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5-Substituted 3-Nitro-1-vinyl-1,2,4-triazoles

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Abstract—A series of 5-substituted 3-nitro-1-vinyl-1,2,4-triazoles were synthesized by alkaline treatment of the corresponding 1-(2-haloethyl- or 2-nitroxyethyl)-3-nitro-1,2,4-triazoles and by transvinylation of NH acids of the same series with vinyl acetate. The scope of applicability of the transvinylation procedure was established with respect to the azole pK_a value. The vinylic double bond on the nitrogen was shown to be inactive toward both nucleophilic and electrophilic reagents, whereas the halogen atom in position *5* exhibits enhanced reactivity. The latter factor provides the possibility for versatile structural modification via nucleophilic replacement of the 5-halogen atom by various groups, including triazolate ion.

Interest in vinyl derivatives of 1,2,4-triazole [1–15] is explained by their ability to form polymers possessing a number of specific properties, in particular solubility in water [1, 2]. Vinyl derivatives of 1,2,4-triazole can be obtained by standard procedures, such as catalytic addition of the corresponding NH acids to acetylene in alkaline medium under pressure [2–4, 12–14], dehydrohalogenation of *N*-(2-haloethyl)-1,2,4-triazoles [5–8], and transvinylation of triazoles with vinyl acetate in the presence of mercury(II) salts and sulfuric acid or boron trifluoride–ether complex [6, 8–10]. An interesting procedure was reported by Shimizu and Ogata [15]; it involves photocatalytic reaction of 1-[bis(trimethylsilyl)methyl]-1,2,4-triazole with carbonyl compounds (Peterson's reaction); however, this procedure has found no wide application.

An important point in the triazole chemistry is the selectivity of N-substitution (or addition). This problem is also inherent to direct vinylation of NH acids of the triazole series. Some aspects concerning mainly vinylation with acetylene were covered in [2, 4, 11–14]. Vinylation of unsubstituted 1,2,4-triazole results in formation of 1-vinyl-1,2,4-triazole in 74% yield, whose structure was determined by comparing the calculated and experimental dipole moments [2]. Trzhinskaya *et al.* [4] showed that the vinylation of both 1,2,4-triazole and its 5-methyl derivative under the conditions given in [2] gives both the corresponding N^1-vinyl compounds (more than 70%) and appreciable amounts of the N^4-vinyl isomers (14 and 25%, respectively). Presumably, this fact remained unnoticed, for the second reaction product resided in the high-boiling fraction. The structure of the second isomer was proved by independent synthesis [8]. Intermolecular cyclization of formylhydrazine, triethyl orthoformate, and 2-aminoethanol gave 1,2,4-triazole with fixed position of 2-hydroxyethyl group (on N^4), which was then converted into vinyl group. The same authors synthesized a series of 1-vinyl-3(5)-R-triazoles from the corresponding hydroxyalkyl derivatives which were in turn prepared by direct alkylation with 2-chloroethanol. However, it was difficult to separate N^1- and N^2-isomers, for their physical properties were very similar.

Vinylation with acetylene was also applied to triazoles with distorted aromaticity of the ring, e.g., 1,2,4-triazole-3-thiones [4, 12, 13] and 1,2,4-triazol-3-ones [14]. These compounds possess nucleophilic centers both in the ring and in the exocyclic group, and the vinylation occurs at all centers. Depending on the conditions and catalyst, 5-substituted 1,2,4-triazole-3-thiones give rise to *S*-mono- or *N*,*S*-divinyl derivatives; the presence of alkali favors formation of *S*-vinyl-1,2,4-triazoles [12] which undergo further vinylation following a usual scheme. *S*,*N*-Divinyl derivatives are obtained in the presence of cadmium acetate. In this case a mixture of N^1- and N^2-substituted isomers is formed when the second substituent in the ring is a bulky group (e.g., furyl or pyridyl [4, 13]); if the latter is hydrogen or methyl, three possible isomers (N^1-, N^2-, and N^4-vinyl) are formed. 1,2,4-Triazol-3-one in alkaline medium gives rise to a mixture of 4- and *O*-vinyl derivatives, and further vinylation of the first of these yields 1,4-divinyl-1,2,4-triazol-3-one. The *O*-vinyl isomer is converted into N^1- and N^2-vinyl-3-vinyloxy-1,2,4-triazoles [14].

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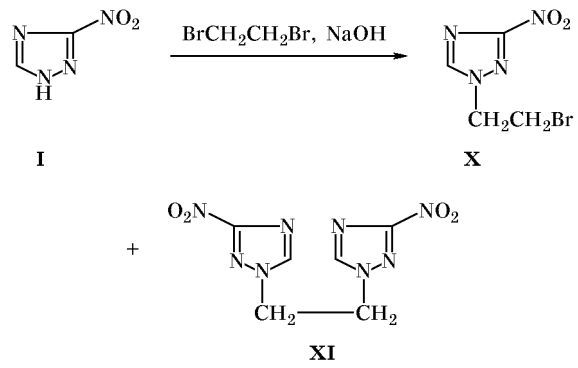
Nonselective vinylation was observed for 3-amino-1,2,4-triazole; according to [11], neither exocyclic amino group nor N^4 atom is involved, but 1- and 2-vinyl derivatives are formed at a ratio of 3 : 2.

On the whole, vinylation reactions were reported for both 1,2,4-triazole [2–9] and its 3(5)-mono- and 3,5-disubstituted derivatives having aliphatic, alicyclic, aromatic, and alkylaromatic groups [3, 5, 8], as well as for 3,5-dichloro-1,2,4-triazoles [9,10], 3-acetylamino-1,2,4-triazoles [8], 5-amino-1,2,4-triazoles [11], 1,2,4-triazole-3-thiones [4, 12, 13], and 1,2,4-triazol-3-ones [14]. However, there are no published data on vinylation of nitro-substituted 1,2,4-triazoles, although a series of available 5-R-substituted 3-nitro-1,2,4-triazoles is fairly large: R = H (**I**), OMe (**II**), Me (**III**), Br (**IV**), Cl (**V**), N_3 (**VI**), NHAc (**VII**), NO_2 (**VIII**), 3-nitro-1,2,4-triazol-5-yl (**IX**). It should be noted that 1-vinyl-3-nitro-1,2,4-triazole was used in [8] as starting compound for the synthesis of the corresponding aminotriazole, but there was no reference to the method of its preparation and its properties were not given.

