DOI 10.1007/s10593-017-2157-y

Chemistry of Heterocyclic Compounds **2017**, *53*(9), 963–975

Synthesis and azido-tetrazole tautomerism of 3-azido-1,2,4-triazines

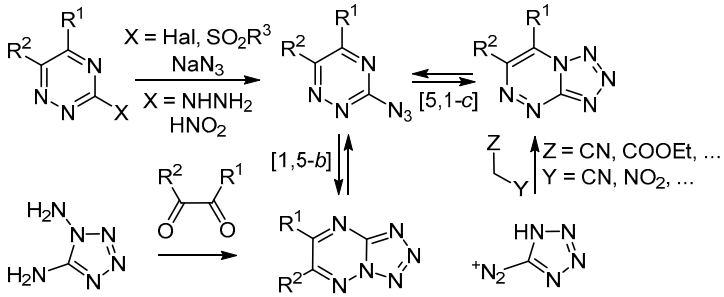
Sergey L. Deev[1]*, Tatyana S. Shestakova[1], Valery N. Charushin[1,2], Oleg N. Chupakhin[1,2]

[1] *Ural Federal University named after the first President of Russia B. N. Yeltsin, 19 Mira St., Yekaterinburg 620002, Russia; e-mail: deevsl@yandex.ru*

[2] *I. Ya. Postovskii Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 22 S. Kovalevskoi / 20 Akademicheskaya St., Yekaterinburg 620990, Russia; e-mail: charushin@ios.uran.ru*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2017, *53*(9), 963–975

Submitted July 19, 2017
Accepted August 24, 2017



This review provides a generalized and systematized literature data from the previous 50 years on the synthesis and azido-tetrazole equilibrium of 3-azido-1,2,4-triazines, which are capable of rearrangement to tetrazole isomers with various types of ring fusion between the azole and azine moieties. Since the cyclization of 3-azido-1,2,4-triazines can lead to the formation of both tetrazolo[5,1-*c*][1,2,4]-triazines and tetrazolo[1,5-*b*][1,2,4]triazines, a particular attention was devoted to the methods for proving the structures of the isomeric tetrazole forms.

Keywords: azides, condensed triazines, tetrazoles, azido-tetrazole tautomerism, IR spectroscopy, NMR spectroscopy, ring-chain transformations, types of fusion.

The ring-chain transformations observed with heterocyclic structures are a characteristic type of reactivity for this broad class of compounds. Such reactions are well known in the chemistry of hetarenes, but not for carbocyclic arenes. At the same time, they are essential from synthetic point of view, especially in planning the routes of synthesis for the preparation of condensed bi- and polycyclic compounds.[1–10]

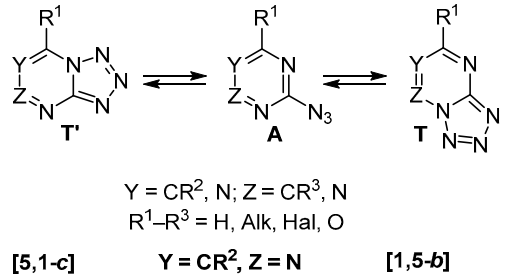
The occurrence of ring-chain transformations and understanding of the factors affecting the shifting of equilibrium and stability of the cyclic or open-chain forms are important for performing directed intramolecular cyclization reactions leading to the formation of condensed molecules.[1–13]

Several types of ring-chain transformations exist, which are based on intramolecular cyclization reactions of open-chain O-, N-, and C-nucleophiles with electron-deficient carbon atoms of cyclic systems containing strongly polar C=O, C=N, or C=S bonds. Another type of cyclization is associated with intramolecular attack by electron-deficient terminal atoms of the open-chain form on the ring system heteroatoms bearing a lone pair of electrons. Theoretical studies of cyclization reactions involving azide group and the lone pair of electrons belonging to nitrogen atom[13] have provided a better theoretical understanding of pericyclic reactions and supported the development of the concept of pseudopericyclic[14] and heteroelectrocyclic[15] reactions. The latter type also includes the cyclization of azido group located at α-position relative to a heterocyclic nitrogen atom belonging to an azole or azine ring, leading to the formation of tetrazole isomer.[16] Such phenomenon is known as azido-tetrazole tautomerism and can be considered to be one of the basic properties of hetaryl azides. This type of ring-chain transformations is reversible and proceeds spontaneously or during the preparation of solutions of such compounds.

A large number of published studies are devoted to the transformations of azide isomer to the tetrazole form in various heterocyclic systems. A substantial contribution to the understanding of these transformations was made by Academician I. Ya. Postovskii, who was one of the first to study these transformations both in the series of tetrazoloazines[17–19] and tetrazoloazoles[20] by using for this purpose IR spectroscopy in solutions, solid state, and melts. The majority of these pioneering studies and the later works by other authors have been described in review articles.[16,21–23] In addition, the cyclization of some hetaryl azides to the tetrazole isomer can produce two cyclic forms (Scheme 1). This type of heterocycles includes compounds **A** derived from 2-azidopyrimidines (Y = CR^2, Z = CR^3), 2-azido-1,3,5-triazines (Y = N, Z = CR^3), and 3-azido-1,2,4-triazines (Y = CR^2, Z = N), lacking *N*-alkyl or *N*-oxide groups at positions 2 and 4 of the triazine ring. This type of azides **A** is capable of transformations both to tetrazole **T'** and to its isomeric cyclic form **T** (Scheme 1). The characteristic structural difference of 1,2,4-triazine derivatives **T'** (Y = CR^2, Z = N) and **T** (Y = CR^2, Z = N) is evident in the type of ring fusion between the azine and azole moieties. In this case, it can be specified as [5,1-*c*] and [1,5-*b*], respectively.

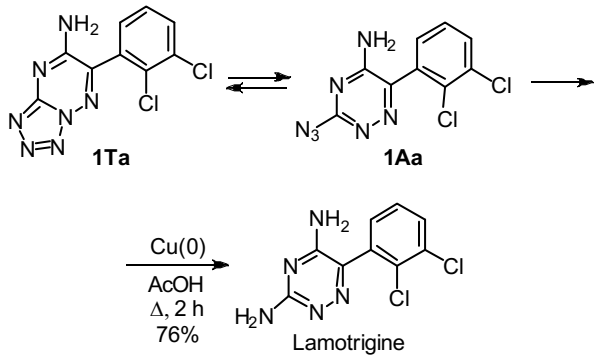
The unpredictable behavior of azide **A** requires that researchers working in this field of chemistry not only perform the synthesis of these hetaryl azides and establish the azido-tetrazole equilibrium, but also pay particular attention to proving the structure of tetrazole isomers **T'** and **T**.

Scheme 1



It should be noted that in recent years there is a renewed interest in 3-azido-1,2,4-triazines and their tetrazole analogs, which belong to the group of heterocycles with high nitrogen content. Due to such structure, this class of compounds is considered as a template for the design of new high energy materials.[24,25] Besides that, the aforementioned series of compounds are also used in search for biologically active compounds.[26–28] For these reasons, it is necessary to study the azido-tetrazole equilibrium of 3-azido-1,2,4-triazines **A** in order to facilitate the future investigations regarding the mechanisms of biological interactions of active structures. An example of practical results from applying tetrazole derivatives of 3-azido-1,2,4-triazines in the synthesis of biologically active compounds is the development of a new method for the preparation of the antiepileptic drug lamotrigine[29] (Scheme 2). This approach was based on the reduction of the corresponding tetrazolo[1,5-*b*][1,2,4]-triazine **1Ta**. Obviously, it would be impossible to perform this transformation without the existence of an azido-tetrazole equilibrium between the isomeric structures **1Ta** and **1Aa**. Thus, it is essential to study the ring-chain transformations in the series of 3-azido-1,2,4-triazines in order to enable practical applications of these compounds.

Scheme 2



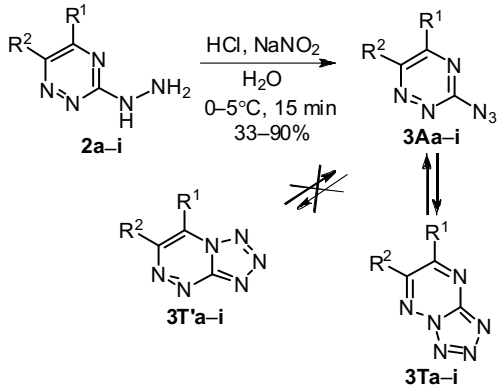
A literature survey showed that the methods for the preparation of 3-azido-1,2,4-triazines **A** can be divided into three main synthetic approaches. The first approach involves the treatment of the respective hetarylhydrazines with nitrous acid. The second approach is based on the substitution of good leaving groups at position 3 of 1,2,4-triazine ring with azide groups. The third variant for the synthesis of compounds **A** involves condensation of the azine moiety with tetrazole ring.

Synthesis from 3-hydrazino-1,2,4-triazines

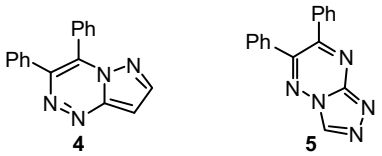
The reaction of 3-hydrazino-1,2,4-triazines with nitrous acid is one of the traditional routes for the preparation of hetaryl azides. This method was successfully used for converting compounds **2a**–**h** to azidotriazines **3Aa**–**h**, which spontaneously isomerized to tetrazolo[1,5-*b*][1,2,4]triazines **3Ta**–**h** (Scheme 3).[30] This fact was confirmed by the absence of an absorption band in the range of 2020–2050 cm^{-1} when examining IR spectra of products **3Ta**–**h**, which were recorded in KBr and in Nujol. Besides that, the signals of azido group appeared after some time in IR spectra of samples **3Ta**–**d** that were recorded in CH_2Cl_2 or $CHCl_3$ solutions. These observations pointed to the reversibility of the conversion of azido species **3Aa**–**h** to the cyclic isomers **3Ta**–**h**. The use of $CDCl_3$ as a solvent enabled the monitoring of this rearrangement by ^1H NMR spectroscopy. However, only one isomer existed in DMSO-d_6 solution, which probably was the tetrazole **3Ta**–**h**. The structure of cyclization products – compounds **3Aa**–**h** – was conclusively established by using X-ray structural analysis of a sample of compound **3Tf**, showing that a type [1,5-*b*] fusion existed between the tetrazole and 1,2,4-triazine rings.

