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Monocyclic and cascade rearrangements of furoxans*

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Abstract: Monocyclic rearrangements of azoles are extensively studied as alternative methods for the preparation of new heterocyclic systems. The present work is devoted to investigation of monocyclic and cascade rearrangements of 1,2,5-oxadiazole 2-oxide (furoxan) derivatives. It was found during investigations that rearrangements of furoxan ring had some peculiarities in comparison with analogous rearrangements of other azoles. Therefore, three different kinds of rearrangements were found. The first of them occurred through a dinitrosoethylene intermediate and resulted in the synthesis of 1,2,3-triazole 1-oxides [oximes of 5-acetyl-4-phenyl(methyl)-2-phenyl-2*H*-1,2,3-triazole 1-oxides and 2-(furoxan-4-yl)-4-nitro-5-R-2*H*-1,2,3-triazole 1-oxides] by thermal recyclization accordingly of 3-methyl-4-acetyl(benzoyl)furoxans phenylhydrazones and 3,3′-(R)-disubstituted-4,4′-azofuroxans. The latter reaction was performed in an oxidizing medium. The second kind of rearrangement (classical variant) was the synthesis of new azoles containing the 1-nitroalkyl substituent. These rearrangements were performed using three examples: base-induced interconversion of furoxanyl ketone phenylhydrazones into 5-(1-nitroalkyl)-2*H*-1,2,3-triazole derivatives and of 1-alkyl(aryl)-3-(furoxan-4-yl)amidines into 1-substituted 3-(1-nitroalkyl)-1,2,4-triazoles as well as a thermally induced rearrangement of 4-thioureido-3-R-furoxans into derivatives of 5-amino-3-(1-nitroalkyl)-1,2,4-thiadiazole including (5-amino-1,2,4-thiadiazol-3-yl)nitroformaldehyde arylhydrazones (where R = N=N–Ar). Rearrangements of the third kind were those of the cascade type. Three new cascade rearrangements of azofuroxan derivatives [3,3′-azo-4,4′-bis(acetylamino)furoxans, 3-arylazo-4-acetylaminofuroxans, and 3-arylazo-4-(3-ethoxycarbonylureido)furoxans] into 4-amino-5-nitro-2*H*-1,2,3-triazole derivatives were discovered. These three reactions were assumed to include two consecutive (cascade) rearrangements: a 1,2,4-oxadiazole ring was formed at the first step and then transformed into a 1,2,3-triazole ring with the participation of an azo group.

INTRODUCTION

Ring-to-ring interconversion of heterocycles is an interesting area that continues to be of great importance in mechanistic studies and synthetic design [1]. An example of such reactions is azole-to-azole interconversion, which can be represented by generally accepted by A. J. Boulton and A. Katritzky [2,3] Scheme 1. The initial azole has a ring-conjugated side chain reacting as a nucleophile toward the pivotal annular nitrogen atom in the S_N^i-type reaction followed by the rupture of the adjacent bond to form a new azole. As a rule, monocyclic rearrangements are initiated thermally, photochemically, or in the

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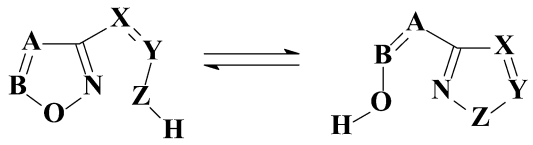
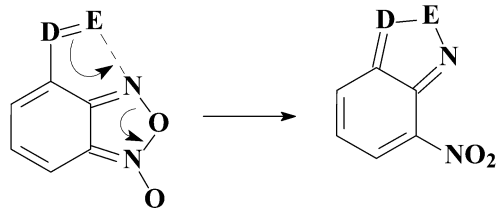


Scheme 1 General scheme of azole-to-azole interconversion.

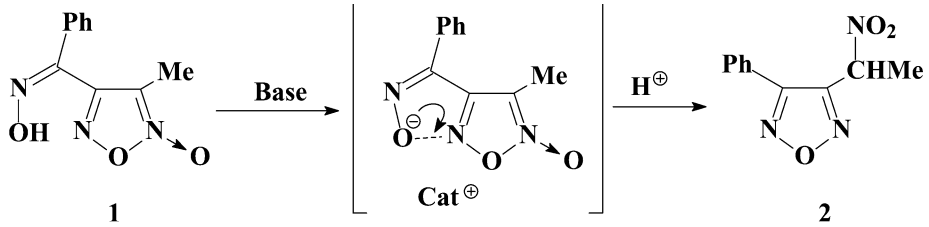
presence of bases and in some cases, they are reversible. Recently, the first example of acid catalysis in such a rearrangement was published [4].

This class of rearrangements, which covers many azole-to-azole interconversions, was reviewed in 1981 and defined as mononuclear heterocyclic rearrangements [5]. The corresponding rearrangements of benzo-fused systems have been discovered by A. J. Boulton and A. R. Katritzky and many rearrangements have been systematized [6–8]. A very important contribution in the study of azole-to-azole interconversions has been made by the Italian group of chemists headed by Prof. N. Vivona [1,5,9–12] and the Belgian group headed by Prof. G. L'Abbe [13–15].

The field of our scientific interest is the chemistry of 1,2,5-oxadiazole 2-oxides (furoxans) [16,17]. The ring transformation of furoxans has been studied in detail for benzo-fused derivatives (Boulton–Katritzky rearrangement) [6–8] (Scheme 2). Rearrangements of noncondensed furoxan derivatives have been described only for oximes of 4-furoxanylcarbonyl compounds [18–20]. In particular, the base-catalyzed rearrangement of *Z*-isomer of 4-benzoyl-3-methylfuroxan oxime **1** to 3-(1-nitroethyl)-4-phenyl-1,2,5-oxadiazole (furazan) **2** has been found [19] (Scheme 3).