It seems unreasonable to effect vinylation of nitrotriazoles with acetylene, for this process requires extremely severe conditions. Dehydrohalogenation of 1-(2-haloethyl)-3-nitro-1,2,4-triazoles may be acceptable, though some limitations are possible. These include experimental difficulties, accessibility of intermediate products, and specific behavior of N-substituted substrates in alkaline medium which is necessary for dehydrohalogenation (nucleophile can attack position *5* of the ring provided that the 5-substituent is sensitive to bases). Therefore, we initially tested the procedure including the synthesis and subsequent vinylation of *N*-(2-Z-ethyl)-1,2,4-triazoles by alkaline treatment with the use of 3-nitro-1,2,4-triazole (**I**) as an example. This compound is readily accessible, it readily undergoes alkylation [16] (pK_a 6.05 [17]), and (what is the most important) its *N*-alkyl derivatives are stable in alkaline medium.

We thought it reasonable to effect alkylation of triazole **I** with such functionalized electrophiles that the resulting *N*-substituted derivative contained a fragment capable of undergoing partial elimination to afford *N*-vinyl-substituted compound. The simplest way seemed to be monoalkylation by heating triazole **I** sodium salt with 1,2-dibromoethane in DMF. Dimethylformamide was selected on the basis of the known general relations holding in the alkylation of ambident anions and its ability to dissolve the initial reactant. Our attempts to effect alkylation in other aprotic solvents, such as acetone, acetonitrile, ethyl acetate, and dioxane, were unsuccessful because of the poor solubility of 3-nitro-1,2,4-triazole salts. In order to find optimal conditions we varied the temperature, reaction time, and reactant ratio. To avoid bis-alkylation a large excess of the reagent was taken. However, in all cases both mono- and bis-alkylation products (compounds **X** and **XI**) were formed (Scheme 1).

Scheme 1.



Products **X** and **XI** differ considerably in their solubilities and ^{1}H NMR spectra. Therefore, we were able to monitor their formation during the process, as well as to separate them when the reaction was over. The optimal ratio of $Br(CH_2)_2Br$ to compound **I** was found to be 4 : 1; further raising the concentration of the alkylating agent did not increase the fraction of the monoalkylation product. Compounds **X** and **XI** are formed at comparable rates; their ratio remains constant over a period of 6 h (80°C), and the overall yield attains 60–65%. The conversion of the initial salt can be increased to 80–90% by raising the temperature or prolonging the reaction, but in this case only the yield of product **XI** increases appreciably.

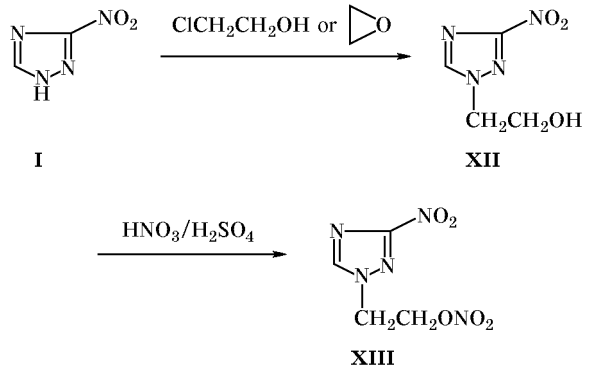
Insofar as the yield of target product **X** can be regarded as only satisfactory, we tried to find an alternative procedure, e.g., by varying functionality of the alkylating agent. In particular, 2-chloroethanol and epoxyethane are acceptable reagents for synthesis of 2-hydroxyethyl derivatives of triazole **I**. The reaction with 2-chloroethanol was carried out under conditions similar to those described above for the bromoethylation. According to the ^{1}H NMR data, the desired 1-(2-hydroxyethyl)-3-nitro-1,2,4-triazole (**XII**) was indeed formed, but the process was low effective and the isolation of the product was difficult. Therefore, we tried the other version which was widely used by us previously for preparation of structurally related alcohols [18–20], namely alkylation with epoxyethane. It should be noted that these reactions were performed with stronger NH acids ($pK_a < 6$) and that the alkylation conditions strongly depended on the

acid–base properties of the substrate. The reaction with triazole **I** at 18–20°C occurred at an appreciable rate only in the presence of a base and was accompanied by increase in pH due to consumption of the substrate. The highest yield of 2-hydroxyethyl derivative was reached at pH 8–9. To avoid further hydroxyethylation, the process should be interrupted by diluting the reaction mixture and neutralizing excess alkali. The synthesis can be performed in both aprotic (acetone, acetonitrile, dioxane) and proton-donor solvents, but the best results were obtained in ethanol. Our results indicate that the alkylation follows the base catalysis mechanism where the oxirane ring is opened by the action of both NH acid and the corresponding anion, as in the case of 3,5-dichloro-1,2,4-triazole (pK_a 5.22) [19] when the role of proton-donor agent (pH > 8) is played by the solvent. The alkylation of 3-nitro-1,2,4-triazole with epoxyethane gave alcohol **XII** in a satisfactory yield.

In principle, the vinyl group can be obtained by dehydration of alcohols, but this process requires as a rule very severe conditions. It is more convenient to initially transform the alcohol into a structure more suitable for subsequent elimination. For this purpose, chlorination with thionyl chloride is used. Taking into account that the nitro group in any position of the ring is capable of being replaced by halogen on treatment with chlorinating agents and HCl [21], we applied less common but milder procedure including the transformation of alcohol **XII** into nitrate **XIII** and subsequent denitration of the latter (Scheme 2). This procedure was used previously for various aliphatic, aromatic, and heterocyclic compounds, in particular for *N*-vinylnitroamines [22].

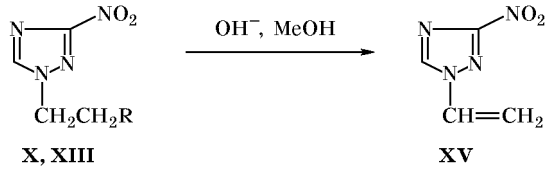
The nitration of alcohols like **XII** to the corresponding nitrates with a mixture of sulfuric and nitric acids occurs smoothly provided that the temperature is maintained at 10–15°C [19, 20]. The target products, nitroxy compounds **XIII** and **XIV** [20], can be

Scheme 2.



protonated by waste acid; as a result, their yield considerably decreases. Therefore, it is advisable to neutralize the mixture (after dilution) to pH 5–6. Compound **XIII** was then denitrated under conditions similar to the conditions for dehydrobromination of **X**, and 1-vinyltriazole **XV** was thus obtained in high yield (Scheme 3).

