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SYNTHESIS AND PROPERTIES OF NITRO-1,2,3-TRIAZOLES (REVIEW)

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Published data on methods for the synthesis of substituted 4(5)-nitro-1,2,3-triazoles and their properties are reviewed.

Keywords: hydrazone oximes, methazonic acid, nitrovinylamines, 4(5)-nitro-1,2,3-triazoles, 1,2,3-triazole 1-oxides, heterocyclization, energy-rich compounds.

Against the background of the extremely large amount of published information about methods for the production of vicinal triazoles and their properties the chemistry of nitro-substituted triazoles of this series is in an embryonic state. At the same time, according to existing data, vicinal nitrotriazoles may find use in the synthesis of medicines, dyes, agents for the struggle against agricultural pests, energy-rich components of propellants, special-purpose powders, and in other regions of technology. However, the practical application of these compounds has been restrained by the lack of technologically convenient methods for their production. Until now sufficiently effective preparative methods have not been developed for their synthesis. With respect to their properties it is known only that the nitro group of the triazoles is capable of being reduced catalytically to an amino group and substituted by various nucleophilic fragments, while the triazole ring is alkylated by alkyl halides and adds to an activated multiple bond. The limited information is probably explained by the poor availability of vicinal nitrotriazoles, which is most likely due to the passivity of the 1,2,3-triazole in electrophilic substitution reactions at carbon atoms and particularly in nitration processes. In this connection it seems expedient to examine methods for the synthesis of nitro-substituted 1,2,3-triazoles by direct nitration with due regard to the conditions determining the entry of the nitro group into the azole ring and also methods for the construction of nitrotriazoles by the cyclization of open-chain nitro compounds and to assess their properties.

1. SYNTHESIS OF NITRO-1,2,3-TRIAZOLES

1.1. Nitration of 1,2,3-Triazoles

The inertness of the carbon atoms of the triazole ring toward electrophilic reagents is due to distribution of the electron density of the ring in such a way that the carbon atoms carry a partial positive charge, preventing the addition of a nitronium cation. Therefore, the path to direct nitration of the ring of unsubstituted vicinal triazole has not so far been realized. Attempts to introduce a nitro group into the ring of the heterocycle of 1-phenyl- and 4-phenyl-1,2,3-triazoles were unsuccessful. 1-Phenyl-1,2,3-triazole (**1**) does not form 4(5)-nitro-substituted triazole during nitration even under rigid conditions. Here, only the phenyl ring is nitrated-initially at the *para* position and then at the *ortho* position [1-3].

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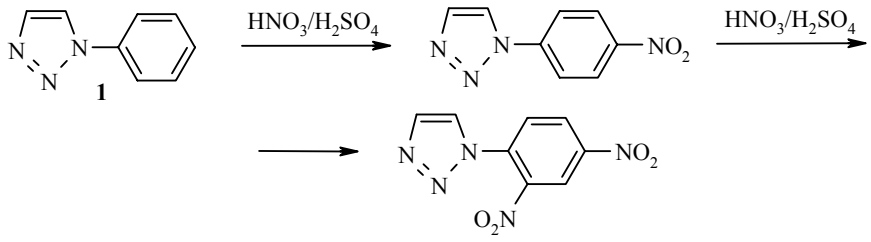
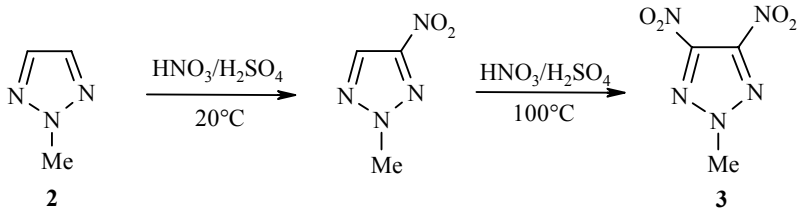
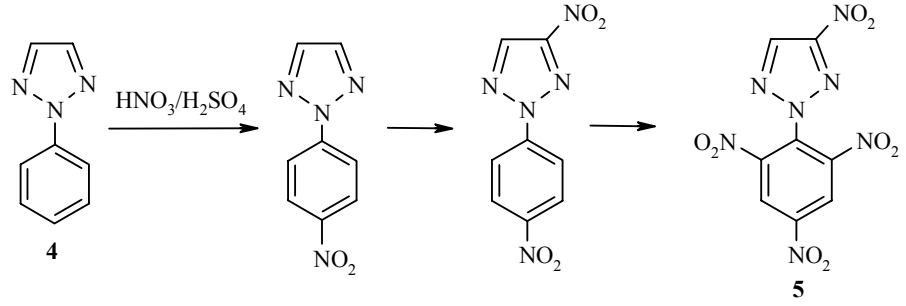


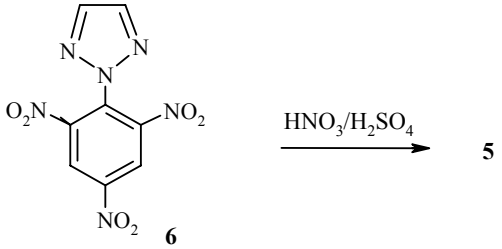
The presence of such substituents as alkyl or *p*-nitrophenyl at position 2 removes the prohibition on direct nitration of the heterocycle. In [4] unexpected results from the nitration of 2-methyl-1,2,3-triazole (**2**) and its 1-oxide were described. It was shown that these compounds form 2-methyl-4-nitrotriazoles during nitration with a mixture of sulfuric and nitric acids at 20°C and even form 4,5-dinitrotriazoles **3** at 100°C. This is a promising development for the production of new energy-rich systems.



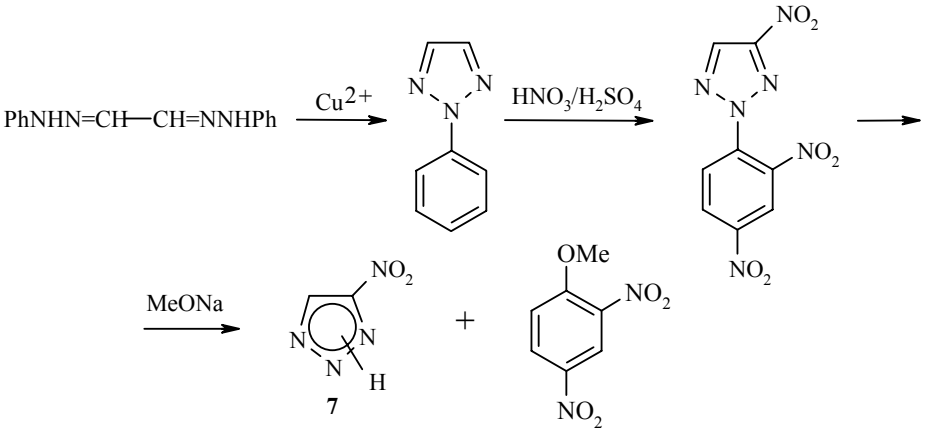
The nitration of 2-phenyl-1,2,3-triazole (**4**) with a nitrating mixture at temperatures in the range of 115-125°C takes place in stages with the successive introduction of nitro groups initially at the *para* position of the phenyl substituent and then at one of the carbon atoms of the heterocyclic fragment, leading finally to the formation of 4-nitro-2-(2,4,6-trinitrophenyl)-1,2,3-triazole (**5**) [5, 6].



