

Strategies and Prospects in Functionalization of Tetrazoles

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Abstract—The review summarizes the methods of functionalization of tetrazoles, which were reported from 2001 to mid 2005, and analyzes main strategies in the development of this field of tetrazole chemistry.

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1. INTRODUCTION

Evident advances achieved in the past decade in the chemistry of tetrazoles are largely determined by wide applications of these compounds as corrosion inhibitors [1], analytical reagents [2], high-energy materials [3–5], and components of ionic liquids [6] and gas-generating compositions [7]. Tetrazoles play an important role in microbiological studies [8, 9] and studies on the effect of environmental factors on vital activity of plants [10]. Radiochromic dyes based on



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Fields of scientific interest: acid and phase-transfer catalysis of organic reactions and methods of synthesis, physicochemical properties, and reactivity of polynitrogen-containing heterocyclic compounds.

tetrazolium salts can be used in dosimetry for radiation treatment of materials [11]. The significance of tetrazoles in oligonucleotide synthesis [12–14] and various catalytic processes [15, 16] also grows. Tetrazole derivatives were successfully used in organic synthesis [17–23], including preparation of complex heterocyclic structures which are difficult or even impossible to obtain by other methods [24–26].

In the recent years, very important results were obtained in the design of new drugs containing a tetrazole ring as structural fragment. First of all, anti-hypertensive drug Losartan and its analogs [27–30] must be noted. In addition, a number of tetrazole derivatives were shown to exhibit antiinflammatory [31], analgetic [32, 33], and antifungal activity [34], as well as to inhibit the growth of papilloma viruses [35] and many others [36–39].

It is quite obvious that wide application of tetrazoles in research work and industry, primarily in pharmaceutical chemistry, has become possible due to development of new and considerable improvement of known methods for the preparation of functionally substituted tetrazoles. This very important period in the development of tetrazole chemistry has started in the late 1990s, and the results of studies in that field have not been discussed so far.

The goal of the present review was to systematize new methods for functionalization of tetrazoles, reveal general trends holding therein and synthetic approaches, and estimate prospects in further research in this line. Therefore, the review covers published data reported during the last 4 years, while general problems of the tetrazole chemistry (for reviews, see [40–50]) are not considered.

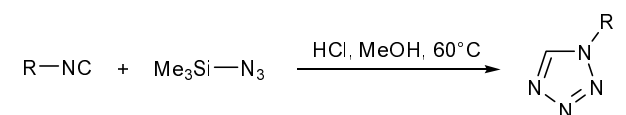
2. MONOSUBSTITUTED TETRAZOLES

This section deals with methods of synthesis of 1-, 2- and 5-monosubstituted tetrazoles. Traditionally, methods for the preparation of 5-substituted tetrazoles were the subject of numerous studies, whereas syntheses of 1- and 2-substituted derivatives were studied to a considerably lesser extent. This problem has received more attention only in the most recent years due to increased application of 1- and 2-substituted tetrazoles in the preparation of drugs [51] and some other fields [52].

2.1. 1-Substituted Tetrazoles

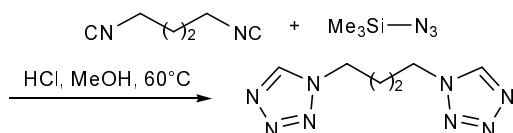
[2+3]-Cycloaddition of isocyanides to hydrazoic acid underlies one of the most known methods of synthesis of 1-substituted tetrazoles. However, until recently the use of this procedure was restricted, obviously due to inconvenience in handling isocyanides and hydrazoic acid. The method was essentially improved via replacement of hydrazoic acid by a more effective and convenient reagent, trimethylsilyl azide (Me_3SiN_3) [53]. Various isocyanides were reported [53] to react with Me_3SiN_3 in methanol in the presence of a catalytic amount of hydrochloric acid to afford 58–92% of 1-substituted tetrazoles (Scheme 1). The reaction is general, and it can be used to obtain bis-tetrazole derivatives from the corresponding bis-

Scheme 1.