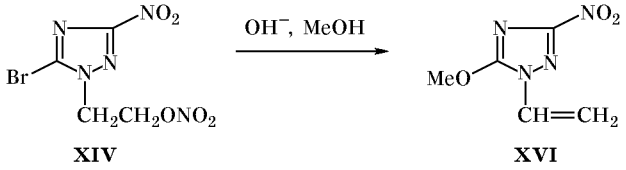
Scheme 3.



X, R = Br; **XIII**, R = ONO_2.

An analogous reaction with 5-bromo-3-nitro-1-(2-nitroxyethyl)-1,2,4-triazole (**XIV**) was accompanied by replacement of the 5-bromine atom, and the only product was 5-methoxy-3-nitro-1-vinyl-1,2,4-triazole (**XVI**) (Scheme 4).

Scheme 4.



The ease of halogen replacement was surprising. It is known that this process usually requires much more severe conditions; according to [23], the halogen atom in position *5* of the triazole ring is deactivated toward nucleophiles due to conjugation with the ring. We believe that *+R*-substituents at C^5 can be involved in direct polar conjugation with the aza group in the *para*-position (N^2), which is responsible for the strongly reduced reactivity of the halogen in most 5-bromo-3-nitro-1,2,4-triazole derivatives. Such a specific "aza effect" was observed in the series of azines [24].

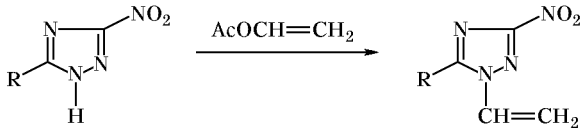
It is clear that the above procedure for generation of vinyl group by alkaline dehydrohalogenation of the *N*-alkyl substituent cannot be applied to synthesis of a wide series of 1-vinyl-3-nitro-5-R-1,2,4-triazoles, especially when the 5-substituent is sensitive to bases. On the other hand, just such derivatives attract increased interest due to the possibility for modifying the structure of *N*-vinyltriazoles through substitution at C^5 by various nucleophiles.

An alternative procedure is direct vinylation of 3-nitro-1,2,4-triazoles with vinyl acetate. This method is usually applied to fairly weak NH acids of the azole series, including 1,2,4-triazole derivatives (pK_a > 10). Among these, only 3,5-dichloro-1,2,4-triazole [19] has an acidity (pK_a 5.22) comparable with the acidity of nitrotriazoles. Depending on the substituent at C^5, the acidity of 3-nitro-1,2,4-triazoles **I**–**IX** ranges from –0.66 to 6.75 [17], i.e., it changes by 8 log units. In this connection, the problem is not only the possibility of vinylation of 3-nitro-5-R-1,2,4-triazoles with vinyl acetate, in principle, but also applicability limits of this reaction within the series of compounds under study. It should be kept in mind that vinyl acetate also possesses properties of an olefin, i.e., it is capable of reacting through the double bond to give addition products; 3-nitro-5-R-1,2,4-triazoles are known to be fairly reactive in such processes [25].

The procedure was developed using 3-nitro-1,2,4-triazole (**I**, pK_a 6.05) as an example. The catalyst, reactant ratio, temperature, and reaction time were varied. Mercury(II) salts in the presence of concentrated sulfuric acid turned out to be the best catalyst. Mercury(II) sulfate or acetate in the absence of a strong mineral acid was not effective within an acceptable temperature range (40–60°C): the target vinyl derivative was formed in an appreciable amount only under more severe conditions (70°C, more than 20 h) which promoted strong tarring. The use of mercury acetate alone as catalyst was also ineffective in the vinylation of benzotriazole; in the vinylation of benzimidazole the yield of the target product was very small [26]. The nitrotriazoles involved in this reaction are stronger NH acids; taking into account that the reaction is catalyzed by acids, the NH acidity of the substrate is likely to be the determining factor.

With the use of $HgO–H_2SO_4$ as catalyst we succeeded in attaining 70–80% conversion of azole **I** in 4–5 h at 40–50°C (increase of the reaction time to 6 h and more had no appreciable effect on the yield of the product). At higher temperature tarring was observed. Addition of hydroquinone as inhibitor of polymerization improves the purity of the product. The reaction also occurs at room temperature, but its rate is low: the conversion of triazole **I** in 14 h is only 20%. The optimal reactant ratio triazole–vinyl acetate is 1 : (5–10), and the reaction can be carried out without a solvent. Our experiments with smaller excess of vinyl acetate in an organic solvent gave worse results. The developed procedure was applied to a wide series of 5-substituted 3-nitro-1,2,4-triazoles **I**–**IX**. However, the synthesis was successful only with NH acids **I**–**VII** whose pK_a values range from 7 to 3 (Scheme 5). The strongest NH acids in this series, 3,5-dinitro-1,2,4-triazole (**VIII**) and 5,5′-bis(3-nitro-1,2,4-triazole) (**IX**) (pK_a 2.1 and 5.3, respectively; determined by M.S. Pevzner using spectrophotometric technique), reacted in an unusual way. From compound **VIII** we obtained a product which showed in the ^{1}H NMR spectrum (Table 1) three signals instead of two quartets typical of vinyl group (Table 2). Two signals were observed in the region of methyl protons: a singlet at δ 2.08 ppm (3H) and a doublet at δ 2.00 ppm (3H), and the third signal was a downfield quartet at δ 7.68 ppm (1H). The IR spectrum of the product indicated the presence of an ester moiety instead of vinyl group. On the basis of the spectral data and elemental composition, the product was assigned the structure of 1-(3,5-dinitro-1,2,4-triazol-1-yl)ethyl acetate (**XXII**). Obviously, it was formed by addition of the azole at the double bond of vinyl acetate, following the Michael reaction pattern (Scheme 6). It should be emphasized that we did not detect even traces of the target *N*-vinyltriazole.

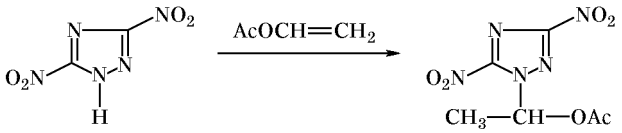
Scheme 5.



I–**VII** **XV**–**XXI**

I, **XV**, R = H; **II**, **XVI**, R = MeO; **III**, **XVII**, R = Me; **IV**, **XVIII**, R = Br; **V**, **XIX**, R = Cl; **VI**, **XX**, R = N_3; **VII**, **XXI**, R = AcNH.

Scheme 6.