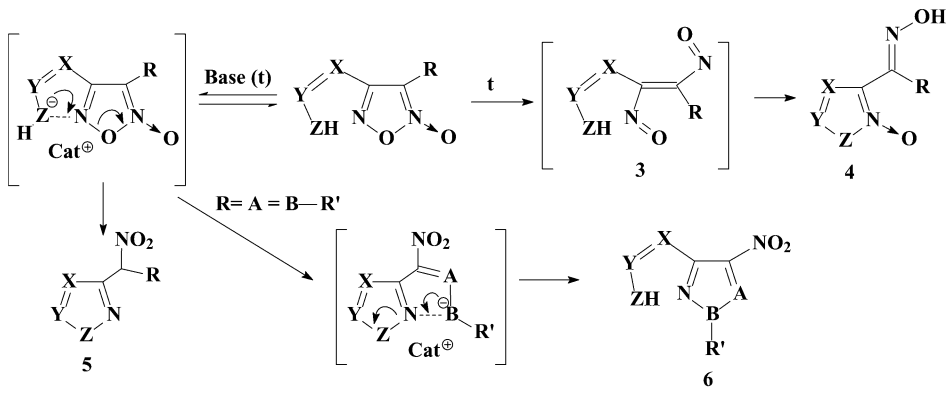


Scheme 2 Boulton–Katritzky rearrangement of benzofuroxans.



Scheme 3 Base-induced rearrangement of 4-benzoyl-3-methylfuroxan oxime **1**.

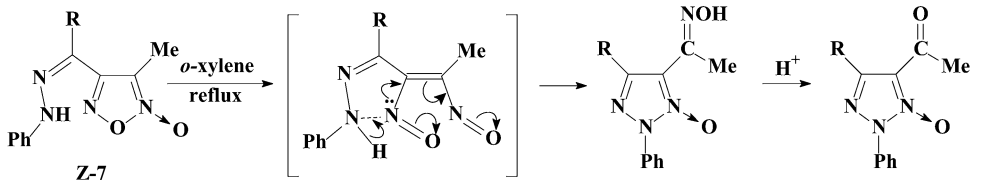
Meanwhile, noncondensed furoxan derivatives are very promising objects for a study of monocyclic rearrangements. Among different azoles, furoxans occupy a special place: (1) they tend to tautomerism occuring through the formation of the dinitrozoethylene intermediate **3** [21], which can react with the substituent resulting in *N*-oxides of azoles **4**; (2) they contain the "latent" nitro group inside of the ring, which allows 1-nitroalkyl-substituted azoles 5 to be obtained by a classical variant of rearrangements; and (3) two successive (cascade) rearrangements may be expected in the presence of an appropriate substituent (e.g., N=N) at the C(3) atom of the furoxan ring. In the last-mentioned case, nitroazoles **6** can be obtained (Scheme 4). In this work, we have investigated all three possible directions of the rearrangements of noncondensed furoxan derivatives.



Scheme 4 Possible directions of noncondensed furoxan derivatives rearrangements.

MONOCYCLIC REARRANGEMENTS OF FUROXAN DERIVATIVES THROUGH THE DINITROSOETHYLENE INTERMEDIATE

To perform rearrangements of this kind, first of all, 4-benzoyl-and 4-acetyl-3-methylfuroxan phenylhydrazones **7** were used as starting compounds [22]. Indeed, it was found that these compounds were capable of entering into monocyclic rearrangements, though the reaction outcome depended on the conditions used. The reactions were initiated either thermally or in the presence of various bases. The thermal rearrangement was performed by refluxing solutions of **7** in *o*-xylene; only *Z*-isomers of parent compounds **7** entered into the reaction. In both cases, oximes of 5-acetyl-4-phenyl(methyl)-2-phenyl-2*H*-1,2,3-triazole 1-oxide **9** were obtained. It is likely that the reaction began with the rupture of the O(1)-N(2) bond in the furoxan ring, which resulted in the formation of dinitrosoethylene intermediates **8** followed by the reaction of one nitroso group with the phenylhydrazone moiety to form 1,2,3-triazole 1-oxide and transformation of the another nitroso group into the oxime group. Taking benzofuroxans as examples, both nitroso groups in the dinitrosobenzene intermediate were trapped by appropriate traps [23]. Such reaction of both nitroso groups derived from a noncondensed furoxan derivative has been reported for the first time. The structures of the obtained compounds have been confirmed by different physicochemical methods. In the ^{14}N NMR spectrum, a signal of the 1-oxide nitrogen atom was detected only after the hydrolysis of the oxime groups to ketone groups with the formation of acetyl derivatives **10** (Scheme 5).



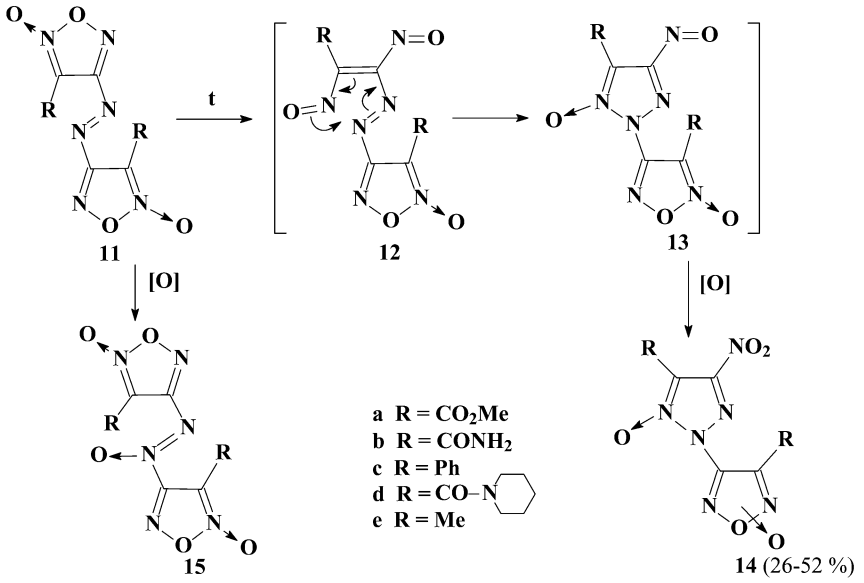
Scheme 5 Thermally induced rearrangement of furoxanylketones phenylhydrazones **7**.