It should be also noted that the formation of alternative tetrazole form **3T'a**–**h** was not observed in this case, and the authors proposed that the formation of tetrazolo[5,1-*c*]-[1,2,4]triazines from 3-azido-1,2,4-triazines is unlikely.

Scheme 3



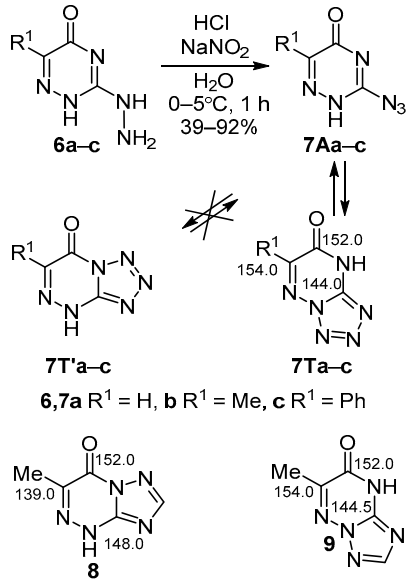
2, **3a** $R^1 = R^2 = H$; **b** $R^1 = H$, $R^2 = Me$; **c** $R^1 = Me$, $R^2 = H$; **d** $R^1 = R^2 = Me$; **e** $R^1 = Ph$, $R^2 = H$; **f** $R^1 = p\text{-}ClC_6H_4$, $R^2 = H$; **g** $R^1 = p\text{-}MeOC_6H_4$, $R^2 = H$; **h** $R^1 = p\text{-}NO_2C_6H_4$, $R^2 = H$; **i** $R^1 = R^2 = Ph$



An analogous result was obtained by diazotation of 3-hydrazino-5,6-diphenyl-1,2,4-triazine (**2i**). This reaction led to azide **3Ai**, which was converted to tetrazole **3Ti**.[31] The type of ring fusion between the tetrazole and triazine moieties in this case was established by comparing the absorption spectra of compound **3Ti** and selected model structures – pyrazolo[5,1-*c*][1,2,4]triazine **4** and triazolo-triazine **5**.

The treatment of hydrazino-1,2,4-triazinones **6a**–**c** with nitrous acid led to azides **7Aa**–**c** (Scheme 4), which spontaneously isomerized to tetrazoles **7Ta**–**c**.[32] Similarly to the case of compounds **3Aa**–**h** (Scheme 3), the signals of azide group in IR spectrum of product obtained from hetarylhydrazine **6a** were observed in the range of 2170–2180 cm^{-1} both in $CHCl_3$ solution and in Nujol. In the rest of the cases only the signals of cyclic form were observed. The type of ring fusion between the azole and azine moieties in tetrazolotriazines **7Ta**–**c** was established by comparing ^{13}C NMR chemical shifts of carbon atoms with the analogous signals of model compounds – deaza analogs 1,2,4-triazolo[5,1-*c*][1,2,4]triazine **8** and 1,2,4-triazolo[1,5-*b*]-[1,2,4]triazine **9**. As shown in Scheme 4, the chemical shifts of 1,2,4-triazine rings in the carbon spectra of compounds **7Tb** and **9** were practically identical. This observation led to the conclusion that the products obtained in cyclization reactions of azides **7Aa**–**c** were tetrazolo[1,5-*b*]-[1,2,4]triazines **7Ta**–**c**. It should be emphasized that the isomerization reactions of compounds **7Ab**,**c** have been investigated previously.[33,34] However, those studies considered only the variant involving the formation of structures **7T'b**,**c**, while data of elemental analysis were used for proving the structure of the tetrazole isomer. Apparently, the conclusions about the structure of the products obtained in cyclization of azides **7Ab**,**c** were erroneous in this case.

Scheme 4*



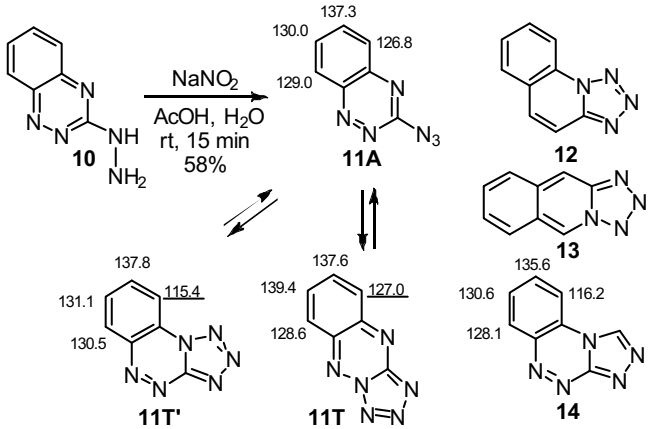
* The chemical shifts (ppm) of 1,2,4-triazine ring, observed in ^{13}C NMR spectra in DMSO-d_6 solution, are indicated for compound **7Tb** (R^1 = Me) and the model structures **8** and **9**.

Azido-tetrazole tautomerism was also investigated for product **11A**, obtained by treatment of 3-hydrazino-1,2,4-benzotriazine **10** with nitrous acid (Scheme 5).[35,36] Thus, IR spectrum recorded for $CHCl_3$ solution showed the absorption band of azido group (2150 cm^{-1}), which was absent when recording the spectrum in KBr. These observations led the authors to a conclusion on the transformation of azide **11A** to isomer **11T'**. At the same time, no solid evidence was presented about the structure of the proposed compound **11T'**, as well as the possibility of the formation of another isomer **11T** was not considered.

Partial attempts were made in another study[37] to establish the direction of isomerization reaction using azide **11A**. For this purpose, the UV spectra of the polycyclic structure **11T'** and model compounds **12** and **13** were compared. It was found that the spectral characteristics of compounds **11T'** and **12** were very close. Further, the authors performed a more detailed analysis of the azido-tetrazole tautomerism by using NMR spectroscopy in DMSO-d_6 solution. This method allowed to observe a triple set of signals for compounds **11T'**, **11A**, and **11T** in the ratio of 6.5:2.5:1. At the same time, the analysis of chemical shift values for some benzene ring signals pointed to the similarity between ^{13}C NMR spectra of tetrazole **11T'** and the model compound – triazolotriazine **14** (Scheme 5). This result provided an additional support to the assumption that the main component of equilibrium mixture, obtained from the reaction product of hetaryl-hydrazine **10** with nitrous acid, was compound **11T'**, featuring a [5,1-*c*] type of ring fusion between the tetrazole and 1,2,4-triazine moieties. Even though this approach is difficult to present as straightforward and ideal, it was possible to establish diagnostic criteria, which allowed to distinguish isomers **11T'** and **11T** in this series of

compounds. Among these characteristics are the chemical shifts of carbon atoms (115.4 and 127.0 ppm, underlined in Scheme 5), which carry hydrogen atoms and are located in the benzene ring, separated by two covalent bonds from the N-4 atom of the triazine ring.

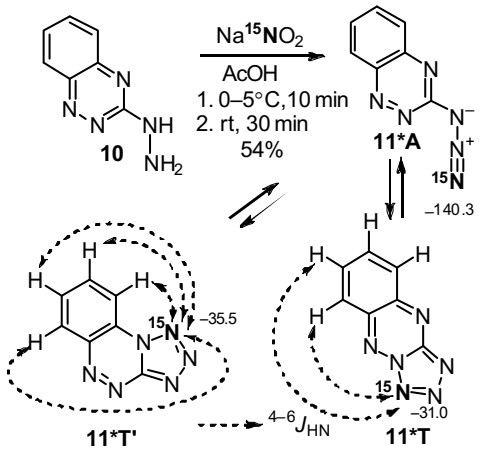
Scheme 5*



* The chemical shifts (ppm) of some ^{13}C NMR signals in DMSO-d_6 solution are indicated for compounds **11A**, **11T'**, **11T** and model compound **14**.

Performing the diazotation reaction of hetarylhydrazine **10** with ^{15}N-labeled $NaNO_2$ (^{15}N, 98%) allowed to selectively introduce this isotopic label into the azido group.[38] As a result, compound **11*A** was synthesized (Scheme 6). The introduction of label allowed to directly study the azido-tetrazole equilibrium *via* the analysis of long-range ^1H–^{15}N coupling constants ($^{4–6}J_{HN}$), without resorting to the use of model compounds, and to observe not only the transitions of cyclic forms to azides, but also to unequivocally prove the structure of the tetrazole isomers. The spin-spin coupling constants between the labeled nitrogen atom and benzene ring protons were measured by using spin echo experiments in 1D ^1H NMR spectra. The determined values of the constants were in the range from 0.17 to 0.04 Hz. Similarly to the previous example,[37] the spectra acquired for DMSO-d_6 solutions showed a mixture of three isomeric species **11*T'**, **11*A**, and **11*T** in 79:12:9 ratio according to the integrated signal intensities. The further analysis of long-range ^1H–^{15}N constants showed that all protons in isomer **11*T'** participated in spin-spin interaction with the labeled atom, while in the case of tetrazole **11*T** the $^{4–6}J_{HN}$ constant was measured only for two proton signals (Scheme 6). Long-range ^1H–^{15}N coupling constants were not observed for azide **11*A**. The values of $^{4–6}J_{HN}$ constant allowed to unequivocally confirm the structure of each isomer. The addition of a small amount of trifluoroacetic acid (TFA) to the DMSO-d_6 solution caused insignificant changes in the isomer ratio. The use of pure deuterated TFA (TFA-*d*) shifted the equilibrium practically toward azide **11*A**. Only small amounts of tetrazole isomer **11*T'** (~1%) could be detected in TFA-*d* solution. However, despite the very low concentration of cyclic isomer **11*T'**, the ^1H–^{15}N constants for this form were successfully detected. The presence of ^{15}N atom in the structure of these isomers gave an additional opportunity to use 1D ^{15}N NMR spectra for the characterization of the equilibrium. The labeled nitrogen signal for tetrazoles **11*T'** and **11*T** was observed in these experiments in the range from –36 to –30 ppm, while the chemical shifts of the azido species were observed in the range from –140 to –130 ppm. It is important to note that the measurements of ^1H–^{15}N spin-spin coupling constants confirmed the correlation of labeled atom signals in one-dimensional ^{15}N NMR spectra.