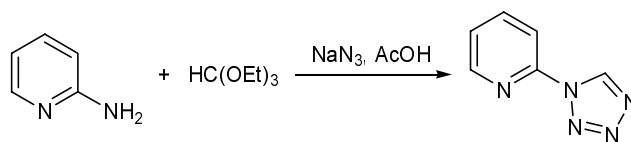
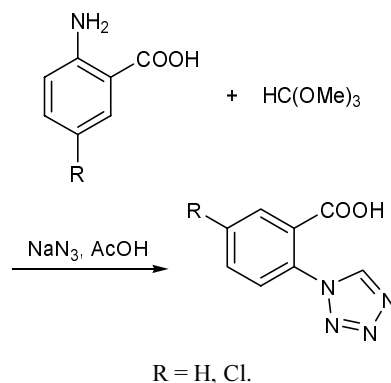
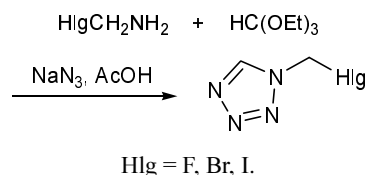
R = Pr, *t*-Bu, Me_3SiCH_2 , cyclohexyl, 2-MeOC₆H₄, 4-MeOC₆H₄, 2,6-Me₂C₆H₃, Ph, 4-MeOCOC₆H₄, 4-O₂NC₆H₄.

Scheme 2.

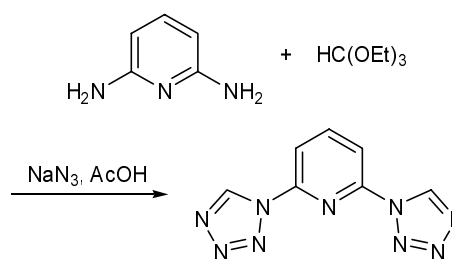


isocyanides (Scheme 2). Another fairly well known method for the synthesis of 1-functionalized tetrazoles is based on reaction of amines with ortho esters and sodium azide in acetic acid. Aliphatic [52], aromatic [23, 51, 54], and heteroaromatic amines [54] are thus converted into 1-substituted tetrazoles with equal efficiency (Scheme 3). Bis-tetrazoles are also available through analogous reaction [55] (Scheme 4).

Scheme 3.

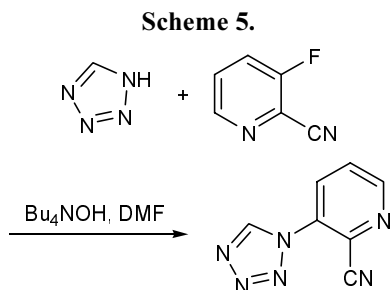


Scheme 4.



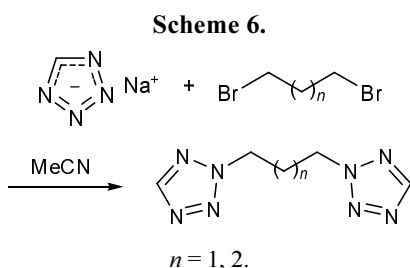
One more reaction frequently used for the synthesis of 1-substituted tetrazoles is alkylation or arylation of unsubstituted tetrazole. The main disadvantage of this method is that mixtures of isomeric 1- and 2-substituted derivatives are always formed; in many cases, separation of the isomeric products involves strong experimental difficulties. Relevant published data have been reviewed recently [44]. Among recent examples, hetarylation of tetrazole with 2-cyano-3-fluoropyridine

[51] (Scheme 5) must be noted. The reaction occurs under mild conditions, but the yield of 3-(tetrazol-1-yl)pyridine-2-carbonitrile is very poor (12%).

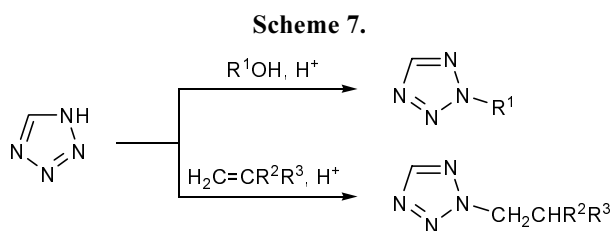


2.2. 2-Substituted Tetrazoles

2-Substituted tetrazoles are usually synthesized by alkylation (or arylation) of tetrazole [44, 48]. However (see above), the reaction is characterized by low selectivity and poor yield of the alkylation products. Examples are reactions of tetrazole with 1,3-dibromopropane [56] and 1,4-dibromobutane [57] (Scheme 6).