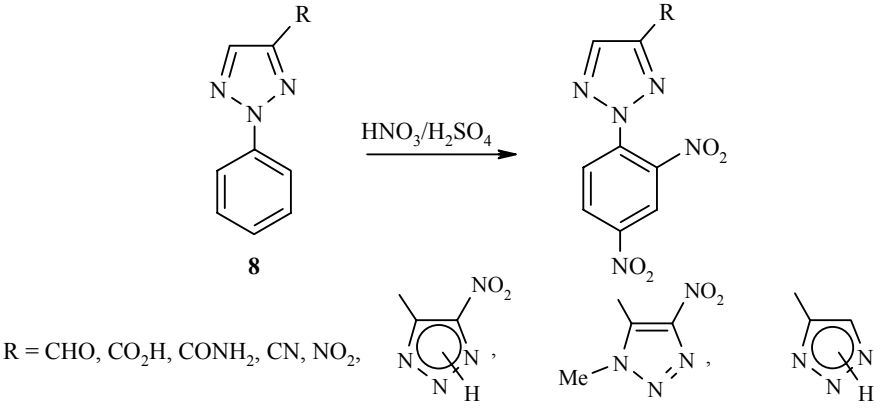
The nitration of triazole with two phenyl substituents at positions 2 and 4 only takes place in the phenyl rings [7]. In turn, the nitration of 2-(2,4,6-trinitrophenyl)-1,2,3-triazole (**6**) at 85°C results in the insertion of one nitro group into the heterocycle [1].



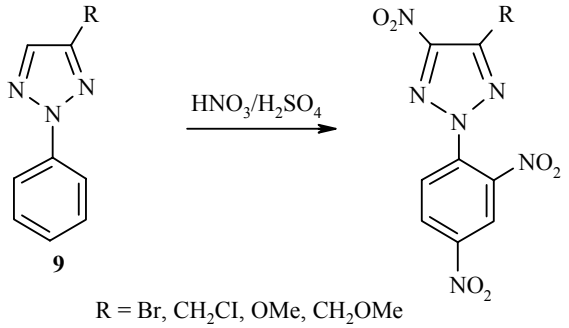
In view of the fact that a di- and trinitrophenyl fragment at position 2 of the 1,2,3-triazole ring is easily removed by the action of alkali-metal alcoholates this method can be considered as the most suitable method for the preparation of 4-nitro-1,2,3-triazole (**7**) [5, 8, 9].



By reducing the electron density at the other atom, electron-withdrawing substituents at one of the carbon atoms of the triazole ring in 4-substituted 2-phenyl-1,2,3-triazoles **8** prevent attack by the nitronium cation on the heterocycle [10]. As a rule, therefore, nitration takes place in the phenyl fragment.

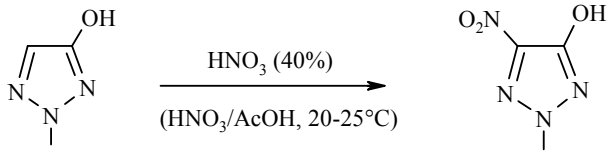


In the case of phenyltriazoles **8**, containing a carbamide or nitrile group at position 4 of the heterocycle, 2-(2,4-dinitrophenyl)-1,2,3-triazole-4-carboxylic acid was isolated as nitration product in addition to those indicated in the scheme, and this demonstrates the unusual ease of hydrolysis of the nitration products at the moment of their release.



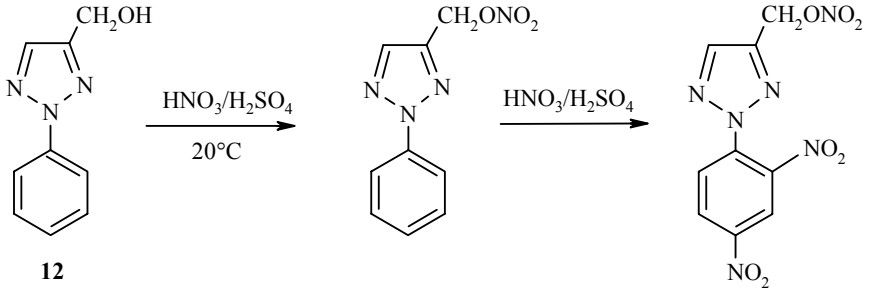
By increasing the electron density in the ring, electron-donating substituents at the carbon atom of triazole lead to the result that 2-phenyltriazoles **9** are readily nitrated with a mixture of sulfuric and nitric acids even at 20°C both in the aromatic ring and in the triazole ring [10].

At the same time in [11] it was shown that the nitration of 4-hydroxy-2-phenyl-1,2,3-triazole **10** and also of the corresponding triazole 1-oxide with a nitrating mixture even with cooling is accompanied by decomposition of the molecule. Nevertheless, the hydroxyl group in the triazole **10**, as in phenol, creates such favorable conditions that nitration of the heterocycle occurs under the influence of milder nitrating agents such as dilute nitric acid or a mixture of nitric and acetic acids. Here nitration takes place in the heterocyclic fragment without affecting the phenyl ring and leads to the formation of compound **11** [12].



10 **11**

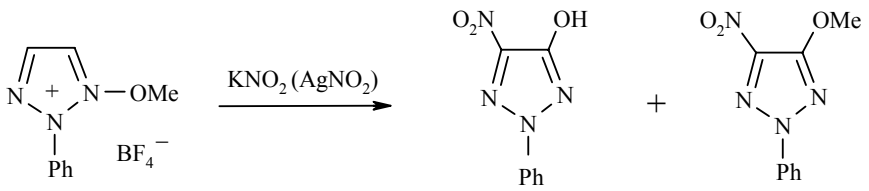
If the hydroxyl group and the triazole ring are separated by a methylene bridge the positive mesomeric effect of the substituent disappears, and as a result the susceptibility of the heterocycle to nitration is greatly reduced. During the action of a nitrating mixture on the triazole **12** the nitronium ion attacks the hydroxyl group and then the phenyl substituent with the formation of compound **13**.



12 **13**

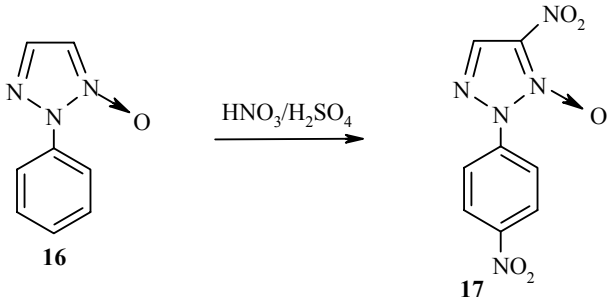
Thus, the main law governing the nitration of 4-substituted 2-phenyl-1,2,3-triazoles, involving activation of one of the carbon atoms by the electron-donating substituents at the other carbon atom of the heterocycle and, conversely, deactivation of the carbon atom in the presence of electron-withdrawing substituents, can be recognized.

In 1983 another possibility for the introduction of a nitro group into the triazole ring by nitration was published [13]. It was found that 1-methoxy-2-phenyl-1,2,3-triazolium borofluoride (**14**) is capable of adding a nitrite ion from potassium or silver nitrites to form hydroxy-substituted (**11**) and methoxy-substituted (**15**) 4-nitro-2-phenyltriazoles.