Thus, even the first attempt to find new monocyclic rearrangements in the series of furoxan derivatives has resulted in the discovery of new rearrangement: thermally induced recyclization of phenylhydrazones **7** to oximes of 5-acetyl-4-phenyl(methyl)-2-phenyl-2*H*-1,2,3-triazole 1-oxides of type **9**.

The second example of the monocyclic rearrangement of furoxan derivatives through the dinitrosoethylene intermediate has been found in a thermally induced transformation of 3,3′-(R)-disubstituted-4,4′-azofuroxans **11** [24]. Test compounds contained no substituents capable of undergoing a

classical rearrangement. We believed that one of the furoxan rings opened to form the dinitrosoethylene intermediate **12** and the subsequent condensation of one of the nitroso groups with the azo group gave, according to ref. [25], 2-(furoxan-4-yl)-4-nitroso-5-R-2*H*-1,2,3-triazole 1-oxides **13** (Scheme 6).

The initial study was performed on the basis of azofuroxan **11a** as an example. We have found that refluxing of **11a** in ethyl acetate, toluene, or xylene resulted in a complete (or partial) decomposition of the parent compound depending on the boiling point of the solvent, or it recovered unchanged from the reaction mixture. Only refluxing of compound **11a** in trifluoroperacetic acid was successful: 5-(methoxycarbonyl)-2-(furoxan-4-yl)-4-nitro-2*H*-1,2,3-triazole 1-oxide **14a** was isolated as a reaction product. It is evident that under these conditions the nitroso group in intermediate nitroso compound **13a** was oxidized to the nitro group with the formation of nitro derivative **14a** (Scheme 6).



Scheme 6 Thermally induced rearrangement of azofuroxans **11** in an oxidizing medium.

The conditions found were used for the rearrangements of azofuroxans **11b–e**. We found that, in addition to the expected rearrangement with the formation of furoxanyltriazole 1-oxides **14**, the direct oxidation of the azo group in the parent azofuroxans to azoxy derivative **15** occurred in a number of cases; the character of substituent R affected the amount of this derivative. Thus, in the case of compound **11e** (R = Me), the formation of azoxy derivative **15e** became the predominant reaction path. In other cases, compounds **15** were formed in insignificant amounts; only compound **15b** was isolated. Use of peracetic acid was more appropriate for the conversion of diphenylazofuroxan **11c**. In this case, however, two isomers **14c** and **14c′** were isolated, which were different only in the position of the *N*-oxide oxygen atom in the furoxan ring: it was arranged on the side of the Ph fragment or the triazole ring in isomer **14c** and **14c′**, respectively. Evidently, due to a higher boiling point of peracetic acid compared to trifluoroperacetic acid, the furoxan ring in the resulting compounds underwent isomerization under reaction conditions; this isomerization is well known to occur also through the dinitrosoethylene intermediate [21].

The structure of new compounds **14** was determined using NMR spectroscopy, mass spectrometry, and an X-ray diffraction study. In these compounds, the molecular ion built up by 16 units because of the introduction of an additional oxygen atom. ^{14}N NMR spectroscopy played an important role; chemical shifts of the nitro- and azoxy groups were –30–32 and –66–68 ppm, respectively. An X-ray diffraction study was performed for rearrangement product **14b** (Fig. 1). It was found that com-

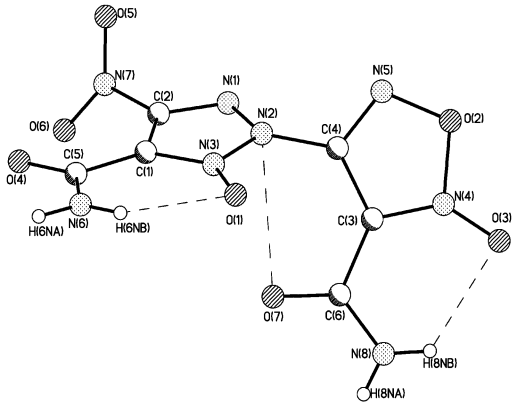


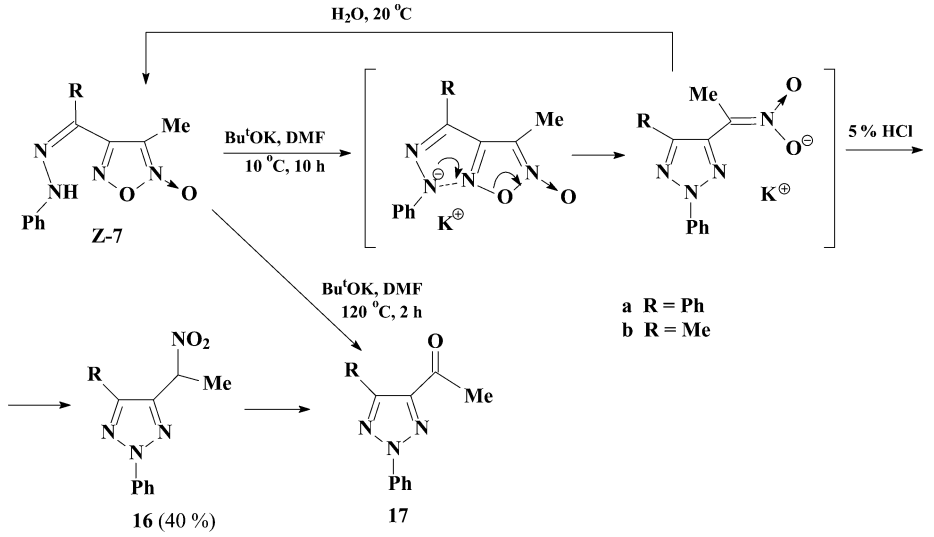
Fig. 1 The general view of compound **14b** structure.