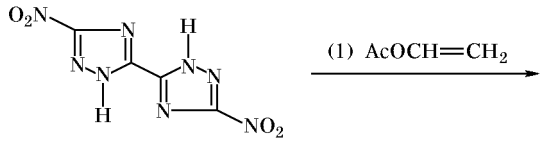


VIII **XXII**

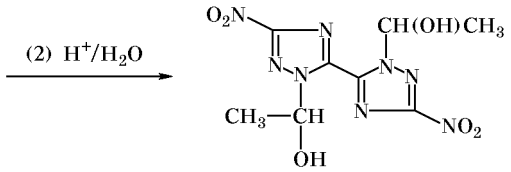
In the reaction with bitriazole **IX**, either vinylation to form mono- or divinyl derivative or addition to vinyl acetate as described above for 3,5-dinitro-1,2,4-triazole (**VIII**) might be expected. Also, the formation of a product with both kinds of substituents on the nitrogen cannot be ruled out. The isolated product was pure (according to TLC), but its spectral parameters and analytical data conformed to none of the expected structures. Compound **XXIII** was insoluble in alkalies, indicating that both hydrogen atoms on the nitrogens were replaced, but it contained neither vinyl

nor ester groups. As in azole **XXII**, the *N*-alkyl moiety of **XXIII** included the $CHCH_3$ fragment but no acetyl group was found: The ^1H NMR spectrum lacked methyl group singlet, and carbonyl absorption was not observed in the IR spectrum. The elemental composition of compound **XXIII** was consistent with the structure of 5,5′-bis[1-(1-hydroxyethyl-3-nitro-1,2,4-triazole) which could be formed in a way similar to compound **XXII** with subsequent acid hydrolysis (Scheme 7).

Scheme 7.



IX



XXIII

The structure of products **XXII** and **XXIII** suggests that in the addition of azoles **VIII** and **IX** to vinyl acetate nucleophilic attack occurs at the internal carbon atom of the double bond.

It is not surprising that triazoles **I**–**VII** ($pK_a > 3$) which are weaker NH acids than compounds **VIII** and **IX** ($pK_a < 3$) do not add across the double bond of vinyl acetate, for their ionization is suppressed in the presence of a strong mineral acid; moreover, partial protonation of azoles **I**–**VII** is possible. As shown in [25], addition of such triazoles to activated olefins requires catalysis by bases. Therefore, all compounds **I**–**VII**, beginning with 5-bromo(chloro)-3-nitro-1,2,4-triazole (pK_a 3.05) react with vinyl acetate to afford the corresponding 1-vinyl derivatives. Stronger NH acids ($pK_a < 3$) need no base to react with olefins according to Michael, and 3,5-dinitro-1,2,4-triazole (**VIII**), being a very strong NH acid, readily adds to olefins in both proton-donor and aprotic media [25]. Presumably, the given vinylation conditions ensure sufficient degree of ionization of strongly acidic triazoles, so that the addition process occurs. We can conclude that the reaction of triazoles with vinyl acetate is governed by the acidity of the former: NH acids with $pK_a > 3$ give rise to vinylation, whereas 1,2,4-triazoles with $pK_a < 3$ add at the double bond of the reagent. Probably, an analogous pattern should be observed for other azole series, e.g., for tetrazole derivatives.

A specific group of NH acids of the triazole series consists of amino derivatives. Successful vinylation of such compounds could give rise to structural modifications through transformation of the amino group (oxidation, diazotization), including the synthesis of the corresponding nitro compounds. This is especially important in cases when direct vinylation is impossible.

Although the acidity of 3-R-substituted 5-amino-1,2,4-triazoles (R = H, NH_2, NO_2) falls into a range suitable for vinylation (pK_a 7–12), we failed to react them with vinyl acetate under the selected conditions: the initial triazole was recovered from the reaction mixture. A possible reason is removal of sulfuric acid from the reaction zone via formation of triazolium salts which are insoluble in vinyl acetate (they precipitated immediately after mixing the reactants). Acylation of the amino group eliminates this problem, and both 5-acylamino-1,2,4-triazole [8] and its 3-nitro analog **VII** undergo vinylation following the general scheme.

Summarizing the above stated, we can conclude that vinylation with vinyl acetate is successful for most 1,2,4-triazoles with $pK_a > 3$; for more acid substrates, Michael addition to vinyl acetate is expected; aminotriazoles should be brought into the reaction with preliminary protected amino group.

Taking into account electron-acceptor properties of the triazolyl group, 1-vinyl-1,2,4-triazoles can be regarded as olefins possessing an activated double bond, which must be capable of reacting with both electrophilic and nucleophilic reagents. There are some data indicating that the *N*-vinyl fragment acts as acceptor with respect to the heteroring (e.g., in pyrroles and carbazoles). The conjugation between the *N*-vinyl group and the heteroring enhances nucleophilicity of the double bond [27].

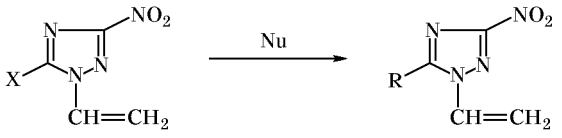
Chemical properties of vinyl derivatives of 1,2,4-triazole were not studied in detail, though a fairly high reactivity was noted for some representatives of this series. For example, 3-amino-1-vinyl-1,2,4-triazole exhibits properties typical of all its molecular fragments: It reacts with HCl to give the corresponding hydrochloride, forms quaternary salts with KI and complexes with manganese, cobalt, and zinc chlorides, and reacts with aldehydes at the amino group; the vinyl group can be involved in bromination, hydrogenation, and polymerization to give water-soluble polymers [11]. The reduction and ready polymerization were reported for 1-vinyl-1,2,4-triazole [2], and

polymerization of 3,5-dichloro-1-vinyl-1,2,4-triazole was described [10]. Nitration of the latter is known to give 1-(3,5-dichloro-1,2,4-triazol-1-yl)-1-nitroethylene which was isolated as tetramer [10]. According to the authors, the nitration occurs as addition at the double bond with formation of 1-nitro-2-nitroxyethyl derivative, followed by elimination of nitric acid and tetramerization.

3-Nitro-1-vinyl-1,2,4-triazoles behave quite differently. As follows from the data of [8], both vinyl and nitro group in these compounds can be reduced; however, reactions at the vinyl group are not typical to 5-substituted 3-nitro-1-vinyl-1,2,4-triazoles. Our attempts to involve them in Michael addition with nitroalkanes or triazoles, including such reactive CH and NH acids as nitroform and 3,5-dinitro-1,2,4-triazole, were unsuccessful. We also failed to effect oxidation with peroxyacids or nitration at the double bond. Under more severe conditions oxidative elimination of the vinyl group occurred to give the corresponding 3-nitro-1,2,4-triazole. Moreover, unlike 1-vinyl-1,2,4-triazole, its nitro derivatives do not undergo polymerization. This means that introduction of a nitro group into position *3* of the triazole ring strongly deactivates the *N*-vinyl fragment.