Scheme 6*



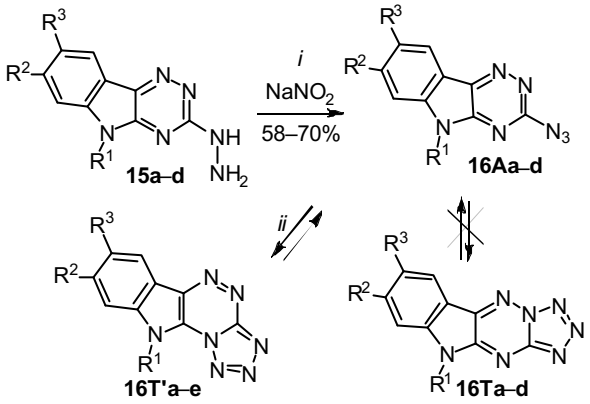
* Chemical shifts (ppm) for ^{15}N atom are indicated relative to $MeNO_2$. The spectrum was acquired in DMSO-d_6 solution.

Various research groups have investigated the interaction of 3-hydrazino-1,2,4-triazino[5,6-*b*]indoles **15a**–**d** with nitrous acid, generated in phosphoric, acetic, or hydrochloric acid media (Scheme 7).[39–42] For example, compounds **16Aa**–**d** were obtained, which spontaneously transformed into the tetrazole form, as confirmed by the absence of absorption bands due to the azido group and the presence of tetrazole ring signals in the range of 1180–1220 cm^{-1} in IR spectra recorded in KBr.[39,40,42] The ring fusion type between the tetrazole and triazine moieties in compounds **16T'a**–**d** was supported by the literature data.[37]

Performing the reaction in concentrated H_3PO_4 allowed to detect the formation of azide **16Aa**, which was converted by refluxing in acetic anhydride into heterocycle **16T'e**, with the cyclization of azido group also accompanied by an acylation reaction (Scheme 7). The preparation of 3-azido-1,2,4-triazine **16Aa** was confirmed by data of IR spectroscopy by the observation of azido group absorption band at 2150 cm^{-1}.[41]

In order to unequivocally establish the direction of the cyclization reaction of azide **16Aa**, experiments were performed with the isotopically labeled compound (Scheme 8).[43] The use of $K^{15}NO_2$ in acidic medium in the diazotation reaction of compound **15a** allowed to obtain azide **16*Aa**, which spontaneously cyclized to tetrazole

Scheme 7

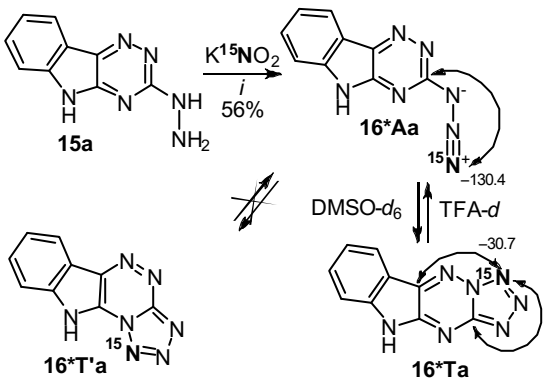


i: H_3PO_4 or HCl or AcOH; 1. 0–5°C, 30 min; 2. rt or 5°C, 2 h
ii: DMF–EtOH or DMF or PhH or Ac_2O
a $R^1 = R^2 = R^3 = H$; **b** $R^1 = R^3 = H$, $R^2 = F$; **c** $R^1 = R^2 = H$, $R^3 = F$; **d** $R^1 = Et$, $R^2 = R^3 = H$; **e** $R^1 = Ac$, $R^2 = R^3 = H$

16*Ta. The study of labeled sample by ^{13}C NMR spectroscopy in DMSO-d_6 solution revealed the presence of $^{2\text{-}3}J_{CN}$ constants for two carbon atoms of the 1,2,4-triazine ring of the tetrazole isomer. These spectral properties proved that compound **16*Aa** was converted by cyclization into structure **16*Ta**, in which the tetrazole and azine moieties were fused according to the type [1,5-*b*]. It is important to note that the alternative cyclic isomer **16*T'a** could not be detected. At the same time, in the case of formation of compound **16*T'a**, ^{13}C–^{15}N constants should be observed in one-dimensional ^{13}C NMR spectrum for all carbon atom signals of the 1,2,4-triazine ring.

The study of azido-tetrazole equilibrium of compound **16*Ta** in TFA-*d* solution allowed to establish that 30 days after dissolution the ratio between structures **16*Aa** and **16*Ta** reached 87:13. The presence of a labeled nitrogen atom provided an opportunity to observe ring-chain interconversion by the method of ^{15}N NMR spectroscopy, while the measurements of ^{13}C–^{15}N spin-spin coupling constants confirmed that the [1,5-*b*] ring fusion type between the tetrazole and triazine moieties in acidic medium was conserved in the case of isomer **16*Ta**. Besides that, azide **16*Aa** was characterized by a single $^3J_{CN}$ constant. Thus, the introduction of ^{15}N isotope in the azole ring of tetrazolo[1,5-*b*][1,2,4]triazines allowed to directly observe not only the transitions of tetrazoles to azides, but also to prove the structure of the cyclic forms.

Scheme 8*



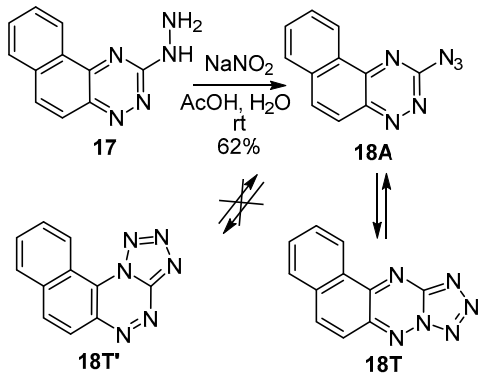
i: H_3PO_4
1. 0–5°C, 15 min;
2. rt, 30 min

* Chemical shifts (ppm) of ^{15}N nuclei are reported relative to $MeNO_2$. The spectrum was acquired in TFA-*d* solution.

The reactivity of the 3-azido-1,2,4-triazine naphtho derivatives **18A** differed from that of 3-azido-1,2,4-benzotriazines **11A**.[44] Thus, compound **18A** obtained by treatment of heterocycle **17** with nitrous acid was cyclized to tetrazolo[1,5-*b*]triazine **18T** (Scheme 9).

The presented process was monitored by the method of IR spectroscopy. The spectrum of the crude product featured a strong azido group absorption band at 2120 cm^{-1} (KBr), which disappeared after recrystallization from dioxane. At the same time, ^1H and ^{13}C NMR spectra acquired in DMSO-d_6 solutions showed the signals of a single tetrazole form **18T**. The performed X-ray structural analysis confirmed the hypothesis about cyclization of azide **18A** to tetrazolo[1,5-*b*][1,2,4]triazine **18T**.

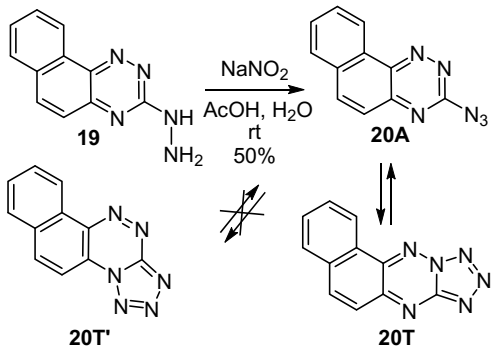
Scheme 9



Furthermore, another case of azido-tetrazole tautomerism for 1,2,4-triazines is discussed in the literature.[44] It was found that the product from interaction between compound **19** and HNO_2, namely, azide **20A**, was isomerized to cyclic form **20T**, in which the tetrazole and triazine moieties were joined by type [1,5-*b*] ring fusion (Scheme 10). The conclusion about the structure of this compound was based on the results of X-ray structural analysis. The conversion of azide **20A** to the tetrazole isomer could be established by using IR spectroscopy. Initially, two absorption bands of azido group were observed in IR spectrum of the diazotation product obtained from compound **19** (2150 and 2120 cm^{-1}, KBr). After compound **20A** was recrystallized from EtOH, the characteristic azide signals were absent from IR spectrum, confirming the conversion of open-chain form to cyclic isomer **20T**.

Two additional examples have been described for the conversion of 3-azido-1,2,4-triazines **22A** and **24A** to tetrazolo[1,5-*b*][1,2,4]triazines **22T** and **24T**[45] (Schemes 11 and 12). When $NaNO_2$ was added to solutions of compounds **21** and **23** in aqueous AcOH, respective azides **22A** and **24A** were formed. The structure of compounds **22A**

Scheme 10

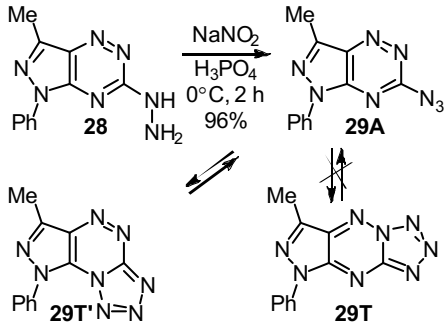


and **24A** was supported by data of IR spectroscopy (absorption band at 2140 cm^{-1} in $CHBr_3$ solution). Refluxing of azidotriazines **22A** and **24A** in EtOH led to polycyclic structures **22T** and **24T**. Alternative structures **22T'** and **24T'** were excluded from consideration on the basis of results presented in earlier publications.[32,37]

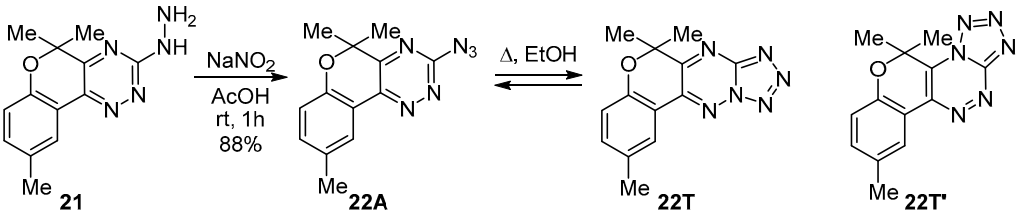
The standard procedure for the conversion of hetaryl-hydrazine **25** to azide **26A** was used for obtaining analogs of the antibiotic 2-methylfervenulone[46] (Scheme 13). The presence of absorption band in IR spectrum at 2200 cm^{-1} confirmed the formation of 3-azido-1,2,4-triazine **26A**. Heating of azide **26A** to 150°C in DMF medium led to tetrazolotriazine **26T**. At the same time, the authors recognized that the isomerization of azide can proceed by an alternative route, leading to the formation of compound **26T'**. The type of ring fusion between the azole and azine moieties, resulting from the cyclization of azide **26A**, was distinguished on the basis of previously published results,[30] as well as comparison of IR and UV spectral data with model compound **27T**, which is known to show only a single type of fusion between the tetrazole and triazine rings.