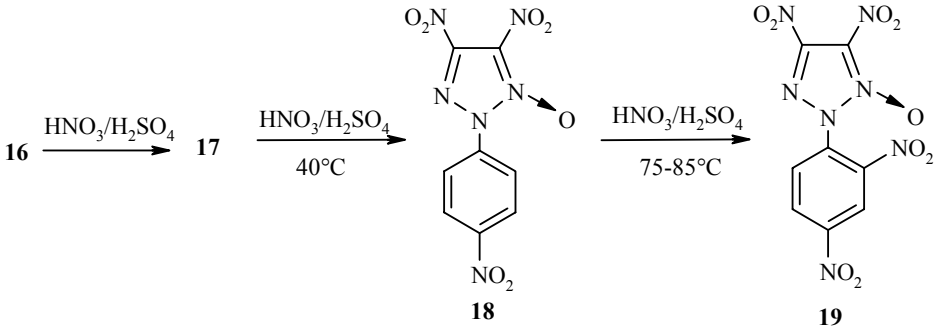


14 **11** **15**

As far as the reactivity of 1,2,3-triazole N-oxides is concerned, the chemical properties of these compounds can be compared to some degree with the properties of 1,2,3-triazoles. In [14] it was suggested that in electrophilic reactions triazole oxides **16** are protonated initially at the N-oxygen atom, making it possible as a result to conduct electrophilic substitution (and nitration in particular) at position 5 with simultaneous deactivation of the C-4 atom, preventing entry of a second nitro group into the triazole ring. As a result compound **17** is formed.

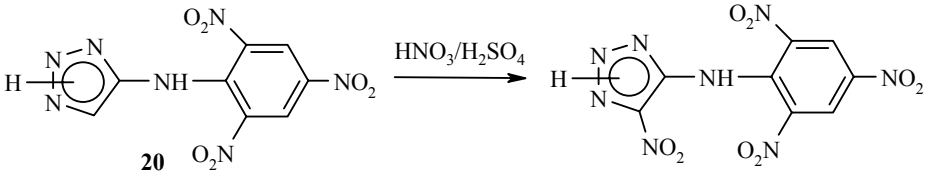


However, more recently it was shown [15] that the electronegative nitro group in 5-nitro-2-(4-nitrophenyl)-1,2,3-triazole 1-oxide (**17**) does not prevent the nitration of this heterocycle at the second carbon atom. Here the activating effect of the N-oxide fragment on the triazole ring appears. The nitration of compound **16** can be conducted in stages, where the order of introduction of the nitro groups is clearly observed.

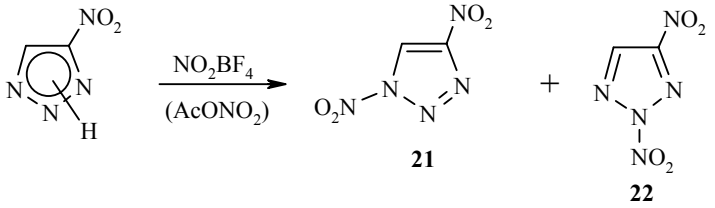


Initially, the mononitrotriazole oxide **17** was obtained at 5°C. By increasing the temperature to 40°C it was possible to introduce a second nitro group into the triazole ring with the formation of 4,5-dinitro-2-(4-nitrophenyl)-1,2,3-triazole 1-oxide (**18**). The final nitration product 4,5-dinitro-2-(2,4-dinitrophenyl)-1,2,3-triazole 1-oxide (**19**) is only produced at 75-85°C [15].

In the literature there are several examples of the nitration of N-unsubstituted derivatives of 1,2,3-triazoles, for which it was shown that the nature of the substituent at one of the carbon atoms of the heterocycle determines the direction of nitration at the carbon or nitrogen atom. Thus, for example, an aminopicryl substituent at one of the carbons in the triazole **20** directs attack by the nitronium cation at the C-2 atom of the heterocycle [16].



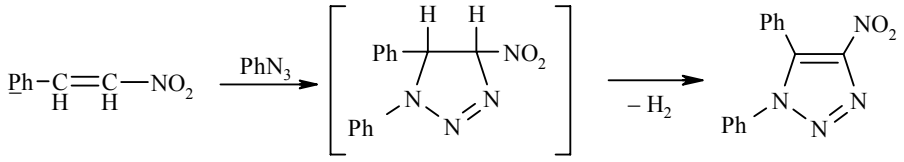
The presence of a nitro group at position 4 of the triazole ring prevents the nitration of 4-nitro-1,2,3-triazole and its 5-alkyl-substituted derivatives with fuming nitric acid or a nitrating mixture on account of destruction of the substrate molecules [11]. At the same time if such nitrating agents as nitronium borofluoride (in acetonitrile at 0°C, in methylene chloride at 20°C) and acetyl nitrate are used nitration takes place at the nitrogen atoms of the ring with the formation of the 1,4-dinitro- (**21**) and 2,4-dinitro-1,2,3-triazoles and (**22**).



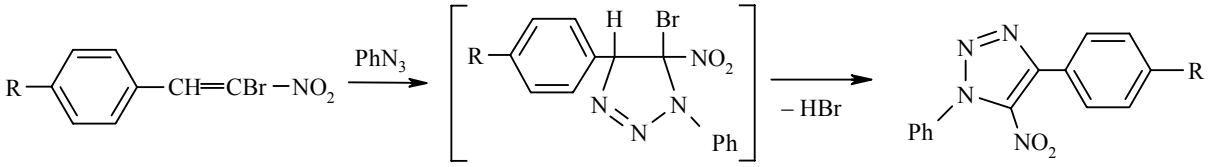
2,4-Dinitrophenyltriazole **22** is thermally unstable and decomposes during isolation. It was not therefore obtained in the pure form.

1.2. Reaction of Azides with Nitroolefins

Several alternative methods of formation of the ring of 4-nitro-1,2,3-triazoles by heterocyclization of open-chain nitro compounds have been described in the literature. In this respect one of the most often employed general methods for the synthesis of vicinal triazoles is the cycloaddition of organic and inorganic azides to nitroethenes having easy leaving groups of the halogen (Cl, Br), RO (R = H, Alk, Ar, Ac), Alk_2N, and NO_2 types at the second carbon atom of the double bond. The process presumably takes place through addition of the azide ion at the double bond of the nitroolefine followed by closure of a triazoline ring and ejection of one of the readily removed substituents at the double bond in the form of nitrate or bromide ions or cyano, alkoxy (aryloxy), and dialkylamino groups with simultaneous spontaneous aromatization of the triazoline heterocycle to a triazole ring. Usually triazoline rings are fairly unstable and are readily transformed into triazoles, aziridines, diazo compounds, and other nitrogen-containing structures. Their stability is increased if aromatic rings are introduced into the ring. When thermally stable triazolines are formed they are successfully dehydrogenated by the action of such oxidants as bromine [17], nickel oxide [18], or potassium permanganate [19]. In principle, the presence of two leaving substituents at the double bond of the nitroethenes is not at all essential for the construction of the triazole ring. In [20, 21] it was shown that nitrotriazoles can be formed by the reaction of organic azides with β-nitrostyrene by heating the reaction mixture to 130°C.



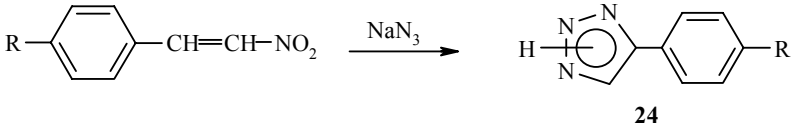
The reaction most likely takes place through a stage involving 1,3-dipolar cycloaddition of the azide to the double bond followed by dehydrogenation of the obtained triazoline. The reaction of phenyl azide with 2-aryl-1-bromo-1-nitroethenes takes place similarly with the formation of the nitrotriazoles **23** [22].



R = H, Me, Cl, Br, OH, OMe

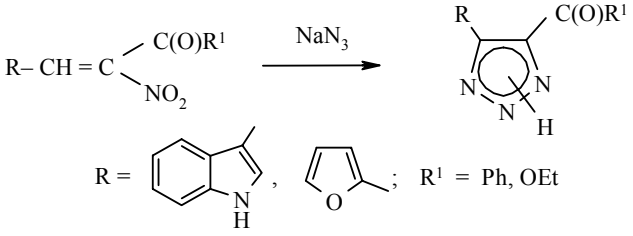
In this case the heteroaromatic triazole system is formed as a result of dehydrobromination of the intermediate triazoline ring.