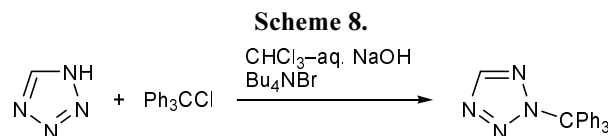


In the first case, preliminarily prepared tetrazole sodium salt was treated with 1,3-dibromopropane in boiling acetonitrile (4 days), and the yield of 1,3-bis-(tetrazol-2-yl)propane was 12.8%. In the alkylation of tetrazole with 1,4-dibromobutane under the same conditions, the corresponding bis-tetrazole was formed in 9.8% yield. 2-Substituted tetrazoles were obtained as the only products when propan-2-ol, 2-methylpropan-2-ol, cyclohexanol, propene, or 2-methylpropene were used as alkylating agents in the presence of 96% sulfuric acid [58] (Scheme 7).



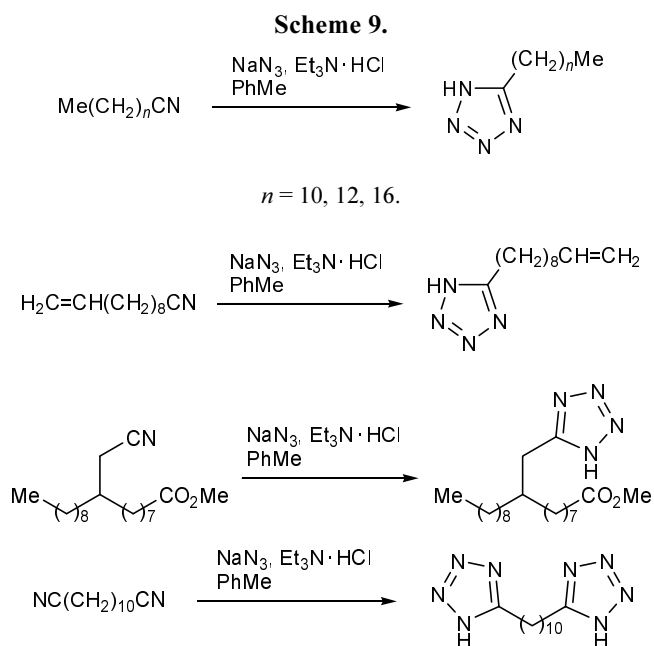
$R^1 = i\text{-Pr, } t\text{-Bu, cyclohexyl}; R^2 = \text{H, } R^3 = \text{Me}; R^2 = R^3 = \text{Me.}$

Analogous pattern was observed in the reaction of tetrazole with chloro(triphenyl)methane under conditions of phase-transfer catalysis [59] (Scheme 8).



2.3. 5-Substituted Tetrazoles

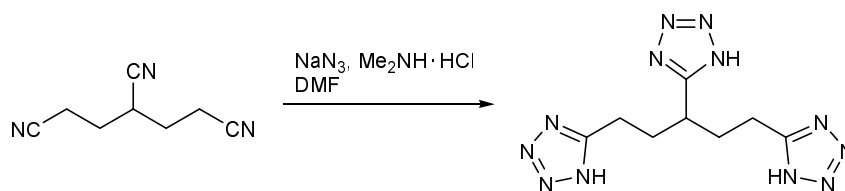
5-Substituted tetrazoles can be prepared in several ways, the main of which is [2+3]-cycloaddition of nitriles to azides [40–42]. The reaction is general and is widely used in the synthesis of tetrazoles having various substituents in position 5. Scheme 9 illustrates the potential of this approach [60]. Unsaturated nitriles, those possessing various functional groups, and dinitriles can be used as initial compounds.



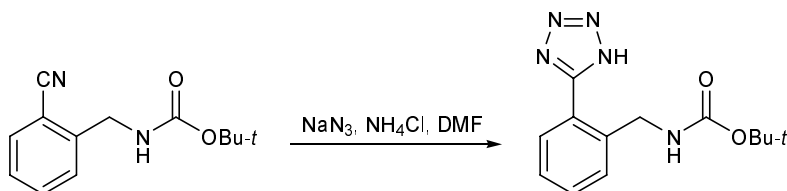
Zubarev *et al.* recently applied this procedure to obtain complex heterocyclic systems including more than two tetrazole rings [61] (Scheme 10).