The reaction of 2-hydrazino-1,2,4-triazine **28** with $NaNO_2$ in concentrated H_3PO_4 medium has been described in the literature[47] (Scheme 14). The authors noted that IR spectrum of the obtained compound did not contain an absorption band in the range of 2120–2150 cm^{-1}. For this reason, tricyclic structure **29T'** was assigned to the product obtained by diazotation reaction of compound **28**. Despite of the two possible directions of cyclization reaction in the case of azide **29A**, there were no arguments presented in support of the formation of heterocycle **29T'**, in which the azole and triazine rings were condensed according to type [5,1-*c*] ring fusion.

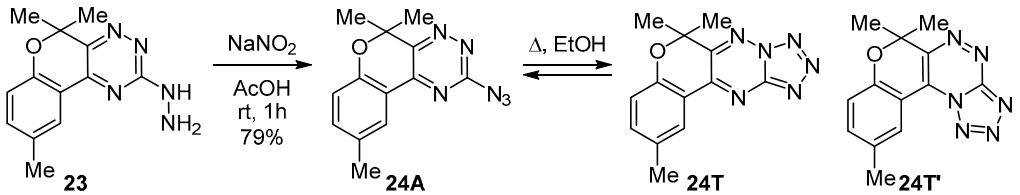
Scheme 14



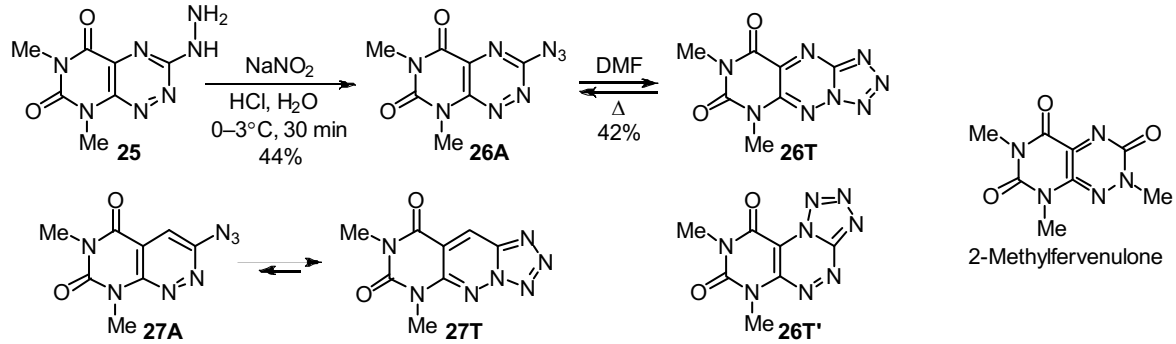
Scheme 11



Scheme 12



Scheme 13

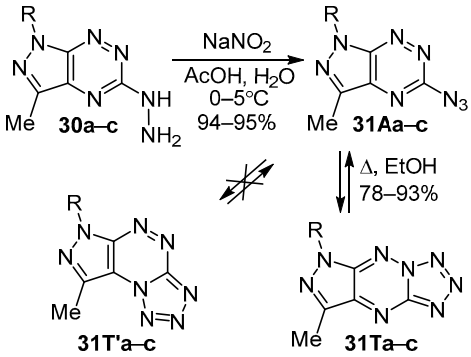


A different manifestation of azido-tetrazole tautomerism was present in studies devoted to diazotation of 3-hydrazinopyrazolo[4,3-*e*]triazines **30a**–**c** and **32**[48–50] (Schemes 15 and 16). It was demonstrated that the reaction resulted in the formation of azides **31Aa**–**c** and **33A**, which upon crystallization from EtOH or spontaneously cyclized to the corresponding tetrazoles **31Ta**–**c** and **33T**.

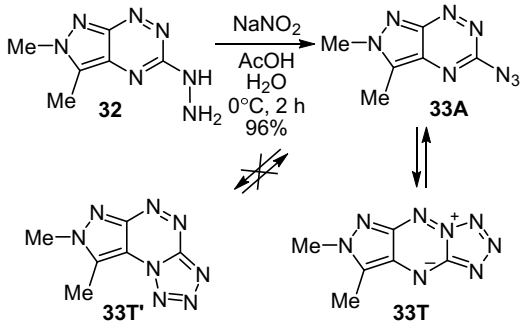
The structure of azides **31Aa–c** and **33A** was confirmed by using the data of IR spectroscopy. In the case of compound **31Aa** the process of conversion into the cyclic isomer **31Ta** was observed by using ^{1}H NMR spectroscopy in $CDCl_3$ solution. The type of ring fusion for compounds **31Ta–c** was unequivocally established by method of X-ray structural analysis.

In the case of cyclization reaction using azide **33A**, the most preferred direction upon initial consideration was the route leading to compound **33T'**. However, the performed X-ray structural analysis showed that the condensation of compound **33A** led to the formation of betaine structure **33T**.

Scheme 15



Scheme 16



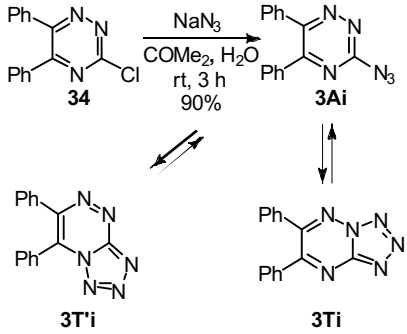
Preparation of 2-azido-1,2,4-triazines by nucleophilic substitution reaction

The second method for the synthesis of 3-azido-1,2,4-triazines and their tetrazole isomers is based on the nucleophilic substitution of a good leaving group at position 3 of 1,2,4-triazine ring with an azido group. Such an approach enabled direct preparation of this class of hetaryl azides.

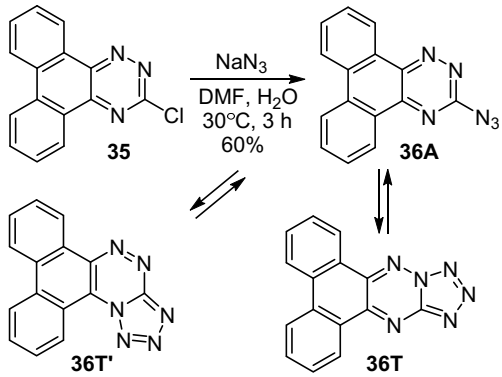
An alternative method of synthesis was proposed for the previously presented compound **3Ai**, including the treatment of chlorotriazine **34** in acetone with aqueous NaN_3 solution (Scheme 17).[51] In the same work, azidotriazine **36A** was obtained by a similar method from chloro derivative **35** (Scheme 18).

The structures of compounds **3Ai** and **36A** were proved on the basis of IR spectra recorded in KBr, which contained characteristic absorption bands at 2137 and 2135 cm^{-1}, corresponding to the signals of azido groups. Despite the fact that compounds **3Ai** and **36A** were capable of conversion into isomers **3Ti** and **36T** or **3T'i** and **36T'**, the authors did not consider the azido-tetrazole tautomerism for the given structures, instead emphasizing the investigation of reactivity toward trialkyl and diethyl phosphonates.

Scheme 17

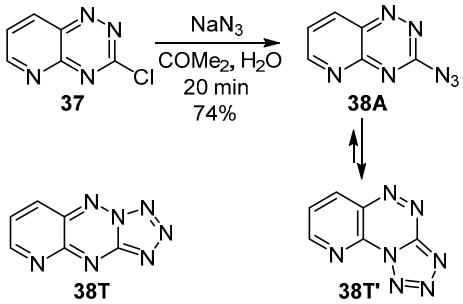


Scheme 18



Another use of NaN_3 was in the case of chloride substitution in pyridotriazine **37** (Scheme 19).[35,36] That reaction proceeded in aqueous acetone, and the authors were able to separate two isomeric forms **38A** and **38T'**. Compound **38A** was observed by IR spectroscopy both in solution phase and in solid state, but was found to be less stable than tetrazole form **38T'**. Thus, compound **38A** underwent gradual spontaneous transformation in DMSO-d_6 solution or in crystalline state, producing tetrazole isomer **38T'**, which was confirmed by ^{1}H NMR and IR spectral data. The main problem during the study of azido-tetrazole tautomerism of compound **38A** was the fact that no consideration was given to the variant of cyclization leading to structure **38T**. Besides that, there was clearly insufficient data to support the formation of structure **38T'**.