Less predictable results are obtained with inorganic azides. According to work by Zefirov and coworkers [23-25], the use of sodium azide in reaction with arylnitroethenes leads to the elimination of the nitro group and the formation of N-unsubstituted 4-aryl-1,2,3-triazoles **24**.

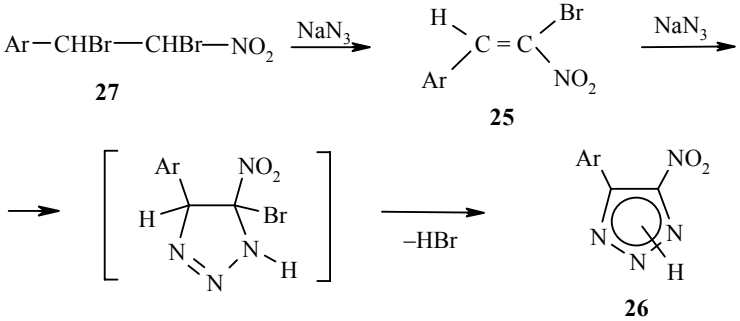


R = H, Cl, Br, NO_2, OMe, NMe_2

Unfortunately, the authors do not give experimental details. Such differences between the results of the reactions and those described earlier [20, 21] quite possibly result from the different conditions under which the reactions were carried out or depend on the nature of the azide. Elimination of the nitro group was also observed in the reaction of nitroethenes containing an electron-accepting carbonyl or carboxylate group at the double bond with sodium azide [26, 27].

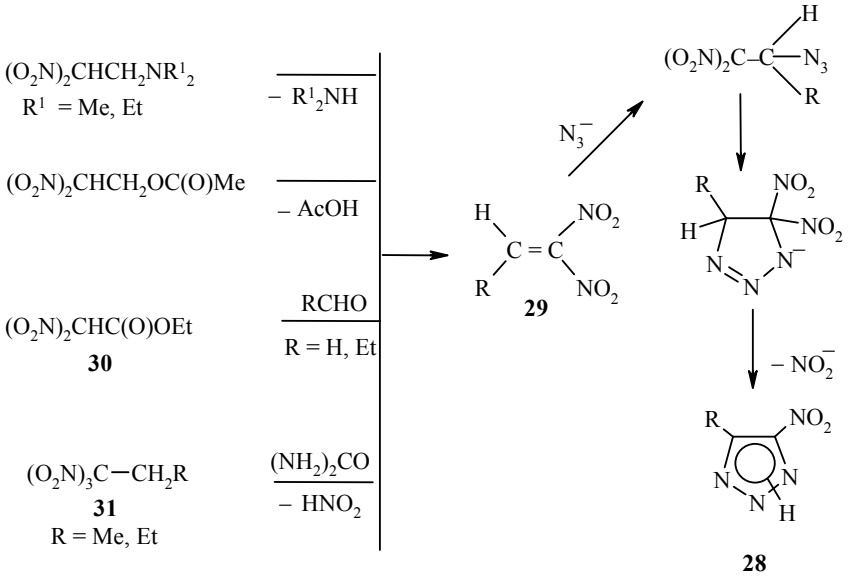


However, the presence of a halogen at the *gem* position in relation to the nitro group in arylnitroethenes favors retention of the nitro group in the final product. The reaction of 2-aryl-1-bromo-1-nitroethene **25** with sodium azide takes place according to a formal scheme of [2+3] cycloaddition leading to the formation of 4-aryl-5-nitro-1,2,3-triazoles **26** [28-30].

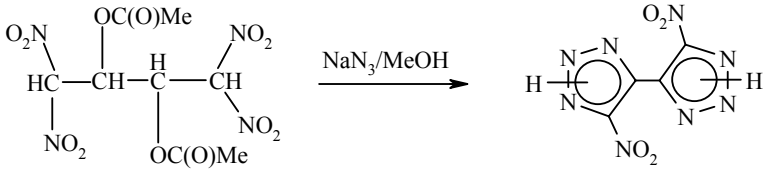


Dibromonitroethanes **27** can be used as starting compounds in such transformations. In this case the reaction takes place through a stage involving the formation of intermediate bromonitroethenes, while the sodium azide performs the function of a dehydrobrominating agent. The yields of the arylnitrotriazoles are fairly high. Unfortunately, the poor availability of compounds **27**, produced by the bromination of nitroethenes, restricts the synthetic possibilities of this method.

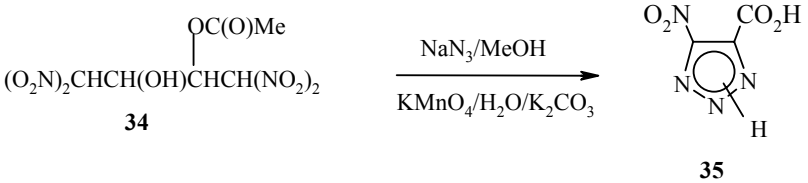
Another method of retaining the nitro group in the final triazole **28** during the action of sodium azide is to use geminal dinitroethenes **29** as substrate. In this case heterocyclization is accompanied by the elimination of one of the nitro groups [11, 31, 32]. In the opinion of the authors the reaction of dinitroalkenes with sodium azide takes place as a two-stage intramolecular cyclization.



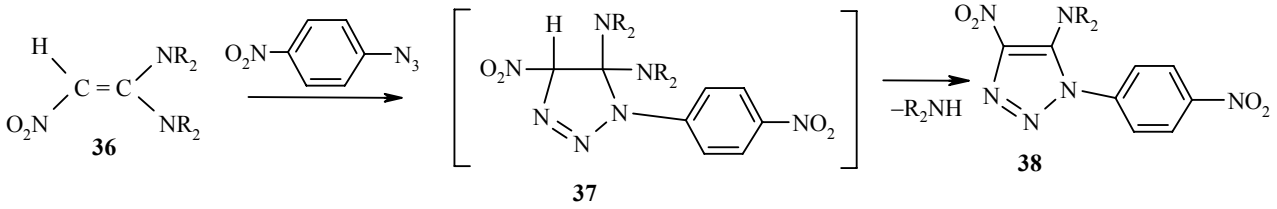
In these papers several approaches to the key dinitroethenes **29** were proposed during searches for a preparative method for the synthesis of N-unsubstituted nitrotriazoles [33]. The esters of dinitroacetic acid **30** and various derivatives of 1,1-dinitro- and 1,1,1-trinitroalkanes **31** were used as initial *gem*-dinitroethenes [11]. A similar approach was used in the synthesis of bis(4-nitro-1,2,3-triazol-5-yl) (**32**) by the reaction of the diacetate of 1,1,4,4-tetranitrobutane-2,3-diol (**33**) with sodium azide in methanol solution at 20°C.



In the opinion of the authors the reaction takes place through the formation of the intermediate tetranitrobutadiene [31]. In contrast to the diacetate, in reaction with sodium azide in methanol the monoacetate of tetranitrobutanediol (**34**) forms 5-substituted 4-nitro-1,2,3-triazole, which the authors oxidized with potassium permanganate without isolation to 5-nitro-1,2,3-triazole-4-carboxylic acid (**35**).