Functionally substituted aromatic mono- and dinitriles [51, 62], benzyl thiocyanates [12], and heterocyclic nitriles [18, 32, 63] smoothly reacted with hydrazoic acid salts to give the corresponding 5-substituted tetrazoles in good yield (Schemes 11–14). When the reaction with benzyl thiocyanate [12] was performed in aqueous dioxane instead of DMF, the reaction time sharply increased (up to 90 h).

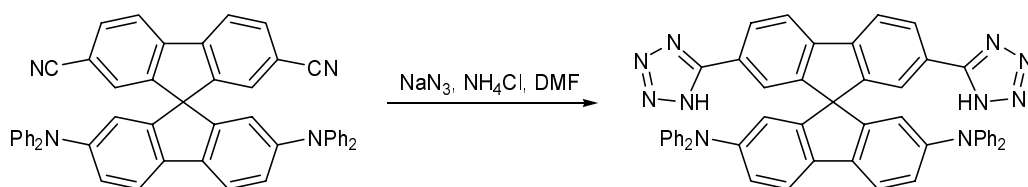
Scheme 10.



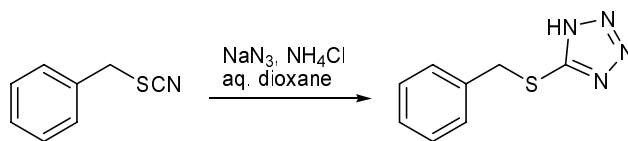
Scheme 11.



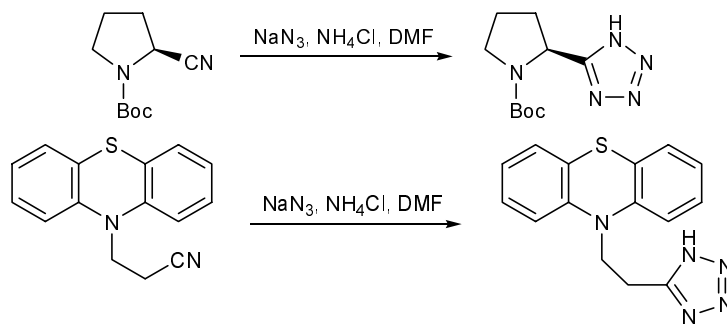
Scheme 12.



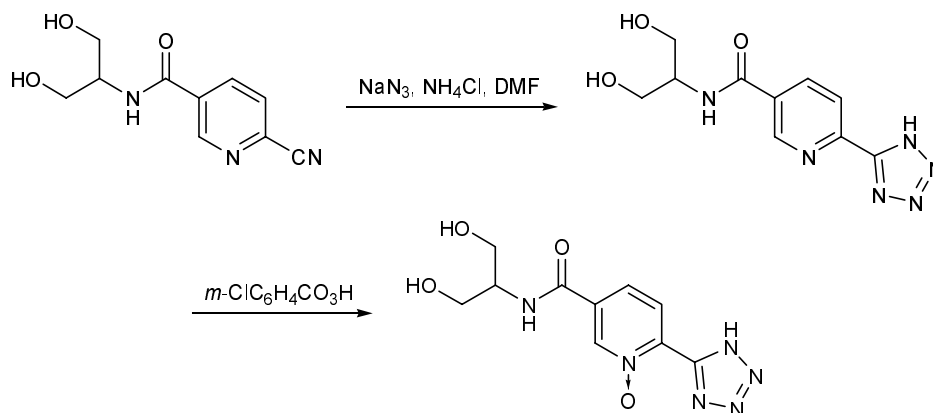
Scheme 13.



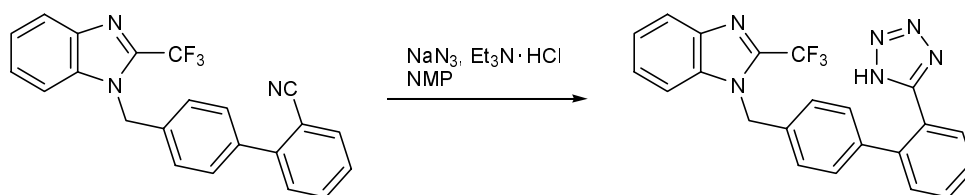
Scheme 14.