Scheme 19

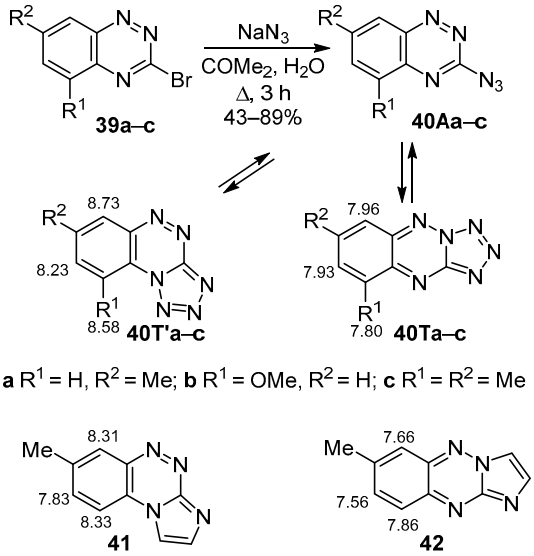


Another example for the application of NaN_3 in the substitution of a halide ion (Scheme 20) has been presented for benzotriazines **39a**–**c**,[52] resulting in the synthesis of azides **40Aa**–**c**. The azido-tetrazole equilibrium of triazine **40Aa**–**c** derivatives was studied by using a combination of methods based on ^{1}H NMR and IR spectroscopy.

Thus, ^{1}H NMR spectra of compounds **40Aa**–**c**, which were acquired in DMSO-d_6 and acetone-d_6 solutions, showed the predominance of tetrazole forms, or the content of one of the tetrazole isomers was close to the azide concentration. In the case of heterocyclic compound **40Ab** and dimethyl derivative **40Ac**, formation of the linear isomers **T** was observed, while the cyclization of azide **40Aa** resulted in the formation of structure **40T'a**. When $CDCl_3$ was used as the solvent, the equilibrium was shifted toward the open form, resulting in the domination of azides **40Aa**–**c**. The assignment of proton signals in azides **40Aa**–**c** contained in complex mixtures in comparison to the tetrazole isomers was performed by taking into account the data of ^{1}H NMR spectra acquired for bromo derivatives **39a**–**c**. It should be noted that the type of ring fusion between tetrazole and triazine moieties was established on the basis of comparing the proton chemical shifts in ^{1}H NMR spectra of the annulated benzene ring of tetrazole forms **40Ta**–**c** and **40T'a**–**c** with those of model compounds, namely, the respective derivatives of imidazo-[1,2-*a*][1,2,4]triazines. An example of comparison between some ^{1}H NMR spectral signals of isomers **40Ta** and **40T'a** with compounds **41** and **42** is shown in Scheme 20. These characteristics show that the chemical shifts of benzene ring protons depend on the type of ring fusion between the azole and azine moieties.

The product obtained by reaction of compound **43** with NaN_3 was studied by method of IR spectroscopy, which allowed to observe spontaneous cyclization of heterocyclic compound **44A** to the tetrazole isomer[44] (Scheme 21). In this case, the formation of compounds **44T'** or **44T** was possible. At the same time, ^{1}H NMR spectrum acquired for DMSO-d_6 solution of the cyclization product obtained from azido-1,2,4-triazine **44A** showed that only one of the two possible tetrazole forms was present. The type of ring fusion between the tetrazole and triazine moieties in this case was established on the basis of ^{13}C NMR spectroscopy data. Following the example of previous work,[37] the selected informative feature was the chemical shift of

Scheme 20*



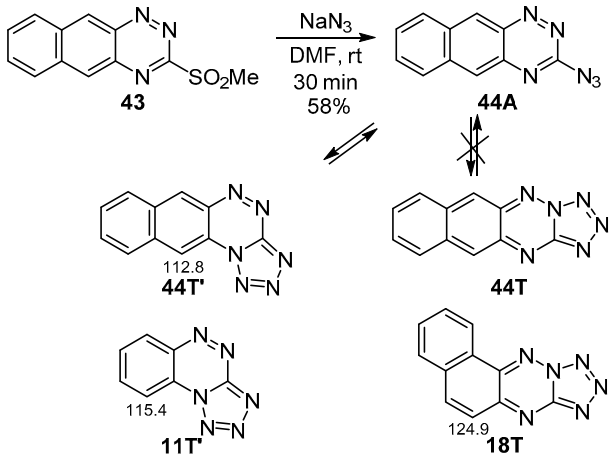
a R^1 = H, R^2 = Me; **b** R^1 = OMe, R^2 = H; **c** R^1 = R^2 = Me

* Chemical shifts (ppm) of benzene ring protons in compounds **40Ta**, **40T'a**, **41**, and **42** in ^{1}H NMR spectra acquired for DMSO-d_6 solutions.

naphthaline ring carbon atom bearing a hydrogen atom and separated by two covalent bonds from the N-4 nitrogen atom of the triazine ring (Scheme 21). When comparing this chemical shift with the analogous signals of benzotriazine **11T'** and compound **18T**, the product obtained by cyclization of azide **44A** was assigned with structure **44T'**.

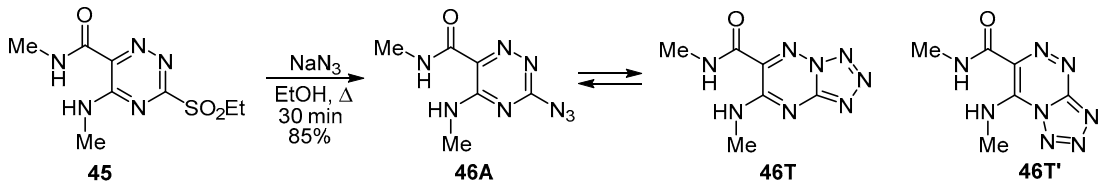
The reaction of heterocyclic compound **45** with an equimolar amount of NaN_3 allowed to obtain tetrazolotriazine **46T** by substitution of the sulfonyl group (Scheme 22).[53] The tetrazole type of structure for the product obtained by sulfonyl group substitution was determined by IR spectroscopy of crystalline sample, which showed an absence of absorption in the range of 2100–2200 cm^{-1}. It is important to note that the opening of tetrazole ring in compound **46T** did not occur even in TFA medium.

Scheme 21*

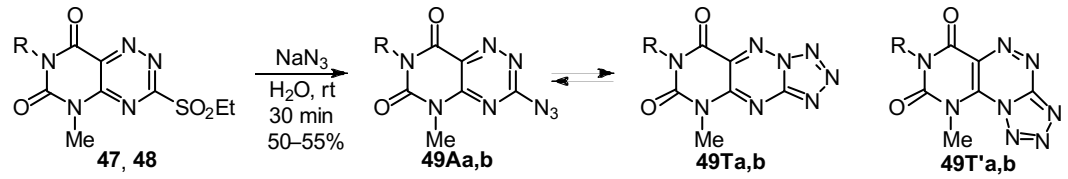


* Chemical shifts (ppm) of the carbon atom signals in naphthyl systems of compound **44T'** and model structures **11T'** and **18T**. ^{13}C NMR spectra were acquired in DMSO-d_6 solution.

Scheme 22



Scheme 23



47, **49a** R = Me; **48, 49b** R = H

Despite the two possible directions for cyclization of azide **46A** (leading to products **46T** and **46T'**), the aforementioned study did not consider the issue of proving the type of triazine ring fusion.

Nucleophilic substitution by using NaN_3 as a reagent was identified as an alternative method for the synthesis of azido and tetrazolo derivatives of azafervenulin, including compound **49Aa**.[54] Thus, the treatment of compounds **47**, **48** with NaN_3 led to heterocyclic products **49Aa** and **49Tb** (Scheme 23). The structures of compounds **49Aa** and **49Tb** were confirmed on the basis of IR spectral data. The further cyclization of azide **49Aa** to tetrazole was not performed, in contrast to another earlier work.[46]

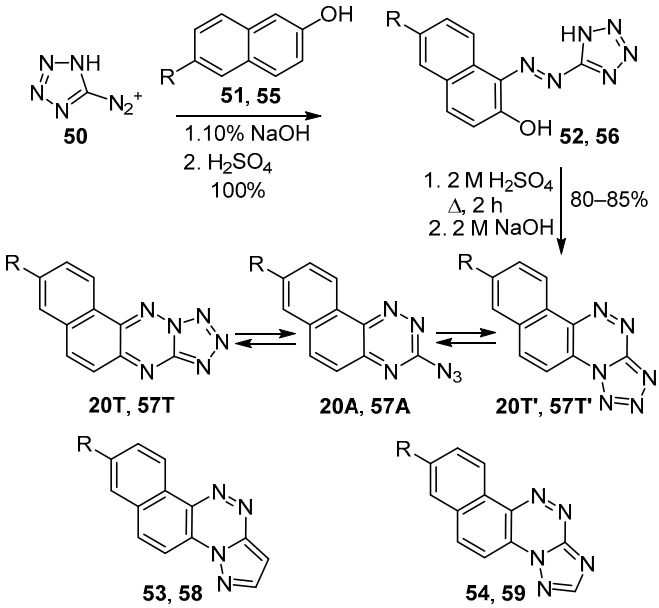
The [1,5-*b*] type of ring fusion between the tetrazole and triazine moieties in compound **49Tb** was unequivocally established by X-ray structural analysis, as was described in a later article.[55] The study of azido-tetrazole equilibrium of compound **49Tb** by ^{1}H NMR spectroscopy showed that two forms existed in DMSO-d_6 solution – tetrazole form **49Tb** and azide form **49Ab**. The addition of TFA resulted in shifting of the equilibrium toward the azide form, while the tetrazole isomer was predominant in pyridine. The diagnostic features in this case were the proton signals of *N*-methyl groups, which did not allow to exclude the possible formation of alternative structure **49T'b**.

Synthesis of 3-azido-1,2,4-triazines and their cyclic isomers on the basis of tetrazole derivatives

The diazotation of 5-aminotetrazole and the subsequent coupling of diazoazole **50** with compounds containing an activated CH group served as obe of the approaches to the construction of 1,2,4-triazine ring on the basis of azole moiety. One of the first synthetic studies in this direction was published in 1974 by uzing β-naphthol **51** as the azo component (Scheme 24).[56] The coupling reaction was performed under basic conditions with efficient cooling and resulted in the preparation of azo compound **52**, which, according to the authors of that study, was converted to tetrazolo[5,1-*c*][1,2,4]triazine **20T'**.