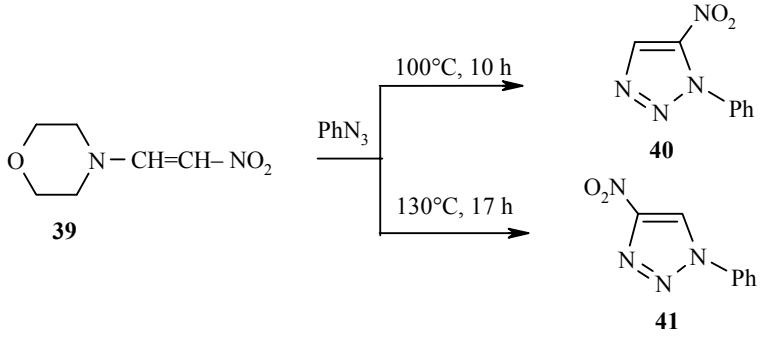


Of the cycloaddition reactions of azides to a double bond it is necessary to mention the fairly often employed reaction of organic azides with 1-amino-2-nitroethenes [21, 34-43], which are usually obtained by the reaction of a secondary amine and nitromethane with orthoesters [42] or of nitromethane with aminoacetals [44]. The cycloaddition of azides to nitroenaminals **36** is accompanied by the elimination of the amine from the intermediate unstable triazoline **37** with retention of the nitro group in the obtained heterocycle **38**.



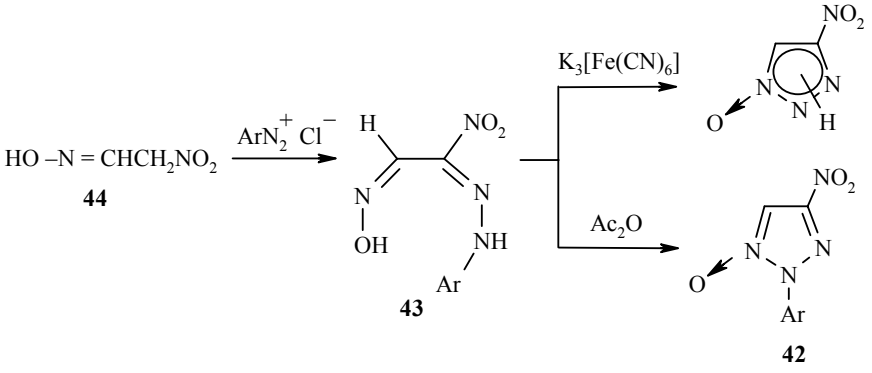
The characteristics of this reaction were discussed in [21, 45, 46]. The method is the only method for the specific production of 1-aryl-substituted 4-nitrotriazoles.

However, it must be borne in mind that reactions of such a type can take place in two directions depending on the temperature conditions. Thus, after 5 h at 100°C 1-morpholino-2-nitroethylene (**39**) and phenyl azide give 5-nitro-1-phenyl-1,2,3-triazole (**40**) with a yield of 60% [36], whereas 4-nitro-1-phenyl-1,2,3-triazole (**41**) was obtained exclusively after heating in toluene solution in a sealed tube at 130°C for 17 h [41].



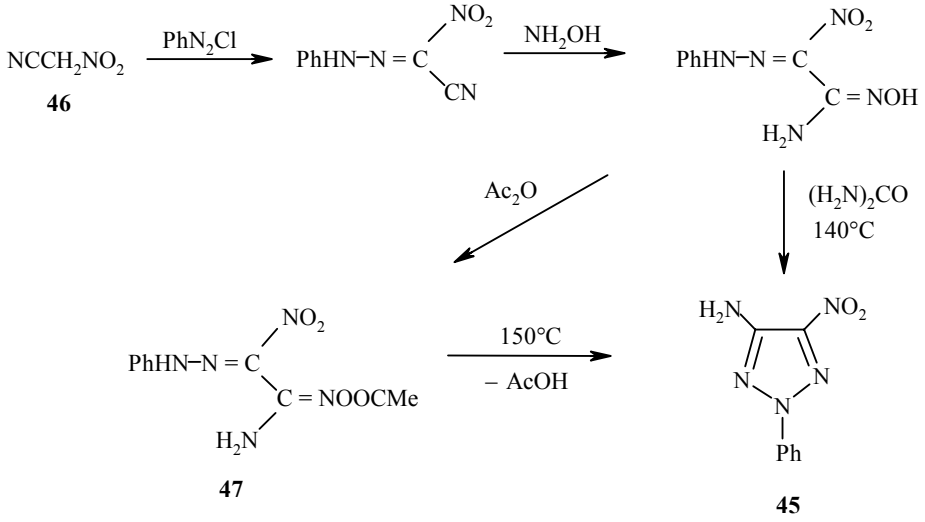
1.3. Heterocyclization of Nitro Group Containing Nitrogen Derivatives of 1,2-Dicarbonyl Compounds

The oxidative cyclization of the α-hydrazone oximes of carbonyl compounds in the presence of copper salts to 1,2,3-triazoles and to the respective N-oxides is used quite widely in synthetic practice. This approach was used for the synthesis of 2-aryl-4-nitrotriazole 1-oxides **42** starting from 2-arylhydrazono-2-nitropropanoacetoximes **43** [47], which were obtained by the reaction of diazonium salts with methazonic acid **44**.



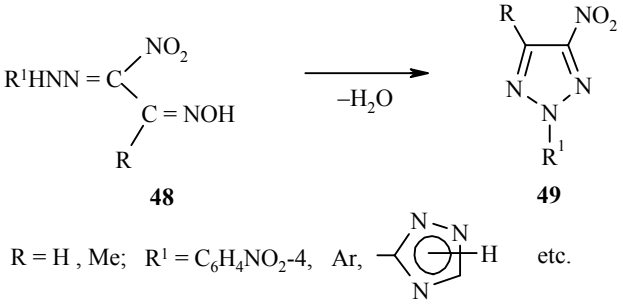
The synthesis of methazonic acid is well known, and the acid is used in the coupling reaction without isolation or special purification. Various aromatic and heterocyclic diazonium salts can be used in the reaction [48-50]. As a rule the yield of the oximes **43** is quantitative. Thus, for example, the reaction of methazonic acid with benzenediazonium and also with substituted benzenediazonium salts followed by cyclization of the 2-arylhydrazono-2-nitroacetoximes in acetic anhydride gave 65% yields of 2-aryl-4-nitro-1,2,3-triazoles with various substituents in the phenyl ring. It should be noted that 4-nitro-1,2,3-triazole 1-oxide was obtained during the cyclization of hydrazone oximes **43** in the presence of $K_3[Fe(CN)_6]$ as oxidizing agent [15, 51]. However, the cyclization stage is unpredictable and requires careful optimization of the conditions in each specific case. The yields of the cyclization products amount to 60-90%.

The general principle of the construction of the triazole ring by the cyclization of substituted phenylhydrazonoacetamidoximes forms the basis of the production of 4-amino-5-nitro-2-phenyl-1,2,3-triazole (**45**). As in the cases described above methazonic acid, the dehydration of which gave the nitroacetonitrile (**46**), was used as starting compound [47].



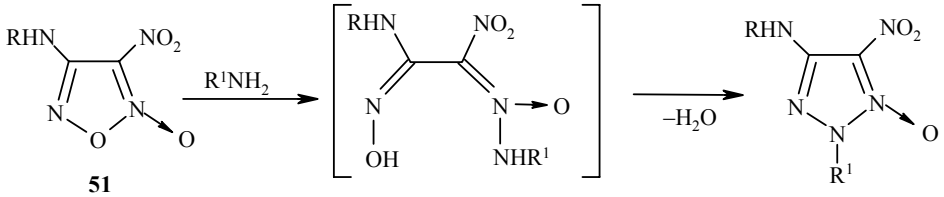
4-Amino-5-nitrotriazole (**45**) can also be synthesized with a 50% yield during vacuum sublimation of the acetate **47** at 150°C.