On the other hand, vinylation of the N^1 atom has a considerable effect on the electron density distribution in the triazole ring. In particular, this concerns the conjugation between the ring and C^5-substituent having an unshared electron pair (R = Br, Cl, N_3, OCH_3). As a result, the mobility of this substituent increases, and it can be replaced by nucleophiles. The effect of the *N*-vinyl group was revealed for the first time in an attempt to obtain 5-bromo-3-nitro-1-vinyl-1,2,4-triazole by alkaline treatment of the *N*-(2-nitroxyethyl) derivative (see above). We then used this reaction to modify the structure of 3-nitro-1-vinyl-1,2,4-triazoles via replacement of the 5-substituent by both conventional nucleophiles (azide ion, hydrazine, methanolic alkali) and salts derived from

Scheme 8.

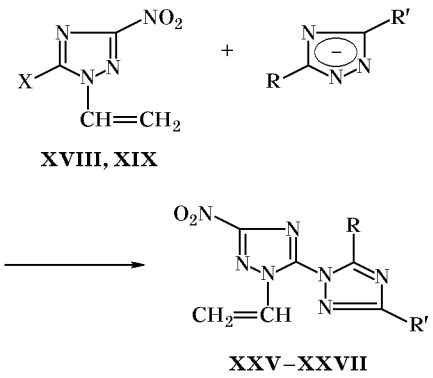


XVI, XVIII–XX **XVI, XX, XXIV**

Nu = MeONa/MeOH: **XVI**, R = MeO; **XVIII**, X = Br; **XIX**, X = Cl; **XX**, X = N_3; Nu = N_3: **XX**, R = N_3; **XVI**, X = MeO; **XVIII**, X = Br; **XIX**, X = Cl; Nu = N_2H_4: **XXIV**, R = $NHNH_2$; **XVIII**, X = Br; **XIX**, X = Cl.

1,2,4-triazoles themselves. Compounds **XVIII**–**XX** were readily converted into 5-methoxy derivative **XVI** by the action of bases in methanol. From triazoles **XVI**, **XVIII**, and **XIX** we obtained under fairly mild conditions the corresponding 5-azidotriazole **XX** and hydrazino derivative **XXIV** (Scheme 8). Halogen derivatives **XVIII** and **XIX** are capable of reacting with such weakly basic nucleophiles as NH acids of the triazole series. As a result, 3-nitro-1-vinyl-5-(3-R-5-R′-1,2,4-triazol-1-yl)-1,2,4-triazoles **XXV**–**XXVII** were obtained (Scheme 9).

Scheme 9.



XVIII, X = Cl; **XIX**, X = Br; **XXV**, R = H, R′ = NO_2; **XXVI**, R = H, R′ = N_3; **XXVII**, R = Cl, R′ = NH_2.

Previously, such heterylation of triazolate ions was possible only through replacement of the nitro group in *N*-substituted 3,5-dinitro-1,2,4-triazoles [28]. 5-Halo-3-nitro-1-vinyl-1,2,4-triazoles **XVIII** and **XIX** showed a comparable reactivity (acetone, 55°C, 8–10 h; the progress of the reaction was monitored by TLC, following disappearance of the sulbstrate). We failed to replace the halogen atom in other 5-bromo-3-nitro-1,2,4-triazole derivatives using even the most basic triazolate ions and under much more severe conditions (DMF, 100–120°C, 20–48 h; only traces of the target products were detected). In the reactions with 5-halo-3-nitro-1-vinyl-1,2,4-triazoles we detected no expected by-product, 3-nitro-1-vinyl-1,2,4-triazol-5-one, which is usually formed in such processes as a result of attack by hydroxide ion on C^5. As a rule, the fraction of triazolone is considerable, and it increases as the reactivity of the reagent and substrate decreases. Thus we have one more evidence for the anomalously high lability of the halogen atom in 5-halo-3-nitro-1-vinyl-1,2,4-triazoles. A plausible explanation is (1) the acceptor effect of the vinyl group on the heteroring and (2) conjugation with N^2 through the $CH_2{=}CH{-}N^1{-}N^2{=}$ bond sequence,

which weakens the bond between C^5 and the substituent. These effects are reflected in the considerable downfield shift of the 5-H signal in the ^{1}H NMR spectrum of compound **XV**, as compared to **I** (Table 1). The chemical shift of the ring proton is larger than 9 ppm for all *N*-heteryl 3-nitro-1,2,4-triazoles [28], where both the above effects are operative. A similar pattern is observed in the ^{1}H NMR spectra of N–C-bitriazoles **XXV** and **XXVI**.

The IR spectra of vinyltriazoles contain bands typical of other nitrotriazole derivatives [$\nu(NO_2)$ 1540–1565, 1300–1350, ν(ring) 1485–1525 cm^{-1}] and a band at 1640–1670 cm^{-1} belonging to stretching vibrations of the C=C bond. The other bands which are usually assigned to vinyl group vibrations [ν(C−H) 3010–3040, 3095–3075, δ(C−H) 995–985, $\delta(CH_2)$ 915–905, 1420–1410, 1300–1290 cm^{-1}] are either poorly resolved or overlapped by bands arising from the other structural fragments. Comparison of the spectra of 1-vinyltriazoles and their precursors, 3-nitro-5-R-1,2,4-triazoles shows that a doublet or triplet in the region 930–980 cm^{-1} can be assigned to vibrations of the vinyl group. Bitriazoles **XXV**–**XXVII** are characterized by additional absorption bands at 1320 and 1580–1590 cm^{-1}; the appearance of these bands in the spectrum of dinitro derivative **XXV** could be explained by the presence of one more nitro group in the triazolyl substituent. However, similar bands are also present in the spectra of compounds **XXVI** and **XXVII**; presumably, they should be assigned to vibrations of the heteroring.

In the ^{1}H NMR spectra of 5-substituted 3-nitro-1-vinyl-1,2,4-tetrazoles, signals from the vinyl protons appear as three asymmetric quartets at δ 7–8 (H_C) and 5.25–6.1 ppm (CH_AH_B), which are typical of an *ABC* spin system.

Taking into account that direct vinylation of triazole **I** and elimination reactions of N^1-alkyltriazoles **X** and **XIII** gave the same product **XV**, we can conclude that N-substitution occurs preferentially at position *1* of the triazole ring.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Perkin–Elmer R-12 spectrometer (60 MHz) in acetone-d_6 using HMDS as internal reference. The IR spectra were measured on a Specord 75IR instrument from samples prepared as thin films.