As established by method of IR spectroscopy, the product from the cyclization of compound **52** existed in crystalline state in its tetrazole form, while in DMSO-d_6 or $CDCl_3$ solutions polycyclic structure **20T'** started to isomerize to azide **20A**. The type of ring fusion between the tetrazole and triazine rings was established by comparing the UV spectra of compound **20T'** and model structures **53** and **54**. As a result of this analysis, the isomerization of heterocyclic compound **20T'** to tetrazole **20T** was excluded.

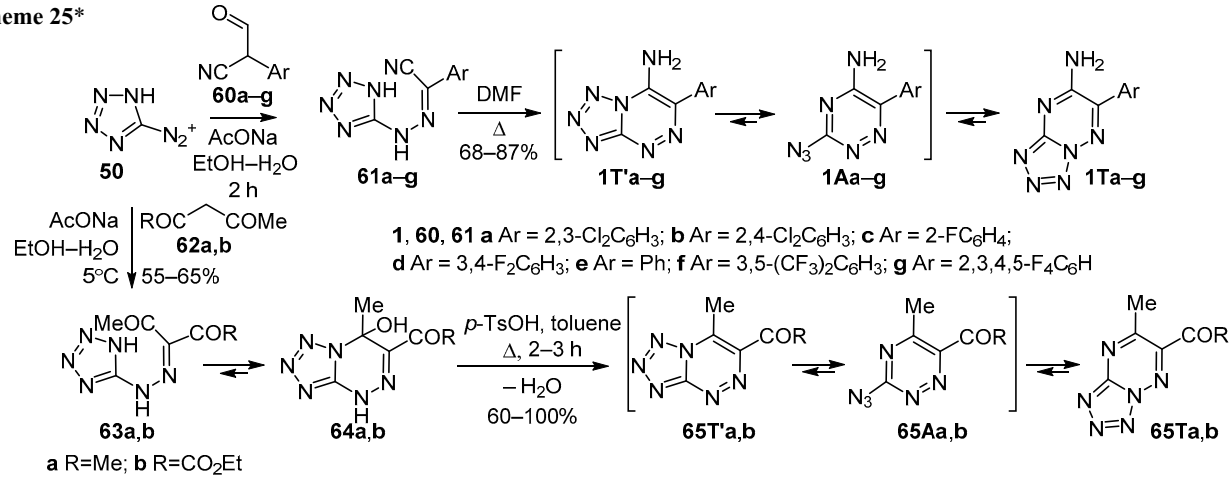
Scheme 24



20, **51**–**54** R = H; **55**–**59** R = Br

The conclusions from this work were subsequently revised in an article by the same authors, where 6-bromo-2-naphthol **55** was used as an additional reagent with activated CH group.[57] Thus, compound **56** was obtained, which was converted to triazine **57T**. The tetrazole character of the obtained isomer was proved by IR spectrum, recorded in KBr pellets. The presence of azido-tetrazole tautomerism was also confirmed by studies performed using ^{1}H NMR spectroscopy. The proton spectrum acquired in $CDCl_3$ solution for the condensation product obtained from azo compound **56** contained a double set of signals due to compounds **57A** and **57T**, showing equal integrated intensity. At the same time, only

Scheme 25*



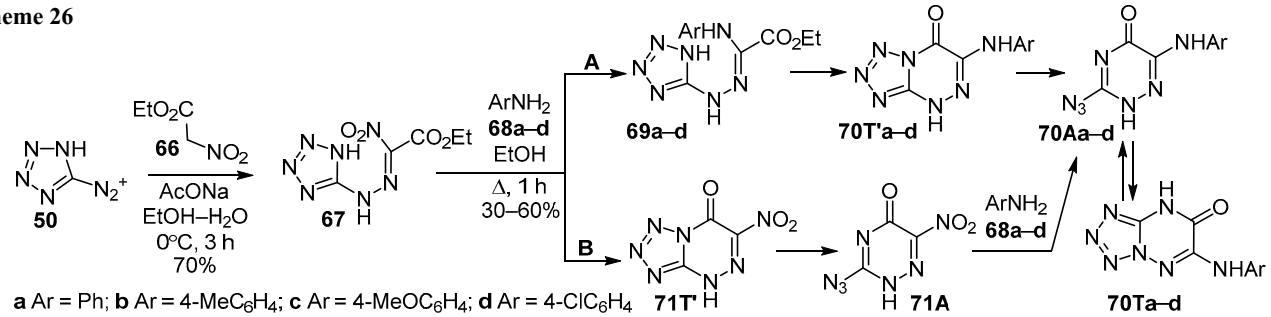
* The overall yield of all stages is indicated for compounds **1Ta**–**g**.

one isomer **57T** was observed in ^{1}H NMR spectra acquired for a DMSO-d_6 solution. The type of fusion between the tetrazole and triazine rings in this case was established by comparing the chemical shifts of proton signals arising from tetracyclic structure **57T** and model compounds **58** and **59** (Scheme 24). The main diagnostic features in ^{1}H NMR spectrum, which were used for determining the structure of compound **57T**, were the signals of naphthyl ring protons. The introduction of bromine atom in this case significantly simplified the coupling pattern compared to the cyclization products obtained from compound **52**. This enabled a more complete comparison of ^{1}H NMR spectra of tetrazolo[1,5-*b*][1,2,4]triazine **57T** and bromo-substituted azolo[5,1-*c*][1,2,4]triazines **58** and **59**. Thus, the main conclusion of this work showed that the condensation of hydrazones **52** and **56** gave linear structures **20T** and **57T**, which represented products from the rearrangement of tetrazole isomers **20T'** and **57T'**. Obviously, the presented process proceeded through respective azides **20A** and **57A**. Besides that, an alternative method was presented for the preparation of compound **20T**, and the conclusions about the structure of this tetrazolotriazine, which were given in the literature,[44,57] were in good agreement.

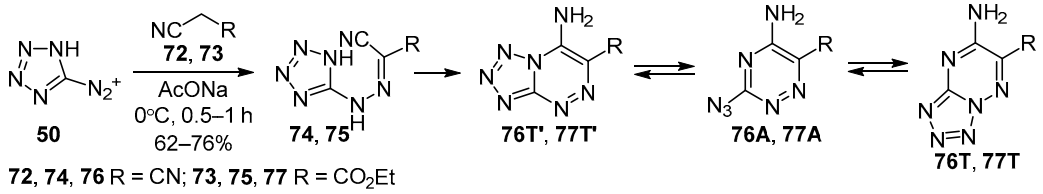
The interaction of diazonium salt **50** with various compounds containing an activated CH group provided a convenient method for the synthesis of 2-azido-1,2,4-triazines and their tetrazole analogs. Thus, the reaction of α-formylphenylacetonitriles **60a**–**g** and compound **50** led to hydrazones **61a**–**g** (Scheme 25).[29] At the same time, the coupling process was accompanied by elimination of the formyl group, which was used for the activation of CH acidity of arylacetonitriles, which themselves did not react with diazotetrazole **50**. The cyclization of hydrazones **61a**–**g** proceeded upon refluxing in DMF and led to structures **1Ta**–**g**. Similar transformations were also described for hydrazones **63a**,**b**, obtained by using β-dicarbonyl compounds **62a**,**b**.[58] It is important to note that the existence of these structures in the cyclic form **64a**,**b** was identified in that study for hydrazones **63a**,**b**, confirming the route of formation for tetrazoles **65T** through azides **65A** and tetrazolo[5,1-*c*][1,2,4]triazines **65T'**. The conversion of compounds **64a**,**b** to triazines **65T'a**,**b** and their further isomerization to tetrazoles **65Ta**,**b** proceeded upon heating in toluene medium in the presence of *p*-TsOH (Scheme 25). The structure of compounds **1Ta**–**g** and **65Ta**,**b** was confirmed by data of X-ray structural analysis.

Another example for the transformation of tetrazolo[5,1-*c*]-[1,2,4]triazines **T'** to isomeric tetrazolo[1,5-*b*][1,2,4]triazines **T** was presented by using products from the cyclization of hydrazone **67**, which was obtained by using nitroacetic ester **66** (Scheme 26).[59] The transformation of compound **67** to tetrazolotriazines proceeded upon refluxing with aromatic amines **68a**–**d**. Two routes are possible for this transformation (Scheme 26). The route A involves substitution of the nitro group in hydrazone **67** and the preparation of compounds **69a**–**d**, which are further cyclized to heterocyclic intermediates **70T'a**–**d**, followed by isomerization to tetrazolo[1,5-*b*][1,2,4]triazines **70Ta**–**d** *via* azido-tetrazole rearrangement. An alternative variant of the reaction route (the route B) involves cyclization of hydrazone **67** as the first step. The substitution of nitro group in that case occurs in the already formed triazine ring

Scheme 26



Scheme 27

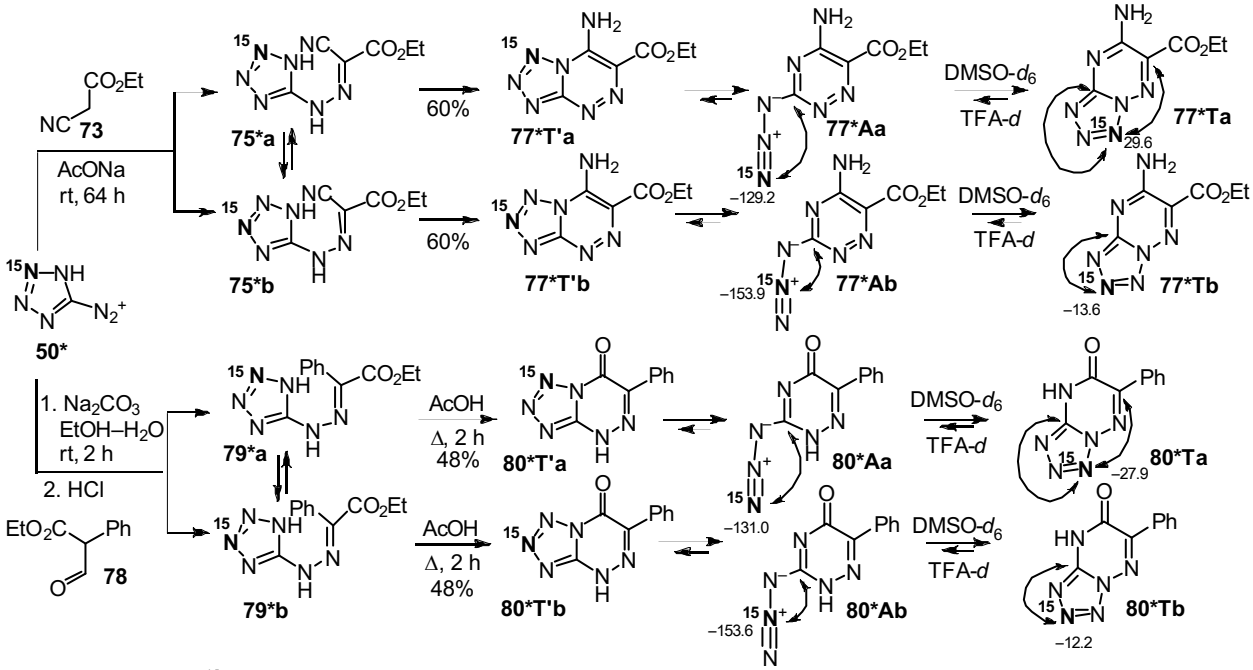


of tetrazole derivative **71T'** or azide **71A**. The lack of IR absorption bands of azido and nitro groups in spectra of tetrazolo[1,5-*b*][1,2,4]triazines **70Ta–d** proved that the formation of tetrazole derivative was accompanied by the substitution of nitro group. The structure of compounds **70Ta–d** was conclusively proved on the basis of X-ray structural analysis of triazine **70Tc**.