The dehydration of hydrazone oximes **48** by the action of various dehydrating agents leads to the production of 4-nitrotriazoles **49** with various substituents at position 2 of the triazole ring [52, 53].



According to data in the patent [53] 2-aryl-4-nitro-1,2,3-triazoles were obtained from α-nitro-hydroxyiminoarylhydrazones by heating them at 100-210°C with urea, which probably acts as a dehydrating agent.

A method for the production of 4-amino-5-nitro-2-R^1-1,2,3-triazole 1-oxides **50** by substitution of the oxygen atom of the heterocycle in 1,2,5-oxadiazole 5-oxides **51** by nitrogen probably according to the following scheme was described in [54-56].



51 **50**

R = H, Me, Et, $(CH_2)_2OH$, $(CH_2)_2CN$; R^1 = Me, Et, $CH_2CH=CH_2$

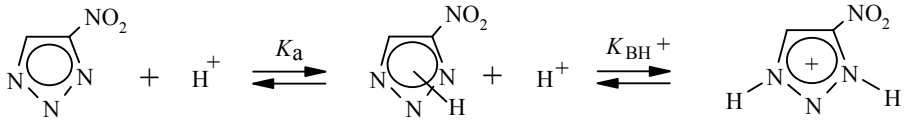
The presented material on the synthesis of nitro-substituted 1,2,3-triazoles probably does no exhaust all the possibilities for the formation of the nitrotriazole ring. As seen, most of the methods are complicated multistage processes and are used at the level of theoretical laboratory investigations. Detailed study of the chemical characteristics of nitrotriazoles in the search for practical applications requires thorough investigations into the development of the most practical and effective methods for their production.

2. CHEMICAL PROPERTIES OF 4(5)-NITRO-1,2,3-TRIAZOLES

The triazole ring is fairly resistant to the action of various reagents and is not as a rule decomposed by the action of such powerful oxidizing agents as nitric acid or potassium permanganate under normal conditions. This makes it possible to conduct chemical transformations of nitrotriazoles both in the heterocycle and in substituents present in the ring.

2.1. Introduction of Substituents into the Heterocycle

The presence of a strong electron-withdrawing nitro group at the carbon atom of the triazole ring substantially reduces the electron density at the ring atoms compared with unsubstituted 1,2,3-triazole. This in turn affects the reactivity of the nitrotriazoles. Being amphoteric compounds, derivatives of 1,2,3-triazole can exhibit both acidic and basic properties. Consequently, protolytic equilibria are possible for the triazole **7** [57].

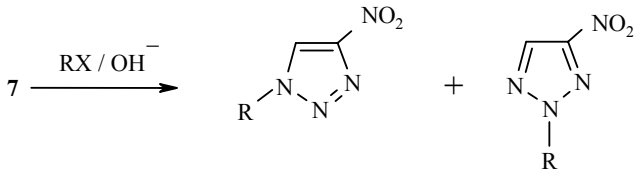


7

The effect of the nitro group shows up in the marked increase of the acidic properties of the triazole ring: the pK_a value for the nitrotriazole **7** is 4.8 (compared with 9.4 for unsubstituted 1,2,3-triazole). Therefore, N-unsubstituted 4-nitro-1,2,3-triazoles readily form salts in reaction with bases and in the form of the triazolate anion undergo attack by various electrophilic reagents with the formation of N-substitution products. The nitro group has the opposite effect on the basicity of the triazole ring: the basicity constant of the nitro derivative **7** (pK_{BH^+} −6.80 [57]) is lower than the basicity constant of unsubstituted 1,2,3-triazole (according to various sources pK_{BH^+} is −0.16 [57] or 1.17 [58]). Similar decrease in the basicity with the introduction of a nitro group into the heterocycle has been observed before in 1,2,4-triazoles [58, 59] and tetrazoles [60]. On account of the

reduced basicity and the reduced electron density at the carbon atom at position 5 the 4-nitro-1,2,3-triazoles are inert in electrophilic addition reactions at the nitrogen atom and also in electrophilic substitution at the carbon atom.

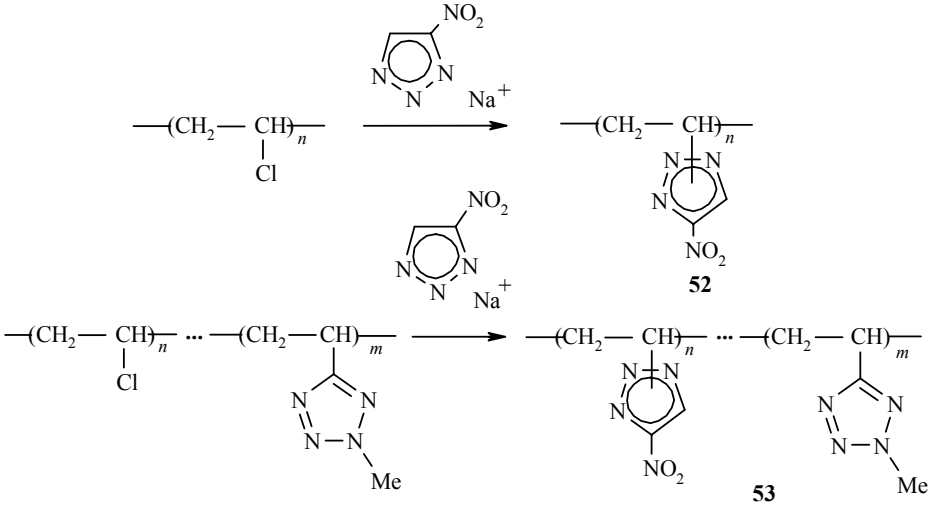
In the form of the triazolate anion the nitrotriazole **7** is alkylated by alkyl halides or dimethyl sulfate with preferred orientation of the substituent at position 1 of the ring [61, 62]. The nature of the solvent does no have a significant effect on the ratio of the isomers.



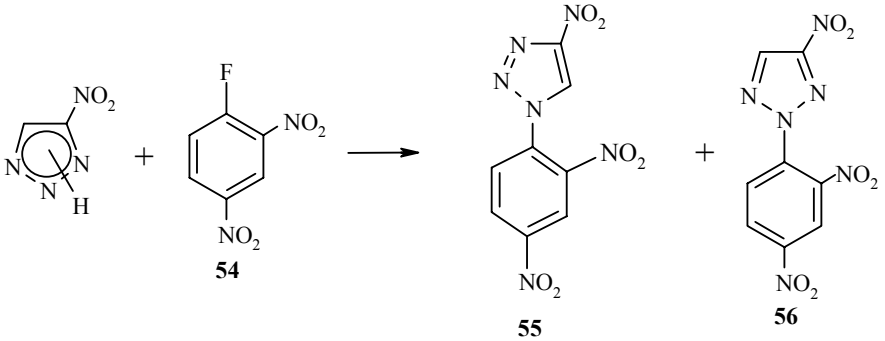
R = Me, Et, Pr, *i*-Pr, CH_2Ph, CH_2CO_2Et, CH_2CO_2Ph

As alkylating agent it is also possible to use high-molecular compounds having substituents in the main chain that can be substituted by the action of nucleophilic agents, one of which can be the nitrotriazolate anion. Thus, substitution of the halogen was used in the synthesis of high-energy polymers **52**, **53**, which could be used as highly effective binding components in solid propellants. Such polymeric compounds were produced in the reaction of sodium 4-nitro-1,2,3-triazolate with polyvinyl chloride or the copolymer of vinyl chloride with 5-vinyl-2-methyltetrazole in DMFA at 120-150°C [63].