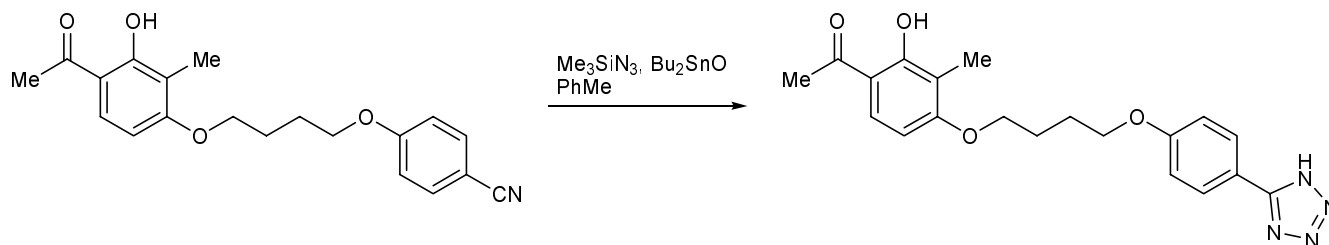
Scheme 15.



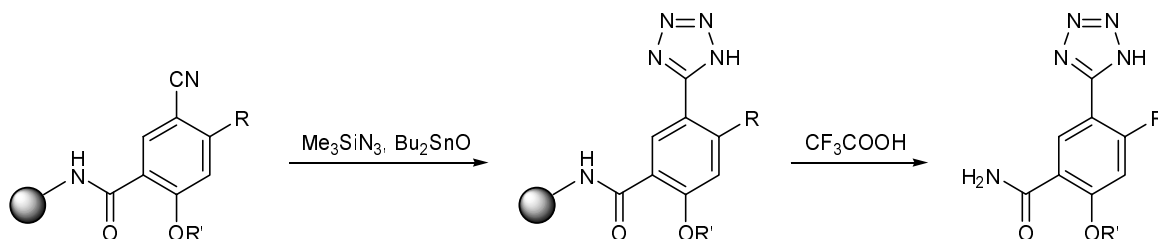
Scheme 16.



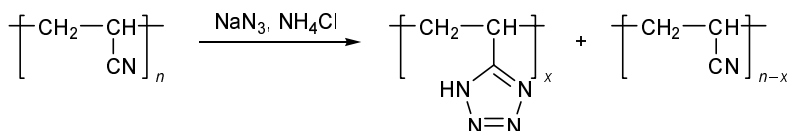
Scheme 17.



Scheme 18.



Scheme 19.



As noted above, the reaction of nitriles with inorganic azides is general. It can be used to obtain polyfunctional 5-substituted tetrazoles, for no other functional group than cyano is involved. This is exceptionally important in the synthesis of medical diagnostic reagents and tetrazole-containing medical agents, primarily of those used in the treatment of cardiovascular diseases and disorders of nervous systems. Scheme 15 illustrates the synthesis of one of such diagnostic reagents [64]. Likewise, other functional groups in polyfunctional nitriles remained intact in analogous syntheses of medical agents shown in Schemes 16 and 17, despite fairly severe conditions (160°C , 12 h), and the corresponding tetrazoles were formed in a good yield [65–68].

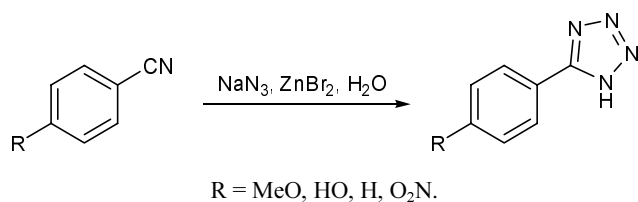
Interesting results were obtained while studying reactions of polymer-supported polyfunctional nitriles with trimethylsilyl azide in the presence of Bu_2SnO in *o*-xylene [69] (Scheme 18). Another interesting ex-

ample is the synthesis of 5-substituted tetrazoles from polymeric nitriles. Such reactions were discussed in detail in the recent review [47]. Among the latest studies, the synthesis of poly(5-vinyltetrazole) from poly(acrylonitrile) and sodium azide should be noted (Scheme 19), where the reaction mixture in dimethylformamide was slowly heated from 60 to 120°C over a period of 12 h [70].