The syntheses of 3-azido-1,2,4-triazine **76A** and tetrazolotriazine **77T'** were reported as examples of azo coupling reactions of diazotetrazole **50** with malonodinitrile **72** and ethyl cyanoacetate **73** (Scheme 27).[60,61] This process proceeded *via* the formation of hydrazones **74** and **75**, which cyclized spontaneously (compound **74**) or upon refluxing in AcOH (compound **75**). The initially formed tetrazolo[5,1-*c*][1,2,4]triazine **76T'** spontaneously converted to open-chain form **76A** according to this mechanism, while the condensation of compound **75** gave heterocyclic product **77T'**. The structure of azide **76A** was confirmed by X-ray structural analysis. The azido-tetrazole equilibrium for the cyclization product obtained from hydrazone **74** was not studied by other methods. The bicyclic structure of compound **77T'** was confirmed by the absence of absorption band in the range of 2100–2200 cm^{-1} in the IR spectrum. Besides that, the structure of triazine **77T'** was additionally proved by using elemental analysis and UV spectroscopy. The methods described for the structural characterization of compound **77T'** did not provide a clear confirmation of the ring fusion type in the bicyclic structure and did not solve the issue about its possible isomerization to tetrazolo[1,5-*b*]triazine **77T**.

The structure of cyclization product obtained from hydrazone **75** could be conclusively established by performing the coupling reaction with cyanoacetate **73** using ^{15}N-labeled diazotetrazole **50*** (Scheme 28).[43] Compound **75***, which was thus obtained, exhibited prototropic tautomerism by existing in two forms **a** and **b**, which spontaneously cyclized through tetrazoles **77*T'a**,**b** and azides **77*Aa**,**b** to a mixture of isotopomers **77*Ta**,**b**. The reaction with ethyl phenylacetate formyl derivative **78** proceeded analogously.[43,62] The cyclization of tautomeric forms **a** and **b** of hydrazone **79*** led to tetrazolotriazines **80*Ta**,**b** with different positions of the ^{15}N isotopic label in the azole ring. The presence of ^{15}N atom in the structures of compounds **77*Ta**,**b** and **80*Ta**,**b** allowed to use the analysis of ^{13}C–^{15}N spin-spin coupling constants for establishing and confirming the structures.[43] The carbon spectra of compounds **77*Ta**,**b** and **80*Ta**,**b** showed interaction of the ^{15}N atom with two carbon atoms of the 1,2,4-triazine moiety. These spectral features unequivocally confirmed the [1,5-*b*] type of ring fusion between the tetrazole and triazine moieties in compounds **77*Ta**,**b** and **80*Ta**,**b**, since the alternative bicyclic structures **77*T'a**,**b**

Scheme 28*



* Chemical shifts (ppm) in ^{15}N NMR spectra are reported relative to $MeNO_2$. The spectrum was acquired in TFA-*d* solution. The overall yield of all stages is indicated for compounds **77*Ta**,**b** and **80*Ta**,**b**.

and **80*T'a**,**b** would show $^{13}C–^{15}N$ coupling constants at each carbon atom of the azine ring, while in the case of azides **77*Aa**,**b** and **80*Aa**,**b** only one carbon atom showed a spin-spin coupling to the labeled atom. Despite the expectations that cyclization of hydrazones **75*a**,**b** and **79*a**,**b** should lead to tetrazolo[5,1-*c*][1,2,4]triazines, the presence of structures **77*T'a**,**b** and **80*T'a**,**b** was not detected. X-ray structural analysis of unlabeled compound **77T** completely confirmed the data obtained on the basis of analysis of $^{13}C–^{15}N$ coupling constants.

Besides that, the $^{13}C–^{15}N$ spin-spin coupling constants and the chemical shift values of labeled atoms in 1D ^{15}N NMR spectra were found to be convenient diagnostic characteristics for studying the azido-tetrazole tautomerism in the given series of compounds (Scheme 28). The significant differences in chemical shifts of the labeled atoms allowed to easily detect ring-chain transformations. By relying on these characteristics it was established that in TFA-*d* solution the mixture of compounds **77*Ta**,**b** completely rearranged over 12 h to azides **77*Aa**,**b**. At the same time, the product from cyclization of hydrazone **79*** in TFA-*d* solution showed a 60:40 ratio of compounds **80*Aa**,**b** and **80*Ta**,**b** when observed 30 days after dissolution.

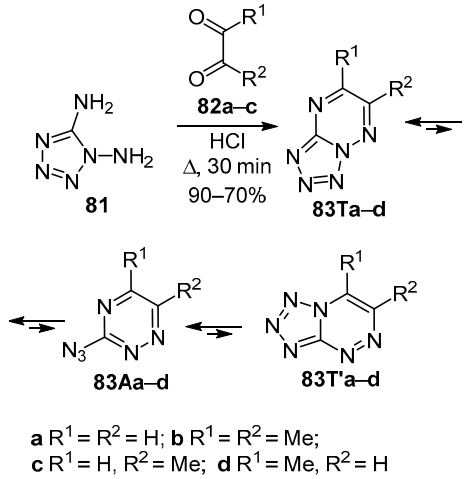
The condensation of diaminotetrazole **81** with α-dicarbonyl compounds **82a**–**c** provided another example for the construction of tetrazolo[1,5-*b*][1,2,4]triazines on the basis of azole ring (Scheme 29).[63] The reaction of azole **81** with glyoxal **82a** and 2,3-butanedione **82b** led to the formation of compounds **83Ta**,**b**. On the other hand, the reaction of diamine **81** with methylglyoxal **82c** provided a mixture of tetrazolotriazines **83Tc**,**d**.

The structures of obtained compounds **83Ta**–**d** were established on the basis of data available in an earlier publication.[30] This conclusion was further confirmed by the results of X-ray structural analysis for compound **83Td**, which were published in another article.[24]

The analysis of literature data and the results of studies from our laboratory show that the azido-tetrazole equilibrium in the series of 3-azido-1,2,4-triazines, as a rule, is shifted toward the formation of tetrazolo[1,5-*b*]-[1,2,4]triazines, and the explanation of this fact requires both additional experimental data and theoretical studies. At the same time, a range of examples are known where the existence of open-chain form and another cyclic isomer (tetrazolo[5,1-*c*][1,2,4]triazine) has been reported. Therefore, the chemists working in this area need to be very careful with structural characterization and observation of ring-chain equilibria in this series of heterocycles.

As already noted above, X-ray structural analysis is certainly the definitive method for unequivocal determination of the isomeric forms of azidotriazines in crystalline state. At the same time, the study of this type of transformations in solution phase can be effectively accomplished by using modern ^{1}H and ^{13}C NMR experiments. Furthermore, the potential benefit from applying NMR methods significantly increases when labeled nitrogen atoms are introduced into the azido group, leading to the appearance of additinal spectral features, such as $^{1}H–^{15}N$ and $^{13}C–^{15}N$ spin-spin coupling constants. Besides that, the introduction of ^{15}N isotopic labels enables the use of ^{15}N NMR spectral data for the characterization of azido-tetrazole equilibrium. Unfortunately, the full potential of this method has not yet been revealed. It can be said with confidence that the further studies using the full range of modern NMR methods with isotopically labeled azaheterocycles will allow to shine the light not only on the nature of azido-tetrazole rearrangements, but also will be useful for the study of other types of ring-chain transformations.

Scheme 29



This work was performed within the framework of the State contract from the Ministry of Education and Science of the Russian Federation (4.6351.2017/8.9) and with financial support from the Russian Foundation for Basic Research (grant 17-03-01029).

References

1. Smith, M. B. *March's Advanced Organic Chemistry: Reactions*, *Mechanisms*, *and Structure*; Wiley: New York, 2013, 7th ed.
2. Guasch, L.; Sitzmann, M.; Nicklaus, M. C. *J. Chem. Inf. Model*. **2014**, *54*, 2423.
3. Charushin, V. N.; Rusinov, V. L.; Chupakhin, O. N. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Eds.; Elsevier: Oxford, 2008, Vol. 9, p. 95.
4. Charushin, V. N.; Chupakhin, O. N. In *Topics in Heterocyclic Chemistry*; Maes, B. U. W.; Cossy, J.; Poland, S.; Series Eds.; Springer: Heidelberg, New York, Dordrecht, London, 2014, Vol. 37, p. 1.
5. Fizer, M.; Slivka, M. *Chem. Heterocycl. Compd.* **2016**, *52*, 155. [*Khim. Geterotsikl. Soedin.* **2016**, *52*, 155.]
6. Gulevskaya, A. V.; Pozharskii, A. F. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Elsevier: New York, 2007, Vol. 93, p. 57.
7. El Ashrya, E. S. H.; Nadeemc, S.; Shahc, M. R.; Kilany, Y. E. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Elsevier: New York, 2010, Vol. 101, p. 161.
8. Pakal'nis, V. V.; Zerov, A. V.; Yakimovich, S. I.; Alekseev, V. V. *Chem. Heterocycl. Compd.* **2014**, *50*, 1107. [*Khim. Geterotsikl. Soedin.* **2014**, 1201.]