pound **14b** included furoxan and 1,2,3-triazole rings arranged at the angle of 70.2°. The geometry parameters of compound **14b** differ significantly from those of previously described 1,2,3-triazole 1-oxide derivatives (e.g., see ref. [26]). This manifests itself in considerable differences between the N–N and N–C bond lengths (0.03 and 0.04 Å, respectively) and in the pyramidalization of the N(2) atom. The distance between the N(2) atom and the plane of N(1), N(3), and C(4) is 0.09 Å, which is maximum for not only this heterocycle, but also for all of the previously described 1,2,3-triazoles, in which a maximum deviation of the nitrogen atom is 0.05 Å, as found by statistical data.

MONOCYCLIC REARRANGEMENTS OF FUROXAN DERIVATIVES RESULTING IN 1-NITROALKYLAZOLES

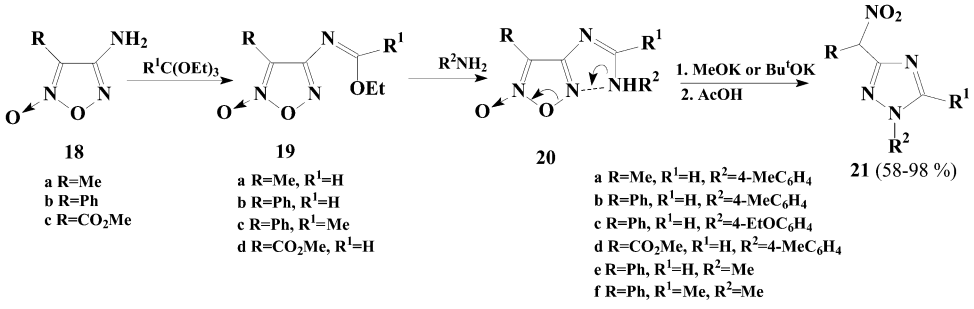
This variant of rearrangement of noncondensed furoxan derivatives (classical variant) was performed for furoxan derivatives involving different side chains: C–N–N (phenylhydrazones), N–C–N (amidines), and N–C–S (thioureides). Rearrangements of parent *Z*-isomers of phenylhydrazones **7a,b** were performed in the presence of bases at different temperatures. In all cases, the reaction mixture was acidified in order to isolate target compounds. Of the bases examined [aqueous NaOH solution, sodium ethoxide, sodium methylsulfinyl carbanion (demsyl sodium), and Bu^{t}OK], a solution of Bu^{t}OK in DMF at 10 °C was found to be most efficient, although a small amount of target product **16a** was separated by preparative thin layer chromatography (TLC) on silica gel after the reaction between compound **7a** with sodium ethoxide. In this case, the major portion of **7a** underwent decomposition under the reaction conditions. This is likely to be due to the well-known sensitivity of acylfuroxans to bases [27,28]. In the case of Bu^{t}OK, decomposition of the parent compounds was also observed, and it was more pronounced with **7b**. In this connection, a higher yield was attained for **16a** (Scheme 7).

An attempt to isolate **16a** by slow dropwise addition of water to the reaction mixture (without acidification) resulted in parent phenylhydrazone **7a**. It is evident that a reversible monocyclic rearrangement of product **16a** (as *aci*-form) into parent furoxan phenylhydrazone **7a** was observed in an aqueous alkaline medium. In this case, the oxygen atom of the *aci*-nitro group anion could attack the nitrogen atom of the 1,2,3-triazole ring. The rearrangement of **7a** in the presence of Bu^{t}OK at heating resulted in 3-acetyl-2,4-diphenyl-2*H*-1,2,3-triazole **17a** (Scheme 7). The formation of compound **17a** may be explained by the participation of 5-(1-nitroethyl)-1,2,3-triazole **16a** formed at the first stage in a Nef-type reaction [29]. The formation of ketone **17a** in insignificant amounts was also observed when the reaction was performed at 10 °C (TLC monitoring).



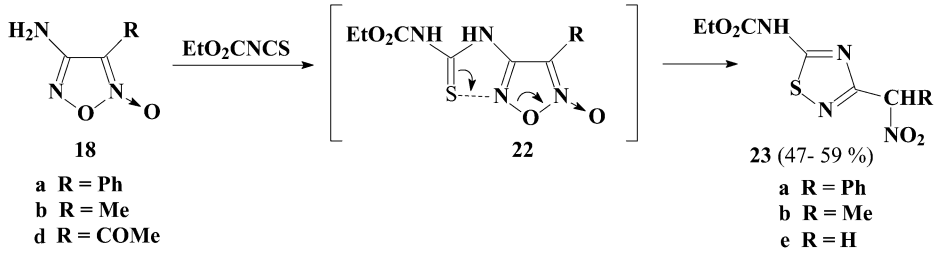
Scheme 7 Base-induced rearrangement of furoxanylketones phenylhydrazones **7**.