1-(2-Bromoethyl)-3-nitro-1,2,4-triazole (X) and 1,2-bis(3-nitro-1,2,4-triazol-1-yl)ethane (XI). To 2 ml of water we added 0.05 mol of NaOH, 0.05 mol of triazole **I**, 50 ml of DMF, 0.3 mol of 1,2-dibromoethane, and 0.1 g of tetraethylammonium bromide, and the mixture was stirred for 6 h at 90°C, cooled, and poured into 150 ml of water. The precipitate of compound **XI** was filtered off and recrystallized. The filtrate was extracted with ethyl acetate (3×50 ml), the extract was evaporated, and the residue (product **X**) was recrystallized.

1-(2-Hydroxyethyl)-3-nitro-1,2,4-triazole (XII). *a*. To a solution of 0.12 mol of sodium hydroxide in 2 ml of water we added 30 ml of DMF, 0.1 mol of triazole **I**, 0.2 mol of 2-chloroethanol, and 0.1 g of sodium bromide. The mixture was heated to 80°C, stirred for 18 h at that temperature, cooled, poured into 100 ml of water, and treated with ethyl acetate (5×30 ml). The extract was dried over calcined $MgSO_4$, the solvent was removed under reduced pressure, and the residue was recrystallized from ethanol.

b. To a solution of 0.005 mol of sodium hydroxide in 2 ml of water we added 40 ml of ethanol, 0.05 mol of triazole **I**, and 0.1 mol of freshly distilled epoxyethane. The mixture was kept for 36–40 h in a closed vessel at 18–20°C with occasional stirring; the pH of the medium was checked periodically. When the pH attained a value of 7.8–8.0, the mixture was diluted with two volumes of water and neutralized with dilute sulfuric acid. Ethanol was removed, and the product was extracted into ethyl acetate. The subsequent procedure was the same as described above in *a*.

3-Nitro-1-(2-nitroxyalkyl)-1,2,4-triazole (XIII). 1-(2-Hydroxyethyl)triazole **XII**, 5 g, was added in portions with stirring and cooling to 20 ml of a mixture prepared from equal volumes of concentrated sulfuric and nitric acids, maintaining the temperature below 10°C. The mixture was stirred for 3 h at that temperature, poured onto a 3-fold amount (by volume) of crushed ice, and neutralized with sodium hydrogen carbonate. The precipitate was filtered off, the filtrate was extracted with ethyl acetate, the solvent was removed, and the residue was combined with the main portion of the product. The product was washed with water, dried in air, and recrystallized.

3-Nitro-1-vinyl-1,2,4-triazole (XV). *a*. To a solution of 0.01 mol of bromoethyl derivative **X** in 50 ml of methanol at 30–35°C we added with stirring in portions a solution of 0.02 mol of potassium hydroxide in 10 ml of methanol. The mixture was kept for 1 h at 30–35°C and cooled. The precipitate of KBr was filtered off, the filtrate was evaporated, and the residue was purified by recrystallization.

b. Nitrate **XIII**, 0.05 mol, was dissolved in 30 ml of ethanol, a solution of 0.1 mol of sodium hydroxide

Table 1. IR and ^{1}H NMR spectra of triazoles **X**–**XIII**, **XXII**, and **XXIII**

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm
X	835, 870, 880, 950, 1050, 1190, 1210, 1300, 1355, 1380, 1415, 1435, 1495, 1540	8.90 s (1H, 5-H), 4.95 t (2H, CH_2), 4.02 t (2H, CH_2)
XI	840, 875, 955, 1040, 1060, 1190, 1230, 1305, 1360, 1380, 1410, 1450, 1505, 1555	8.70 s (1H, 5-H), 5.12 s (4H, CH_2)
XII	845, 870, 890, 980, 1040, 1160, 1210, 1310, 1365, 1375, 1415, 1425, 1510, 1560, 3200–3600	8.80 s (1H, 5-H), 4.50 t (2H, CH_2), 4.35 t (2H, CH_2), 5.60 t (1H,[a] OH)
XIII	855, 875, 900, 980, 1180, 1230, 1310, 1360, 1375, 1425, 1510, 1560, 1650	8.80 s (1H, 5-H), 5.16 m (4H, CH_2)
XXII	940, 1020, 1050, 1110, 1225, 1320, 1340, 1350, 1380, 1440, 1540, 1580, 1750	2.00 d (3H, CH_3), 2.08 s (3H, CH_3), 7.68 q (1H, CH)
XXIII	950, 980, 1065, 1100, 1320, 1360, 1410, 1550, 1555	1.95 d (3H, CH_3), 6.65 q (1H, CH)

[a] Exchanges with D_2O.

Table 2. IR and ^{1}H NMR spectra of 1-vinyltriazoles **XV**–**XXI** and **XXV**–**XXVII**

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum,[a] δ, ppm		
		H_A, H_B, q	H_X, q	other protons
XV	935, 950, 965, 1190, 1320, 1390, 1420, 1505, 1555, 1650	6.03, 5.38	7.58	9.05 s (1H, 5-H)
XVI	920, 960, 1160, 1180, 1310, 1380, 1420, 1510, 1560, 1645	5.85, 5.30	7.30	4.35 s (3H, CH_3)
XVII	930, 970, 1145, 1315, 1410, 1540, 1560, 1660	6.00, 5.41	7.60	2.70 s (3H, CH_3)
XVIII	940, 960, 1085, 1310, 1380, 1430, 1500, 1565, 1650	6.10, 5.58	7.55	–
XIX	930, 950, 1105, 1310, 1365, 1435, 1500, 1565, 1650	6.61, 5.55	7.52	–
XX	940, 970, 1145, 1240, 1310, 1385, 1510, 1565, 1650, 2175	5.90, 5.35	7.15	–
XXI	950, 970, 1165, 1240, 1260, 1320, 1380, 1490, 1570, 1660, 1725	6.80, 5.25	7.23	2.70 s (3H, CH_3)
XXV	940, 960, 990, 1140, 1210, 1305, 1320, 1390, 1430, 1520, 1560, 1580, 1650	6.25, 5.65	8.00	9.65 s (1H, 5-H)
XXVI	920, 970, 990, 1195, 1310, 1320, 1360, 1440, 1530, 1570, 1590, 1655, 2165	6.05, 5.45	8.00	9.25 s (1H, 5-H)
XXVII	940, 980, 1130, 1315, 1360, 1515, 1560, 1590, 1650, 1670	5.95, 5.40	7.97	7.80 (2H, NH_2)

[a] J_{AB} = 2.0 Hz, J_{AX} = 17 Hz, J_{BX} = 10 Hz.

in 5 ml of water was added with stirring, and the mixture was heated to 40°C, kept for 0.5 h at that temperature, cooled, and poured into 100 ml of water. The mixture was filtered, the filtrate was extracted with ethyl acetate (3 × 30 ml), the extract was dried over calcined magnesium sulfate and evaporated, and the residue was recrystallized.

c. Triazole **XV** was synthesized by reaction of 3-nitro-1,2,4-triazole with vinyl acetate following the transvinylation procedure (see below).