9. Shchegol'kov, E. V.; Sadchikova, E. V.; Burgart, Ya. V.; Saloutin, V. I. *Russ. J. Org. Chem.* **2009**, *45*, 572. [*Zh. Org. Khim.* **2009**, *45*, 586.]
10. Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* **2003**, 3025.
11. Alkorta, I.; Blanco, F.; Elguero, J.; Claramunt, R. M. *Tetrahedron* **2010**, *66*, 2863.
12. Alkorta, I.; Blanco, F.; Elguero, J. *Tetrahedron* **2010**, *66*, 5071.
13. Burke, L. A.; Elguero, J.; Leroy, G.; Sanal, M. *J. Am. Chem. Soc*., **1976**, *98*, 1685.
14. Birney, D. M. *J. Org. Chem.* **1996**, *61*, 243.
15. Bakulev, V. A.; Gloriozov, V. P. *Chem. Heterocycl. Compd.* **1989**, *25*, 420. [*Khim. Geterotsikl. Soedin.* **1989**, 504.]
16. Pochinok, V. Ya.; Avramenko, L. F.; Grigorenko, P. S.; Skopenko, V. N. *Russ. Chem. Rev.* **1975**, *44*, 1028. [*Usp. Khim.* **1975**, *44*, 1028.]
17. Ershov, V. A.; Postovskii, I. Ya. *Chem. Heterocycl. Compd.* **1971**, *7*, 668. [*Khim. Geterotsikl. Soedin.* **1971**, 711.]
18. Postovskii, I. Ya.; Goncharova, I. N. *Zh. Obshch. Khim.* **1963**, *33*, 2334.
19. Vereschagina, N. N.; Postovskii, I. Ya. *Zh. Obshch. Khim.* **1964**, *34*, 1745.
20. Sheinker, J. N.; Postovskii, I. Ya.; Bednyagina, N. P.; Senyvina, L. B.; Lipatova, L. F. *Dokl. Chem.* **1961**, *141*, 1388. [*Dokl. Akad. Nauk SSSR* **1961**, 1388.]
21. Tišler, M. *Synthesis* **1973**, *3*, 123.
22. Butler, R. N. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R.; Boulton, A. J., Eds.; Elsevier: New York, 1977, Vol. 21, p. 323.
23. Ostrovskii, V. A.; Koldobskii, G. I.; Trifonov, R. E. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor R. J. K., Eds.; Elsevier: Oxford, 2008, Vol. 6, p. 257.
24. Han, Z.; Yao, Q.; Du, Z.; Tang, Z.; Cong, X.; Zhao, L. *J. Heterocycl. Chem.* **2016**, *53*, 280.
25. Wu, J.-T.; Zhang, J.-G.; Yin, X.; He, P.; Zhang, T.-L. *Eur. J. Inorg. Chem.* **2014**, 4690.
26. Taha, M. A. M. *Monatsh. Chem.* **2007**, *138*, 505.
27. Taha, M. A. M.; El-Badry, S. M. *Monatsh. Chem.* **2008**, *139*, 1261.
28. Shchegol'kov, E. V.; Khudina, O. G.; Ivanova, A. E.; Burgart, Ya. V.; Sadchikova, E. V.; Kravchenko, M. A.; Saloutin, V. I. *Pharm. Chem. J*. **2014**, *48*, 383. [*Khim.-Farm. Zh*. **2014**, *48*, 29.]
29. Ulomskii, E. N.; Shestakova, T. S.; Deev, S. L.; Rusinov, V. L.; Chupakhin, O. N. *Russ. Chem. Bull.*, *Int. Ed.* **2005**, *54*, 726. [*Izv. Akad. Nauk*, *Ser. Khim.* **2005**, 1993.]
30. Goodman, M. M.; Atwood, J. L.; Carlin, R.; Hunter, W.; Paudler, W. W. *J. Org. Chem.* **1976**, *41*, 2860.
31. Stevens, M. F. G. *J. Chem. Soc.*, *Perkin Trans. 1* **1972**, 1221.
32. Goodman, M. M.; Paudler, W. *J. Org. Chem.* **1977**, *42*, 1866.
33. Dornow, A.; Menzel, H.; Marx, P. *Chem. Ber.* **1964**, *97*, 2185.
34. Dornow, A.; Pietsch, H.; Marx, P. *Chem. Ber.* **1964**, *97*, 2647.
35. Messmer, A.; Hajós, G.; Benko, P.; Pallas, L. *J. Heterocycl. Chem.* **1973**, *10*, 575.
36. Messmer, A.; Hajós, G.; Benko, P.; Pallos, L. *Magy. Kem. Foly.* **1974**, *80*, 527.
37. Messmer, A.; Hajós, G.; Tamás, J.; Neszmélyi, A. *J. Org. Chem.* **1979**, *44*, 1823.
38. Shestakova, T. S.; Shenkarev, Z. O.; Deev, S. L.; Chupakhin, O. N.; Khalymbadzha, I. A.; Rusinov, V. L.; Arseniev, A. S. *J. Org. Chem.* **2013**, *78*, 6975.
39. Joshi, K. C.; Chand, P. *J. Heterocycl. Chem*. **1980**, *17*, 1783.
40. Younes, M. I.; Abbas, H. H.; Metwally, S. A. *Arch. Pharm*. **1987**, *320*, 1191.
41. Abdel-Latif, F. F.; Shaker, R. M.; Mahgoub, S. A.; Badr, M. Z. A. *J. Heterocycl. Chem.* **1989**, *26*, 769.
42. Ram, V. J. *Arch. Pharm*. **1980**, *313*, 108.
43. Deev, S. L.; Shenkarev, Z. O.; Shestakova, T. S.; Chupakhin, O. N.; Rusinov, V. L.; Arseniev, A. S. *J. Org. Chem*. **2010**, *75*, 8487.
44. Hajós, G.; Messmer, A.; Neszmèlyi, A.; Párkányi, L. *J. Org. Chem*. **1984**, *49*, 3199.
45. Vinot, N.; Maitte, P. *J. Heterocycl. Chem.* **1986**, *23*, 721.
46. Nishigaki, S.; Ichiba, M.; Senga, K. *J. Org. Chem.* **1983**, *48*, 1628.
47. Youssef, M. S. K.; Hassan, Kh. M.; Atta, F. M.; Abbady, M. S. *J. Heterocycl. Chem.* **1984**, *21*, 1565.
48. Mojzych, M.; Karczmarzyk, Z.; Rykowski, A. *J. Chem. Crystallogr.* **2005**, *35*, 151.
49. Mojzych, M.; Karczmarzyk, Z.; Wysocki, W.; Urbanczyk-Lipkowska, Z.; Zaczek, N. *J. Mol. Struct.* **2014**, *1067*, 147.
50. Karczmarzyk, Z.; Mojzych, M.; Rykowski, A. *J. Mol. Struct.* **2007**, *829*, 22.
51. El-Khoshien, Y. O. *Phosphorus*, *Sulfur Silicon Relat. Elem.* **1998**, *139*, 163.
52. Castillón, S.; Meléndez, E.; Pascual, C.; Vilarrasa, J. *J. Org. Chem.* **1982**, *47*, 3886.
53. Azev, Yu. A.; Vereshchagina, N. N.; Postovskii, I. Ya.; Pidémskii, E. L.; Goleneva, A. F. *Pharm. Chem. J.* **1981**, *15*, 789. [*Khim.-Farm. Zh*. **1981**, *15*, 50.]
54. Azev, Yu. A.; Postovskii, I. Ya.; Pidémskii, E. L.; Goleneva, A. F. *Pharm. Chem. J.* **1980**, *14*, 230. [*Khim.-Farm. Zh*. **1980**, *14*, 39.]
55. Klyuev, N. A.; Aleksandrov, G. G.; Azev, Yu. A.; Sidorov, E. O.; Esipov, S. E. *Chem. Heterocycl. Compd.* **1986**, *22*, 95. [*Khim. Geterotsikl. Soedin.* **1986**, 114.]
56. Villarrasa, J.; Granados, R. *J. Heterocycl. Chem.* **1974**, *11*, 867.
57. Castillón, S.; Villarrasa, J. *J. Org. Chem*. **1982**, *47*, 3168.
58. Shchegol'kov, E. V.; Ivanova, A. E.; Burgart, Y. V.; Saloutin, V. I. *J. Heterocycl. Chem.* **2013**, *50*, E80.
59. Rusinov, V. L.; Dragunova, T. V.; Zyryanov, V. A.; Aleksandrov, G. G.; Chupakhin, O. N. *Chem. Heterocycl. Compd.* **1984**, *20*, 455. [*Khim. Geterotsikl. Soedin.* **1986**, 1668.]
60. Rusinov, V. L.; Dragunova, T. V.; Zyryanov, V. A.; Aleksandrov, G. G.; Klyuev, N. A.; Chupakhin, O. N. *Chem. Heterocycl. Compd.* **1984**, *20*, 455. [*Khim. Geterotsikl. Soedin.* **1984**, 557.]
61. Gray, E. J.; Stevens, M. F. G.; Tennant, G.; Vevers, R. J. S. *J. Chem. Soc.*, *Perkin Trans. 1* **1976**, 1496.
62. Shestakova, T. S.; Deev, S. L.; Ulomsky, E. N.; Rusinov, V. L.; Chupakhin, O. N.; D'yachenko, O. A.; Kazheva, O. N.; Chekhlov, A. N.; Slepukhin, P. A.; Kodess, M. I. *Russ. Chem. Bull*., *Int. Ed.* **2006**, *55*, 2071. [*Izv. Akad. Nauk*, *Ser. Khim.* **2006**, 1993.]
63. Willer, R. L.; Henry, R. A. *J. Org. Chem*. **1988**, *53*, 5371.