In order to introduce a side chain N–C–N to the C(4) atom of the furoxan ring, 3-aryl(alkyl)-1-(3-R-furoxan-4-yl)amidines **20a–f** were synthesized by the reaction of aminofuroxans **18a–c** with triethyl ortoformiate or triethyl ortoacetate followed by the action of various amines on the resulting iminoethers **19a–d** (Scheme 8). Aromatic amines were used for the synthesis of amidines **20a–d** and aliphatic amines for the synthesis of amidines **20e,f**. The rearrangements of amidines **20** were initiated by various bases (MeONa in MeOH, Bu^{t}OK in DMF and NaOH in water). It was found that MeOK in MeOH at 20 °C was effective for the conversion of amidines **20a–d** into 1,5-disubstituted 3-[1-nitroethyl(benzyl)]-1,2,4-triazoles **21a–d.** Heating of amidines **20e,f** with Bu^{t}OK in DMF at 100 °C was needed for the synthesis of corresponding 3-(1-nitrobenzyl)-1,2,4-triazoles **21e,f** (Scheme 8). In addition, it was found that the use of 10 % NaOH solution in water was effective for carrying out the rearrangement of both kinds of amidines (**22b,f**). However, in this case, 3-benzoyl-1,2,4-triazole derivatives were isolated which evidently were the products of a Nef-type reaction of compounds **21b,f** formed at the first stage of a process.



Scheme 8 Base-induced rearrangement of furoxanylamidines **20**.

For the introduction of the side chain N–C–S to the C(4) atom of the furoxan ring, we attemped to synthesize 4-(3-ethoxycarbonylthioureido)-3-R-furoxans **22a–e** by the interaction of ethoxycarbonyl isothiocyanate with corresponding 4-amino-3-R-furoxans **18a,b,d** (Scheme 9). We intended to initiate the rearrangements either thermally or in the presence of bases.



Scheme 9 Thermally induced rearrangement of 4-(3-ethoxycarbonylthioureido)-3-R-furoxans **22**.

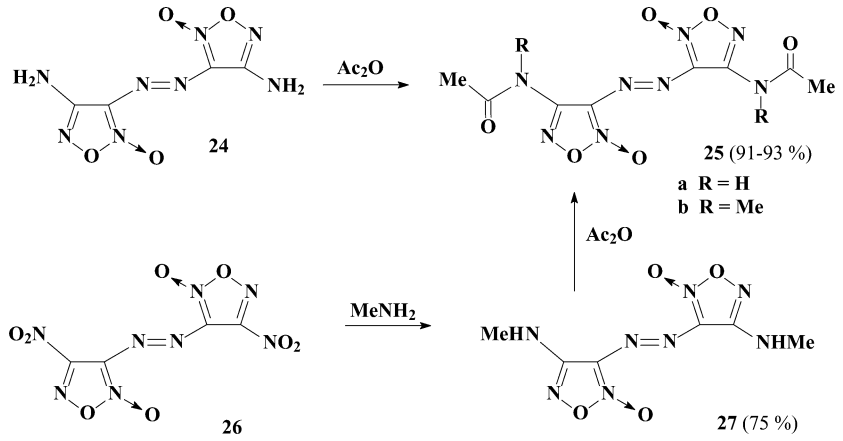
Ethoxycarbonyl isothiocyanate was chosen as most reactive of the isothiocyanates commonly used in analogous reactions [30]; this is associated with very low basicity of the amino group in furoxans. [31] The reaction was performed by refluxing of a mixture of aminofuroxans **18a,b,d** with ethoxycarbonyl isothiocyanate in various aprotic solvents (chloroform, diethyl ether, acetone, benzene, and ethyl acetate) and monitored by TLC. Among the tested solvents, ethyl acetate was the best. With this solvent, the reaction was complete in 2 h. However, rearrangement products **23** were obtained instead of expected 4-(3-ethoxycarbonylthioureido)-3-R-furoxans **22a,b,d**. In particular, for **18a,b** (R = Me and Ph), corresponding 5-amino-3-(1-nitroalkyl)-1,2,4-thiadiazole derivatives **23a,b** were obtained. In the case of **18d** (R = Ac), the reaction was assumed to proceed analogously with the formation of **23c**; however, under the isolation conditions, the hydrolysis of the acetyl group occurred, and 3-nitromethyl-5-ethoxycarbonylamino-1,2,4-thiadiazole **23e** was isolated as the product [32] (Scheme 9). Such feasibility of these rearrangements is evidently related to a higher nucleophilicity of the sulfur atom in comparison with that of the nitrogen atom.

So, in this part of the investigation, the base-induced classical rearrangement of 3-methyl-4-benzoyl(acetyl)furoxan phenylhydrazones to 4-phenyl(methyl)-5-(1-nitroethyl)-2-phenyl-2*H*-1,2,3-triazoles and 3-aryl(alkyl)-1-(3-R-furoxan-4-yl)amidines to 1,5-disubstituted 3-[1-nitroethyl(benzyl)]-1,2,4-triazoles as well as the thermally induced rearrangement of 4-(3-ethoxycarbonylthioureido)-3-R-furoxans to 5-ethoxycarbonylamino-3-(1-nitroalkyl)-1,2,4-thiadiazoles have been achieved for the first time.