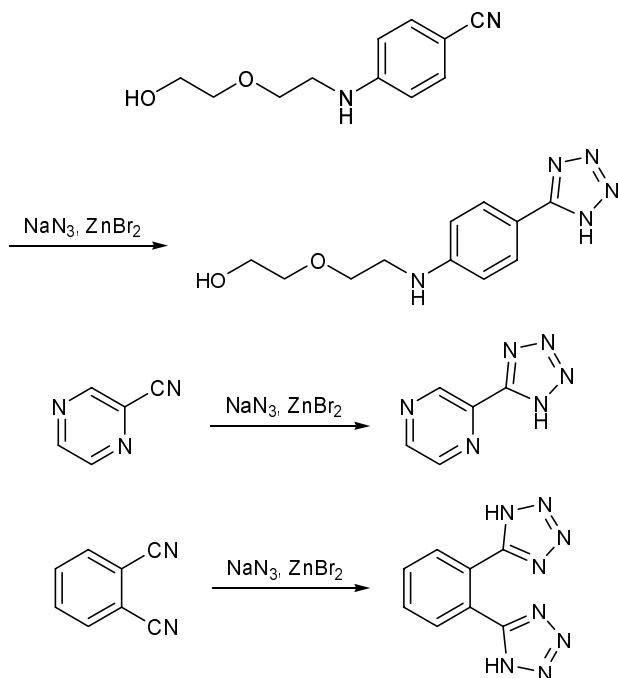
Analysis of vast experimental data, including the pioneering study by Finnegan *et al.* (1958) [71] on reactions of nitriles with hydrazoic acid salts as a universal synthetic route to 5-substituted tetrazoles, leads to the following important conclusions. Despite obvious advantages of this method, some its drawbacks must be pointed out, namely fairly high reaction temperature (110 – 160°C) and long reaction time (in some cases, 80–90 h is necessary for the reaction to be complete). In addition, such processes cannot be regarded as safe. Sharpless and co-workers [72–74] succeeded

in solving the above problems: they found that various nitriles smoothly react with sodium azide in water in the presence of Lewis acids, e.g., ZnCl_2 or ZnBr_2 (Scheme 20). Under these conditions, 5-substituted tetrazoles are successfully formed from functionally substituted, heterocyclic, and aromatic nitriles [72, 75–78] (Scheme 21). In all cases, the yields of the target products are good, and the use of aqueous medium makes the process almost safe. Moreover, zinc(II) bromide turned out to be quite effective catalyst in the synthesis of poly(5-vinyltetrazole) [79].

Scheme 20.



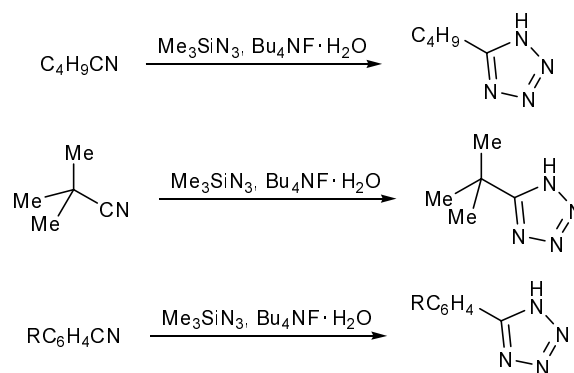
Scheme 21.



High yields (80–97%) of 5-substituted tetrazoles were achieved in reactions of various nitriles with trimethylsilyl azide in the presence of tetrabutylammonium fluoride as catalyst and a small amount of water [80] (Scheme 22).