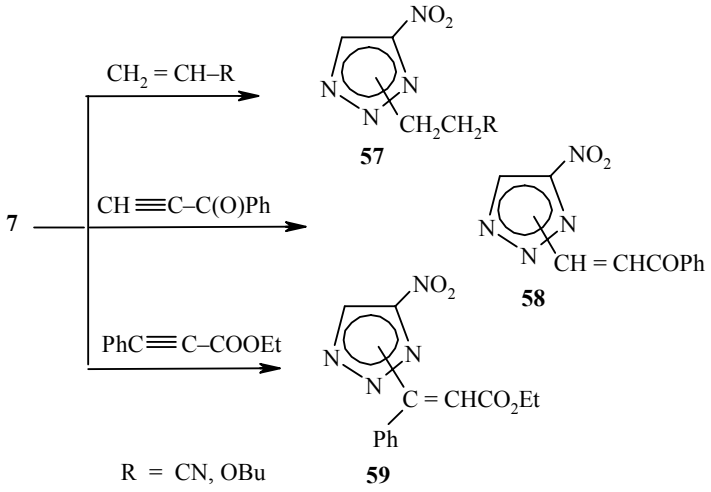
The obtained polymers contain two isomeric vinylnitrotriazole monomer units.



The nitrotriazole **7** is capable of reacting with 4,4-dinitrofluorobenzene (**54)** as a nucleophilic reagent. As a result the 1-aryl-4-nitrotriazole (**55**) and 2-aryl-4-nitrotriazole (**56**) were obtained [64].

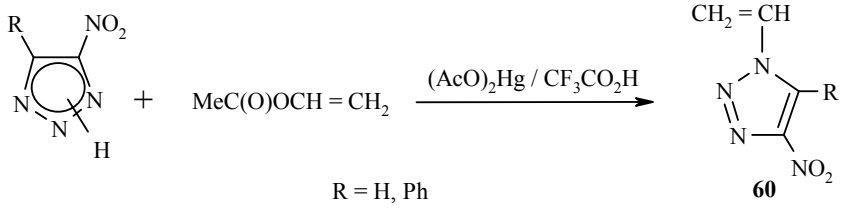


The nitrotriazole **7** is also capable of nucleophilic addition to activated alkenes of the acrylonitrile, α-carbonyl-, and carboxylacetylene type and can also act as electrophilic reagent during addition to vinyl ethers.



In the indicated reactions, as in alkylation, a mixture of two isomeric nitrotriazole-substituted compounds **57**-**59** with a preference for the isomer with the substituent at position 1 of the ring is formed. The exception is the reaction with acrylonitrile, in which the ratio of the obtained isomers is close to equimolar. Another feature of the products from the addition of nitrotriazole to acrylonitrile is the possibility of transformation of the N(1) isomer to the N(2) isomer. Specially set up experiments showed that the transition from one isomer to the other at room temperature takes place very slowly; after two years the content of the N(2) isomer in the mixture had increased by only 15%. After heating in DMF at 120°C for 8 h the ratio of the isomers changed by 4-5% [61, 65, 66].

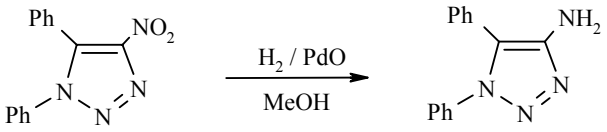
Under conditions where the vinyl group is activated by coordination with the cations of metals, particularly with Hg^{2+}, N-unsubstituted 4-nitro-1,2,3-triazoles are capable of entering into vinyl exchange with vinyl acetate.



In the presence of the mercuric acetate–trifluoroacetic acid catalytic system at 70°C the reaction takes place with the complete absence of side processes and gives 4-nitro-1-vinyl-5-R-1,2,3-triazoles **60** with yields of 70-88% [67].

2.2. Reactions of the Substituents

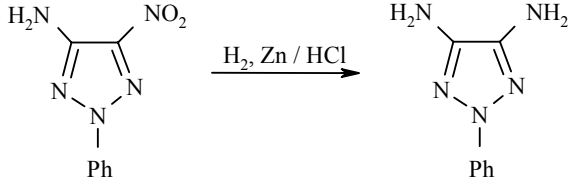
Classical reduction of the nitro group is also characteristic of nitrotriazoles. Reduction takes place in the presence of palladium and platinum catalysts at room temperature both at atmospheric pressure and at increased pressure [16, 36, 22]. Thus, 4-amino-1,5-diphenyl-1,2,3-triazole (**61**) was obtained with a 93% yield by the reduction of 4-nitro-1,5-diphenyl-1,2,3-triazole at palladium oxide in methanol [22].



61

4-Amino-2-β-D-ribofuranosyl-1,2,3-triazole was obtained similarly from 4-nitro-2-β-D-ribofuranosyl-1,2,3-triazole [68].

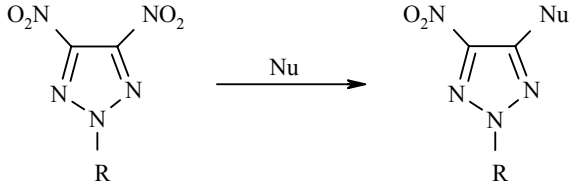
Good results were obtained during the noncatalytic reduction of 4-nitro-2-phenyl- and 5-amino-4-nitro-2-phenyl-1,2,3-triazole (**62**) with nascent hydrogen in systems with zinc dust or $SnCl_2$ in hydrochloric acid and also in the Fe/H_2SO_4 system in water–alcohol solution.



62

The reaction took 1-2 h and led to the respective aminotriazoles with yields of 50-75% [48].

π-Electron-deficient 2-alkyl-4,5-dinitro-1,2,3-triazoles **63** enter into nucleophilic substitution reactions, in which the leaving group is one of the nitro groups [69].



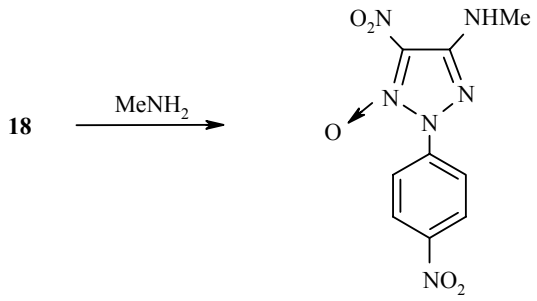
63

R = Me, Et, Pr; Nu = MeO, N_3, $MeNH_2$, $EtNH_2$

The reaction with very active nucleophiles such as the methoxide anion is exothermic. Here one of the nitro groups is substituted, and high yields of 2-alkyl-4-methoxy-5-nitro-1,2,3-triazoles are obtained. The methoxy group in nitrotriazoles appreciably reduces the π-electron deficiency of the heterocyclic system, leading to loss of the reactivity of the second nitro group in nucleophilic substitution reactions. Analogous deactivation of the remaining nitro group occurs in the presence of the electron-donating amine fragment in 2-alkyl-4-amino-5-nitro-1,2,3-triazoles, which are produced smoothly as a result of nucleophilic substitution of the nitro group by the action of softer nucleophiles – ammonia, primary and secondary amines in aprotic solvents.

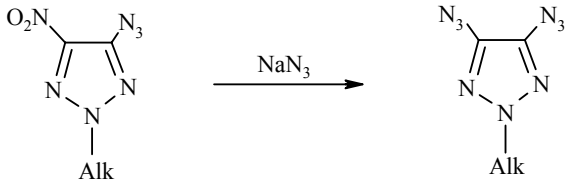
2-Aryl-4,5-dinitro-1,2,3-triazole 1-oxides behave similarly in nucleophilic substitution reactions, and substitution of the nitro group in the triazole oxides takes place exclusively at position 4 of the heterocycle. The direction of nucleophilic attack for the case of the reaction of 4,5-dinitro-2-(4-nitrophenyl)-1,2,3-triazole 1-oxide (**18**) containing a labeled $^{15}NO_2$ group at position 5 with methylamine is shown.