CASCADE REARRANGEMENTS OF 4-(X-Y-Z)-SUBSTITUTED-3-FUROXANYL(ARYL)AZOFUROXANS

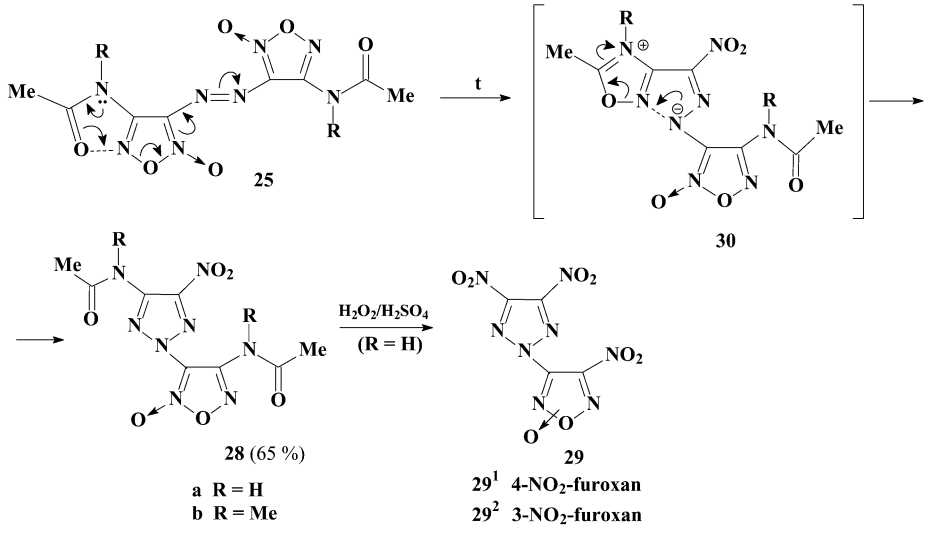
To perform two successive (cascade) rearrangements, it was necessary to synthesize furoxans with the side chain X-Y-Z at the C(4) atom and with an appropriate substituent (e.g., N=N) at the C(3) atom of the furoxan ring. This kind of rearrangements was studied using four examples of 3-azofuroxans with X-Y-Z = N-C-O and N-C-S: 4,4′-bis(acetylamino)-3,3′-diazenofuroxans, 4-acetylamino-3-arylazofuroxans, 3-arylazo-4-(3-ethoxycarbonylureido)furoxans, and 3-arylazo-4-(3-ethoxycarbonylthioureido)furoxans.

The first example of the cascade rearrangements was found at heating of 4,4′-bis(acetylamino)-3,3′-diazenofuroxans **25**. Diazenofuroxan **25a** was synthesized by acetylation of 4,4′-diamino-3,3′-diazenofuroxan **24** under the action of acetic anhydride in the presence of the catalytic amount of concentrated H_2SO_4. Its analog **25b** was synthesized by nucleophilic substitution of the nitro groups in 3,3′-diazeno-4,4′-dinitrofuroxan **26** by methylamino groups [33] under the action of methylamine followed by acetylation of formed 4,4′-bis(methylamino)-3,3′-diazenofuroxan **27** with Ac_2O/H_2SO_4 (Scheme 10).



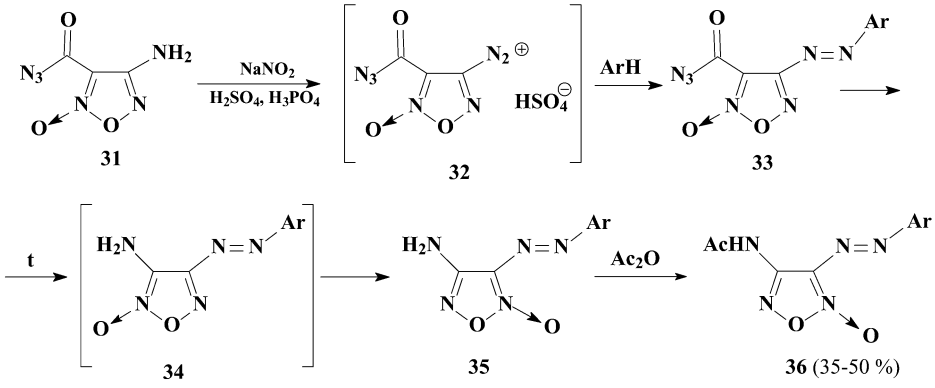
Scheme 10 Synthesis of 4,4′-bis(acetylamino)-3,3′-azofuroxans **25**.

It was found that heating of compound **25a** in a mixture of AcOH:Ac_2O at 50 °C resulted in 4-acetylamino-3-(5-acetylamino-4-nitro-2*H*-1,2,3-triazol-2-yl)furoxan **28a** [34]. Later, the same reaction was carried out by refluxing in other solvents (AcOH, dioxane, EtOAc). In order to increase the solubility of the synthesized compounds, triazolylfuroxan **28a** was oxidized to trinitro derivative **29** under the action of concentrated H_2O_2 in H_2SO_4. This compound was obtained in the same way as two furoxan isomers **29[1]** and **29[2]**, which were separated. The structure of **29[1]** was established by a comparison of the elemental analysis and NMR spectra data. ^{15}N NMR spectra (δ, ppm) were especially informative. They proved the presence of a triazole ring [–36.31 for N(1) and N(3) and –162.75 for N(2)] and nitro groups (–38.7 for NO_2 of the triazole ring and –40.05 for NO_2 of the furoxan ring). The conditions found were successfully used for the rearrangement of diazenofuroxan **25b** into triazolylfuroxan **28b**. It was suggested that the found transformation of compounds **25** into compounds **28** included two successive (cascade) rearrangements: the 1,2,4-oxadiazole ring is formed at the first step (intermediate **30**); next, this ring is transformed into the 1,2,3-triazole ring with the participation of the azo group (Scheme 11). Generally, *one-pot* thermal recyclization of the diazenofuroxanyl unit into the 4-nitro-2*H*-1,2,3-triazole ring has been for the first time discovered.



Scheme 11 Thermally induced cascade rearrangement of 4,4′-bis(acetylamino)-3,3′-azofuroxans **25**.