5-Substituted 3-nitro-1-vinyl-1,2,4-triazoles XV–**XXI (***transvinylation procedure***), 1-(3,5-dinitro-1,2,4-triazol-1-yl)ethyl acetate (XXII), and 5,5′-bis(1-hydroxyethyl-3-nitro-1,2,4-triazole) (XXIII).** Triazole **I**–**IX**, 44 mmol, HgO, 0.2 g, concentrated sulfuric acid, 3–4 drops, and hydroquinone, 0.3 g, were added to 30 ml of vinyl acetate. The mixture was heated under stirring to 50°C, kept for 4–6 h at that temperature, cooled, and poured into 100 ml of water. The precipitate was filtered off and washed with water. An additional amount of the product can be obtained by extraction of the filtrate with ethyl acetate. The yields, melting points, analytical data, and spectral parameters of the products are given in Tables 1–3.

Table 3. Yields, melting points, and elemental analyses of compounds **X**–**XIII**, **XV**–**XXI**, and **XXV**–**XXVII**

Comp. no.	Yield, % (method)	mp, °C (solvent	Found, %			Formula	Calculated, %			*M*	
			C	H	N		C	H	N	found	calcd.
X	30	97–98 (acetone/EtOH)	21.88, 22.01	2.51, 2.42	25.44, 25.32	$C_4H_5BrN_4O_2$	21.74	2.28	25.35	221.00	230.10
XI	42	187–188 (chloroform)	28.72, 28.47	2.45, 2.29	44.14, 44.28	$C_6H_6N_8O_4$	28.35	2.38	44.09	254.16	260.50
XII	25 (*a*), 55 (*b*)	71–72 (EtOH)	30.35, 30.48	4.00, 3.95	35.65, 35.84	$C_4H_6N_4O_3$	30.39	3.83	35.44	158.11	163.00
XIII	85	46–47 (EtOH)	23.77, 23.93	2.63, 2.24	34.52, 34.37	$C_4H_5N_5O_5$	23.65	2.48	34.48	203.11	211.20
XV	60 (*a*), 70 (*b*, *c*)	68–69 (CCl_4)	34.33, 34.15	2.79, 2.70	40.49, 40.37	$C_4H_4N_4O_2$	34.29	2.88	40.00	140.10	145.10
XVI	40 (*a*, *b*)	133–134 ($CHCl_3$)	35.01, 35.16	3.49, 3.31	32.79, 32.64	$C_5H_6N_4O_3$	35.30	3.56	32.93	170.13	175.30
XVII	75	145–146 (EtOH)	38.96, 38.78	4.09, 3.94	36.65, 36.58	$C_5H_6N_4O_2$	38.96	3.92	36.35	154.13	160.30
XVIII	75	122–123 (EtOH)	22.93, 22.10	1.61, 1.40	25.47, 25.81	$C_4H_3BrN_4O_2$	21.94	1.38	25.58	219.00	226.50
XIX	65	82–83 ($CHCl_3$)	27.66, 28.01	2.00, 1.99	31.72, 32.00	$C_4H_3ClN_4O_2$	27.52	1.73	32.10	174.54	168.00
XX	75	88–89 (EtOH)	26.58, 26.55	1.78, 1.81	54.25, 54.00	$C_4H_3N_7O_2$	26.53	1.67	54.14	181.11	187.00
XXI	40	161–162 (dichloroethane)	36.12, 36.63	3.93, 3.48	35.30, 35.72	$C_6H_7N_5O_3$	36.55	3.58	35.52	170.13	176.20
XXV	65	145–146 (EtOH)	28.96, 28.97	1.65, 1.69	44.64, 44.84	$C_6H_4N_8O_4$	28.58	1.60	44.44	252.15	248.40
XXVI	70	80–81 (EtOH)	29.29, 29.33	1.88, 1.64	56.23, 56.25	$C_6H_4N_{10}O_2$	29.04	1.62	56.44	248.17	245.00
XXVII	55	215–216 (EtOH)	28.23, 27.99	1.78, 2.08	43.95, 43.70	$C_6H_5ClN_8O_2$	28.08	1.96	43.67	256.61	254.20

5-Methoxy-3-nitro-1-vinyl-1,2,4-triazole (XVI) was synthesized from 1-(2-nitroxyethyl)triazole **XIV** [20] or azidotriazole **XX** by the procedures described above for compound **XV** (methods *b* and *c*).

5-Azido-3-nitro-1-vinyl-1,2,4-triazole (XX) and 5-hydrazino-3-nitro-1-vinyl-1,2,4-triazole (XXIV). To a solution of 19.5 mmol of 3-nitro-1-vinyl-1,2,4-triazole **XVI**, **XVIII**, or **XIX** in 70 ml of ethanol we added a solution of 21.5 mmol of sodium azide (or 40 mmol of hydrazine hydrate) in 5 ml of water, and the mixture was heated to 40–45°C and was kept for 3 h at that temperature. The solvent was removed, and the residue was washed with water and purified by recrystallization.

3-Nitro-1-vinyl-5-(3-R-5-R′-1,2,4-triazol-1-yl)-1,2,4-triazoles XXV–**XXVII.** A solution of 8.8 mmol of 3-R-5-R′-1,2,4-triazole in 5 ml of water containing 0.36 g (8.8 mmol) of sodium hydroxide was added to a solution of 8 mmol of 5-halo-3-nitro-1-vinyl-1,2,4-triazole **XVIII** or **XIX** in 50 ml of acetone. The mixture was heated to the boiling point and was stirred for 8–10 h at 55–60°C (until the initial compound disappeared, TLC). The solvent was removed, and the residue was washed with water and recrystallized.

REFERENCES

1. Tatarova, L.A., Ermakova, T.G., Lopyrev, V.A., Kedrina, N.F., and Razvodovskii, E.F., USSR Inventor's Certificate no. 647310, 1979; *Chem. Abstr.*, 1979, vol. 90, no. 204841.
2. Makhno, L.P., Ermakova, T.G., Domnina, E.S., Tatarova, L.A., Skvortsova, G.G., and Lopyrev, V.A., USSR Inventor's Certificate no. 464584, 1975; *Byull. Izobret.*, 1975, no. 11, pp. 66–67; Ermakova, T.G., Tatarova, L.A., and Kuznetsova, N.P., *Russ. J. Gen. Chem.*, 1997, vol. 67, no. 5, pp. 805–807.