The signal of the labeled nitrogen atom of the nitro group at position 5 of the heterocycle remains in the ^{15}N NMR spectra of the nucleophilic substitution product **64** [69]. Substitution of the second nitro group by the action of nucleophiles does not occur even under rigid conditions on account of deactivation of the heterocycle as a result of the electron-donating effect of the amino group.



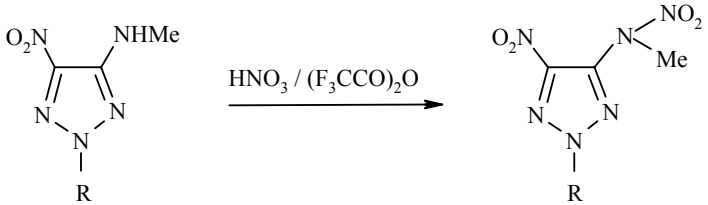
64

Nucleophilic substitution of one of the nitro groups by an azide fragment takes place very readily. The electron-withdrawing azido group in the obtained 2-alkyl-4-azido-5-nitro-1,2,3-triazoles leads to the result that it is possible to substitute the second nitro group after prolonged reaction and to obtain 2-alkyl-4,5-diazido-1,2,3-triazoles **65** [69].



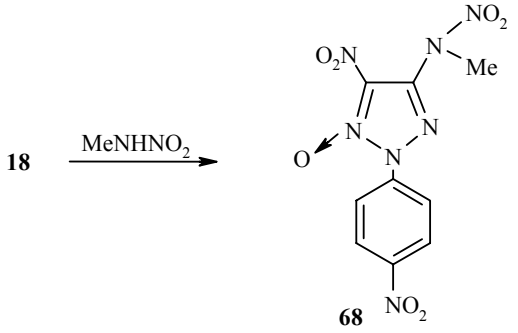
65

The dinitrotriazoles **63** react with the methylnitramine anion with greater difficulty. Substitution of even one of the nitro groups leads to the formation of 2-alkyl-4-methylnitramino-5-nitro-1,2,3-triazole **66** with a yield in the region of 10%. For the preparation of this compound it is better to use the nitration of 2-alkyl-4-methylamino-5-nitro-1,2,3-triazole **67** with concentrated HNO_3 in trifluoroacetic anhydride.



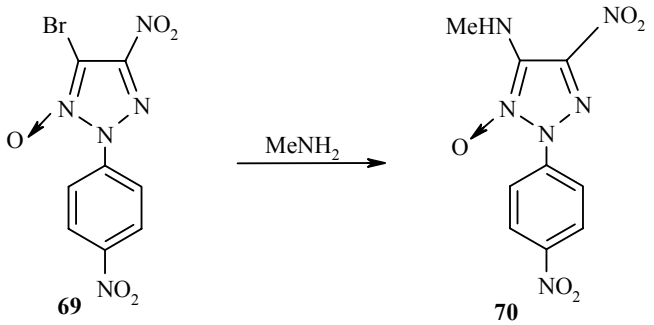
67 **66**

Nucleophilic substitution of the nitro group by the action of such a weak nucleophile as the methylnitramine anion takes place much more readily in 4,5-dinitro-2-(4-nitrophenyl)-1,2,3-triazole 1-oxide (**18**) and leads to the formation of 4-methylnitramino-5-nitro-2-(4-nitrophenyl)-1,2,3-triazole 1-oxide (**68**) [69].



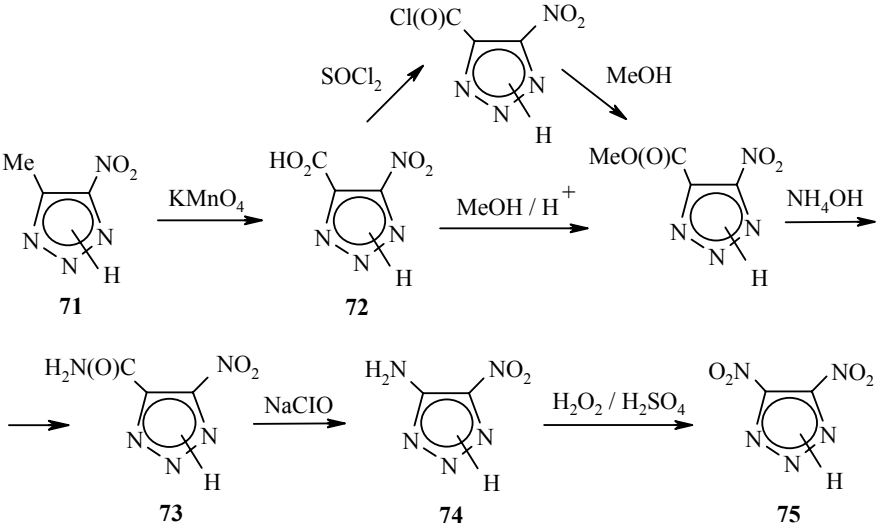
68

As in the reaction with methylamine the nitro group at position 4 of the triazole oxide ring undergoes nucleophilic substitution. However, the regioselectivity of nucleophilic substitution at the carbon atoms in the heterocycle depends largely on the different reactivity of the groups being substituted. Thus, in 5-bromo-4-nitro-2-(4-nitrophenyl)-1,2,3-triazole 1-oxide (**69**) only the halogen atom at position 5 is substituted selectively in reaction with methylamine [69].



69 **70**

Apart from the nitro group, chemical modifications of other substituents in nitrotriazole molecules have been described in the literature. Thus, a whole series of derivatives of N-unsubstituted 4-nitro-1,2,3-triazoles, including the difficultly obtainable 4,5-dinitro-1,2,3-triazole, were synthesized by successive transformation of the functional groups [11].



71 **72** **73** **74** **75**

The starting compound for these transformations was 5-methyl-4-nitro-1,2,3-triazole (**71**). The methyl group at the carbon is readily oxidized with potassium permanganate by the usual procedures for the oxidation of side chains in aromatic compounds. The nitrotriazolecarboxylic acid **72** obtained here is esterified by alcohols without complications through the respective acid chloride or in the presence of mineral acids. 5-Amino-4-nitrotriazole (**74**) was synthesized from the amide **73** by a Hoffmann rearrangement in the presence of sodium hypochlorite or hypobromite. The same aminonitrotriazole was obtained with a small yield by the action of diphenylphosphoryl azide on 4-amino-1,2,3-triazole-5-carboxylic acid [70]. By oxidizing 4-amino-5-nitrotriazole with a mixture of 30% hydrogen peroxide and concentrated sulfuric acid the authors were able for the first time [11] to obtain 4,5-dinitro-1,2,3-triazole (**75**), which represented a noncrystallizing yellow oil, fairly stable at 20°C but decomposing at 110°C. The potassium, sodium, and ammonium salts of this triazole were obtained.

In conclusion it must be said that the properties of these compounds have been studied far from adequately due, possibly, to the lack of experimentally convenient methods for their preparation. This is probably why little is known about their practical value and application in the national economy. On the surface it is possible by determining the structure of this molecule, which contains unstable nitro groups, to expect that it will have high-energy characteristics and may serve as the basis of explosives and components of propellants [48, 50, 71]. In the patent [62] it is claimed that 4-nitrotriazoles with various substituents at the nitrogen can be used as radiosensitizers in anticancer radiation therapy. Probably, the most practical and promising ways of using vicinal nitrotriazoles are in the synthesis of new drugs [2], dyes, agents against agricultural pests [72], and other branches to do with problems of fine organic synthesis.

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