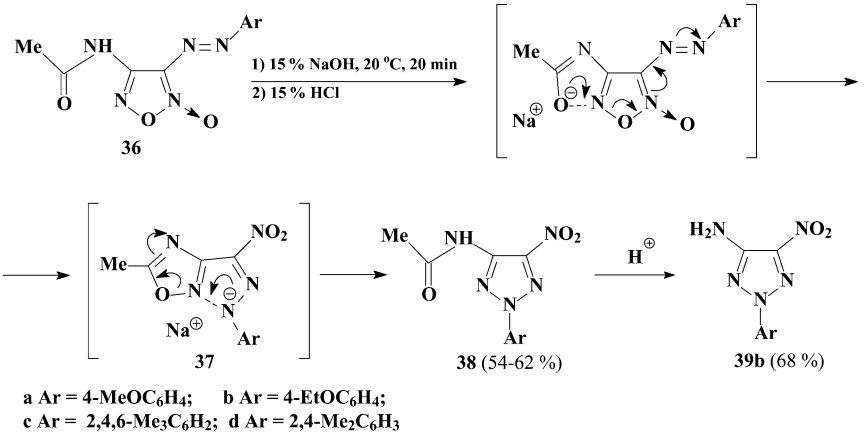
The second example of the cascade rearrangements of azofuroxans was a base-induced rearrangement of 4-acetylamino-3-arylazofuroxans **36** into 4-acetylamino-2-aryl-5-nitro-2*H*-1,2,3-triazoles **38**. 4-Amino-3-azidocarbonylfuroxan **31** [35] served as a common parent compound for azofuroxans **36**. On this basis, diazonium salt **32** was prepared by a well-known procedure [36], and this salt was introduced into azo coupling reactions with the corresponding aromatic compounds. The diazotization of aminofuroxan **31**, which was a weak-base amine (like other aminofuroxans [31]), was performed in a mixture of concentrated sulfuric and phosphoric acids. Of aromatic compounds, anisole, phenetole, mesitylene, and m-xylene were introduced in this reaction. Next, the azidocarbonyl group in azo compounds **33** obtained was transformed into amino groups using the Curtius rearrangement [37] with the formation of 3-amino-4-arylazofuroxans **34**, which were thermally isomerized without isolation into 4-amino-3-arylazofuroxans **35**. Acetylation of compounds **35** resulted in initial 4-acetylamino-3-arylazofuroxans **36** (Scheme 12).



Ar = 4-MeOC$_6$H$_4$, 4-EtOC$_6$H$_4$, 2,4,6-Me$_3$C$_6$H$_2$, 2,4-Me$_2$C$_6$H$_3$

Scheme 12 Synthesis of 4-acetylamino-3-arylazofuroxans **36**.

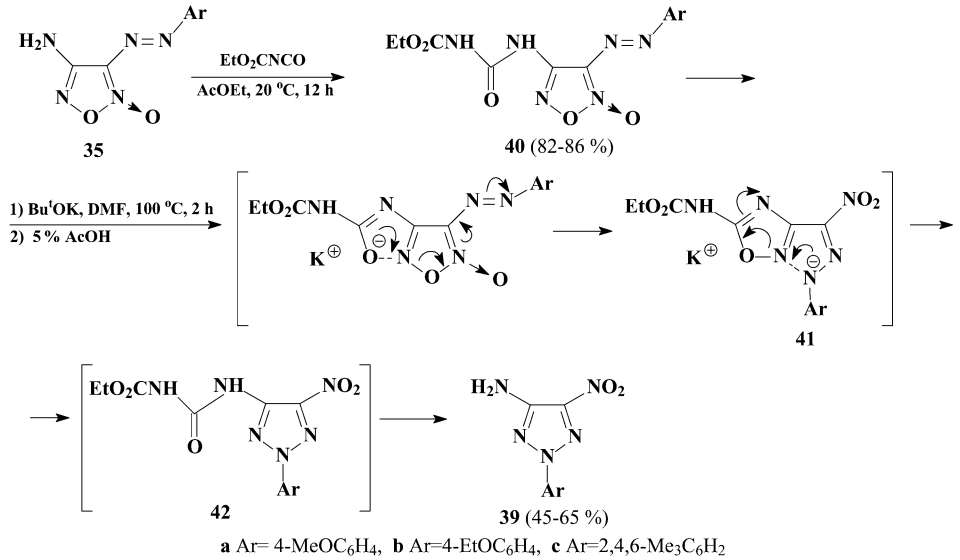
Attempts to perform a thermal rearrangement of synthesized azofuroxans **36** (refluxing in ethyl acetate, dioxane, or toluene) by analogy with the rearrangement of compounds **25** were unsuccessful. The rearrangement of compounds **36** into 4-acetylamino-2-aryl-5-nitro-2*H*-1,2,3-triazoles **38** was performed only under conditions of the basic catalysis in water at room temperature (15 % solution of NaOH) [38]. It can be assumed by analogy with the synthesis of triazolylfuroxans **28** that the nitrotriazoles **38** are formed via two successive (cascade) rearrangements. As a result of the first rearrangement, intermediate 1,2,4-oxadiazole derivatives **37** are formed, which are rearranged into final compounds **38** with the participation of the azo group. A removal of the acetyl protection in compound **38b** by acid hydrolysis resulted in the 4-amino-5-nitro-2*H*-1,2,3-triazole **39b** (Scheme 13).



Scheme 13 Based-induced cascade rearrangement of 4-acetylamino-3-arylazofuroxans **36**.

To estimate the influence of substituents at the amino group in 4-amino-3-arylazofuroxans **35** on their tendency to rearrange we intended to synthesize 3-arylazo-4-(3-ethoxycarbonylureido)furoxans **40** and 3-arylazo-4-(3-ethoxycarbonylthioureido)furoxans **43** (R = N=N–Ar).

