to dwell on the tremendous importance of this reaction in the aromatic series. However, the reduction of aliphatic nitro-compounds has been studied in a less detailed manner and the literature on this question has not been specially systematised. Isolated information on some particular problems may be found in a number of monographs and review articles on the nitro-compounds[1-7].

Since the question of the reduction of nitro-compounds containing other functional groupings in addition to the nitro-group is of fundamental chemical and pratical interest, only examples of selective reduction of aliphatic functional nitro-compounds will be considered in this review. This question is considered in two aspects. Thus, in the first part the reduction of the nitro-group to the amino-group without change of other functions is considered, and in the second the reduction of functional groups without changing the nitro-group.

It was not our purpose to produce an exhaustive review of all instances of selective reduction of nitro-compounds, and the material of the review has been selected in such a way as to illustrate the use of various reducing agents or catalysts, suitable for the selective (in the above sense) reduction of functional aliphatic nitro-derivatives.

II. SELECTIVE REDUCTION OF THE NITRO-GROUP IN ALIPHATIC NITRO-COMPOUNDS WITH OTHER FUNCTIONAL GROUPS

1. Reduction of Nitro-Alcohols to Amino-Alcohols

Of all aliphatic nitro-compounds, the reduction of the nitro-alcohols has been most fully studied. The leading motive of many investigations in this field is the wide use