3. JPN Patent no. 75-04 074, 1974; *Chem. Abstr.*, 1975, vol. 83, no. 114 414 g.
4. Trzhinskaya, B.V., Apkina, E.V., and Afonin, A.V., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, no. 4, pp. 928–931.
5. JPN Patent no. 74-35 384, 1974; *Chem. Abstr.*, 1974, vol. 81, no. 120 637 g.
6. Hopff, H. and Lippay, M., *Macromol. Chem.*, 1963, vol. 66, no. 1, pp. 157–167; Lippay, M. and Faller, M., *J. Appl. Chem.*, 1965, vol. 15, no. 3, p. 310; *Chem. Abstr.*, 1965, vol. 63, p. 7119 b.
7. FR Patent no. 1 389 363, 1965; *Chem. Abstr.*, 1965, vol. 63, p. 7119 b.
8. Bol'shedvorskaya, R.L., Gareev, G.A., Pavlova, G.A., Vereshchagin, L.I., and Chernyshova, G.V., *Osnovn. Org. Sintez Neftekhim.*, 1986, no. 22, pp. 96–102.
9. Lebedeva, N.P. and Klasek, A., *Khim. Geterotsikl. Soedin.*, 1989, no. 6, pp. 859–864.
10. Stotskii, A.A., Fomina, V.V., Lebedeva, N.P., and Klasek, A., *Izv. Vyssh. Uchebn. Zaved., Ser. Khim. Khim. Tekhnol.*, 1986, vol. 29, no. 5, pp. 41–43.
11. Skvortsova, G.G., Domnina, E.S., Makhno, L.P., Voronov, V.K., Toryashinova, D.-S.D., and Chipanina, N.N., *Khim. Geterotsikl. Soedin.*, 1973, no. 11, pp. 1566–1569.
12. Skvortsova, G.G., Trzhinskaya, B.V., Teterina, L.F., Voronov, V.K., and Popova, M.N., *Khim. Geterotsikl. Soedin.*, 1977, no. 11, pp. 1561–1563.
13. Trzhinskaya, B.V., Rudakov, E.V., Afonin, A.V., Voronov, V.K., and Pertsikov, B.Z., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, no. 12, pp. 2745–2747.
14. Trzhinskaya, B.V., Rudakova, E.V., Afonin, A.V., Keiko, V.V., and Voronov, V.K., *Khim. Geterotsikl. Soedin.*, 1987, no. 9, pp. 1224–1226.
15. Shimizu, S. and Ogata, M., *J. Org. Chem.*, 1987, vol. 52, no. 11, pp. 2314–2315.
16. Bagal, L.I., Pevzner, M.S., Sheludyakova, N.I., and Kerusov, V.M., *Khim. Geterotsikl. Soedin.*, 1969, no. 2, pp. 265–268.
17. Pevzner, M.S., Kofman, T.P., and Gorbunova, N.N., *Zh. Org. Khim.*, 1978, vol. 14, no. 10, pp. 2024–2029.
18. Kofman, T.P., Manuilova, V.I., Pevzner, M.S., and Timofeeva, T.N., *Khim. Geterotsikl. Soedin.*, 1975, no. 5, pp. 705–707; Kofman, T.P., Vasil'eva, I.V., and Pevzner, M.S., *Khim. Geterotsikl. Soedin.*, 1977, no. 10, pp. 1407–1410.
19. Kofman, T.P., Vasil'eva, I.V., and Pevzner, M.S., *Khim. Geterotsikl. Soedin.*, 1976, no. 9, pp. 1281–1285.
20. Kofman, T.P., Zykova, G.A., Manuilova, V.I., Pevzner, M.S., and Timofeeva, T.N., *Khim. Geterotsikl. Soedin.*, 1974, no. 7, pp. 997–1002.
21. Bagal, L.I., Pevzner, M.S., Samarenko, V.Ya., and Egorov, A.P., *Khim. Geterotsikl. Soedin.*, 1970, no. 12, pp. 1701–1703.
22. Korchagin, M.P., Blinova, L.S., Karpov, G.A., Mikhailova, I.S., Aleksandrova, E.V., and Korol', O.V., *Khim.-Farm. Zh.*, 1999, vol. 33, no. 1, pp. 40–43; Gafarov, A.N., Zakirova, G.T., Novikov, S.S., Ermolaeva, V.A., and Vorob'eva, V.V., *Zh. Org. Khim.*, 1973, vol. 9, no. 1, pp. 46–49.
23. Pevzner, M.S., Samarenko, V.Ya., and Bagal, L.I., *Khim. Geterotsikl. Soedin.*, 1972, no. 6, pp. 848–851.
24. Pozharskii, A.F., *Teoreticheskie osnovy khimii geterotsiklov* (Theoretical Foundations of the Chemistry of Heterocycles), Moscow: Khimiya, 1985.
25. Kofman, T.P., Krivosheeva, G.S., and Pevzner, M.S., *Zh. Org. Khim.*, 1993, vol. 29, no. 11, pp. 2304–2310; Kofman, T.P., Uspenskaya, T.L., Medvedeva, N.Yu., and Pevzner, M.S., *Khim. Geterotsikl. Soedin.*, 1976, no. 7, pp. 991–994.
26. Hapff, H., Wyss, U., and Zussi, H., *Helv. Chim. Acta*, 1960, vol. 43, no. 2, pp. 135–139.
27. Trofimov, B.A., Golovanova, N.I., Mikhaleva, A.I., Korostova, S.E., Vasil'ev, A.N., and Balabanova, L.M., *Khim. Geterotsikl. Soedin.*, 1977, no. 7, pp. 915–920; Filimonov, V.D., Afinogenov, V.A., and Matkonov, M.E., *Khim. Geterotsikl. Soedin.*, 1976, no. 10, pp. 1318–1323.
28. Kofman, T.P., Kartseva, G.Yu., Namestnikov, V.I., and Paketina, E.A., *Russ. J. Org. Chem.*, 1998, vol. 34, no. 7, pp. 1032–1039; Pevzner, M.S., Kofman, T.P., Kibasova, E.N., Sushchenko, L.F., and Uspenskaya, T.L., *Khim. Geterotsikl. Soedin.*, 1980, no. 2, pp. 257–261.