Compounds **40** were prepared by the reaction of corresponding 4-amino-3-arylazofuroxans **35** with ethoxycarbonyl isocyanate (Scheme 14). This isocycnate was chosen due to its high reactivity [39–41] because the amino group in aminofuroxans has very low basicity [31]. The reactions were carried out in dry ethyl acetate at 20 °C for 12 h. To examine the possibility of cascade rearrangement of synthesized compounds **40**, a 15 % aqueous solution of NaOH at 20 °C was first used. However, the starting compounds remained unconsumed under the conditions chosen. We succeeded in carrying out the desired cascade rearrangement only with the use of Bu^{t}OK in anhydrous DMF as a base, heating at 100 °C for 2 h being necessary for the reaction to proceed [42] (Scheme 14).

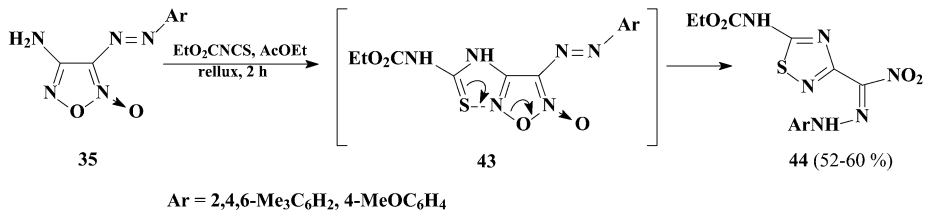


Scheme 14 Based- and thermally induced cascade rearrangement of 3-arylazo-4-(3-ethoxycarbonylureido)furoxans **40**.

This reaction required much more stringent conditions compared to those that had been used for the rearrangement of 4-acetyl-3-arylazofuroxans **36**, apparently due to the fact that the ureido fragment was of much lower acidity than the amide group [43]. After the rearrangement completion, the reaction mixture was cooled and acidified with acetic acid to pH 6. The products containing the unsubstituted amino group, viz., 4-amino-2-aryl-5-nitro-2*H*-1,2,3-triazoles **39**, were isolated as the final products (Scheme 14). Evidently, the reaction proceeds through 1,2,4-oxadiazole intermediates **41** and the formation of 2-aryl-4-(3-ethoxycarbonylureido)-5-nitro-2*H*-1,2,3-triazoles **42**. However, under the conditions of isolation of the final products, the ethoxycarbamoyl protection is removed.

In addition to the base-induced rearrangement, a possibility of a thermal rearrangement of ureido derivatives **40** (taking **40a,c** as the examples) by refluxing their solutions in various solvents (toluene, m-xylene, bromobenzene, and DMSO) was studied. Only heating in DMSO at 120 °C for 3 h appeared to be efficient. Interestingly, the ethoxycarbamoyl protection is also removed during the isolation of final products **39** by column chromatography on SiO_2.

For the study of the next cascade rearrangement, we intended to synthezize 3-arylazo-4-(3-ethoxycarbonylthioureido)furoxans **43** by a reaction of 4-amino-3-arylazofuroxans **35** with ethoxycarbonyl isothiocyanate. The formation of 2-aryl-4-amino-5-nitro-2*H*-1,2,3-triazole derivatives **39a,c** could be expected for R = 4-$MeOC_6H_4$ and 2,4,6-$Me_3C_6H_2$, accordingly by analogy with a similar rearrangement of 3-arylazo-4-(3-ethoxycarbonylureido)furoxans **40**. However, this case gave an unexpected result. On refluxing with ethoxycarbonyl isothiocyanate in ethyl acetate, these compounds also entered into a rearrangement without a release of intermediates **43**; but, instead of the expected cascade rearrangement to form 1,2,3-triazole derivatives **39a,c**, the reaction stopped after the formation of 1,2,4-thiadiazole derivatives, which did not enter into a subsequent rearrangement, and the molecules were stabilised as nitrohydrazones **44** [32] (Scheme 15). The structure of compound **44** was confirmed by both physicochemical methods and X-ray diffraction study (for **44a**, Fig. 2). Although compounds **43** did not enter into the cascade rearrangement, isolation of nitrohydrazones **44** indirectly supports the previously proposed mechanism of the cascade rearrangements of various 4-amino-3-aryl(heteroaryl)azofuroxan derivatives. Thus, the methodology of the cascade rearrangements in the furoxan series has been developed for the first time, and their mechanism has indirectly supported.



Scheme 15 Thermally induced rearrangement of 3-arylazo-4-(3-ethoxycarbonylthioureido)furoxans **43**.

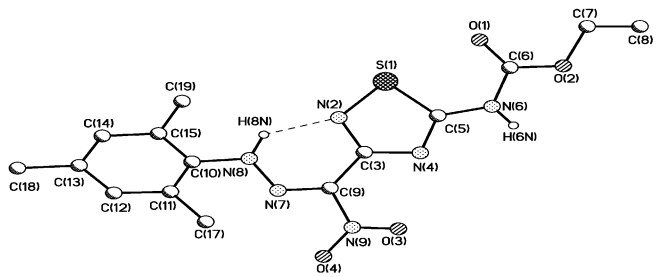


Fig. 2 The general view of compound **44a** structure.

CONCLUSION

Generally, the study of rearrangements of noncondensed furoxan derivatives allowed identification of three kinds of rearrangements: (1) rearrangements through dinitrosoethylene intermediate; (2) rearrangements resulting in 1-nitroalkylazoles; and (3) cascade rearrangements of 4-(X-Y-Z)-substituted 3-furoxanyl(aryl)azofuroxans. The use of these rearrangements has led to the development of new alternative approaches to the synthesis of 1,2,3-triazole 1-oxides, 1-nitroalkyl derivatives of 1,2,3-triazoles, 1,2,4-triazoles and 1,2,4-thiadiazoles as well as 4-amino-5-nitro-1,2,3-triazole derivatives. It is quite evident that the results attained are only a starting point for extending the investigations of monocyclic rearrangement of furoxan derivatives.

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