A novel and exceptionally promising field in the chemistry of heterocyclic compounds, including tetrazoles, covers studies on their synthesis under microwave (MW) activation [81]. Alterman and Hallberg

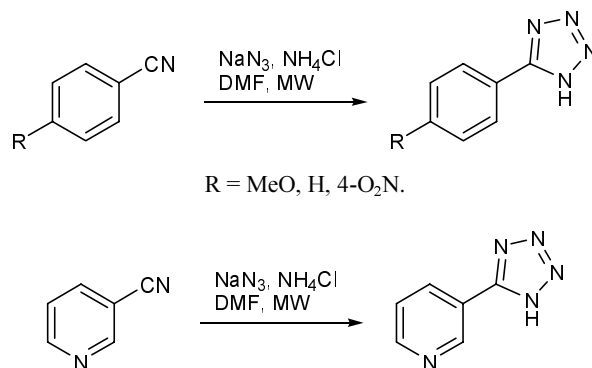
Scheme 22.



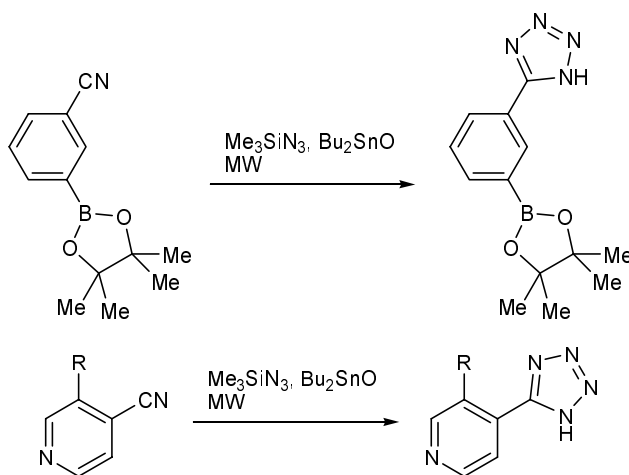
$\text{R} = 3\text{-MeO}, \text{H}, 4\text{-O}_2\text{N}.$

[82] recently showed that reactions of nitriles with sodium azide in DMF under microwave irradiation give the corresponding 5-substituted tetrazoles in high yield and that the reaction time is shortened by 1–2 orders of magnitude as compared to conventional process (Scheme 23).

Scheme 23.



Scheme 24.

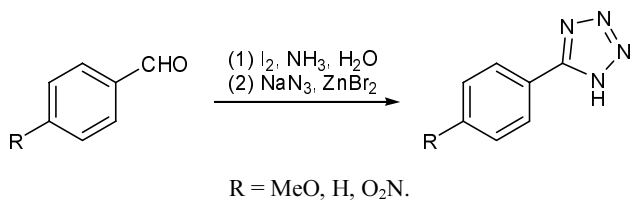


$\text{R} = i\text{-Pr}, t\text{-Bu}, \text{Ph}.$

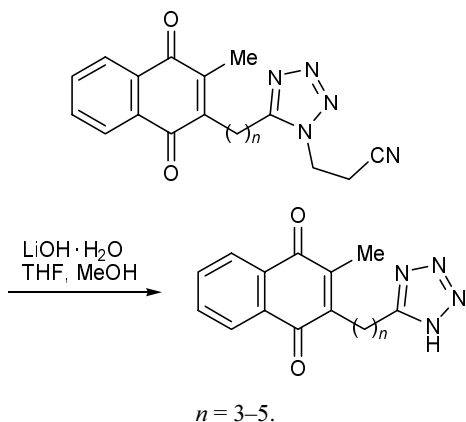
Functionally substituted and heterocyclic nitriles react in a similar way with trimethylsilyl azide in the presence of Bu_2SnO in such solvents as 1,2-dimethoxyethane or dioxane [83, 84] (Scheme 24).

To conclude discussion on the methods for preparation of 5-substituted tetrazoles, some procedures which have not still received wide application should be noted. First of all, these include multistep reaction of aldehydes with iodine in aqueous ammonia, followed by treatment with sodium azide and zinc(II) bromide [85] (Scheme 25), and transformation of 1,5-disubstituted tetrazoles into 5-substituted derivatives as a result of a process analogous to retro-Michael addition [33, 37] (Scheme 26). Mo *et al.* [86] described a novel synthesis of 5-(pyridin-2-yl)tetrazole via reaction of (pyridin-2-yl)methanamine with benzaldehyde and subsequent treatment of the Schiff base thus formed with sodium azide in the presence of magnesium or copper salts.

Scheme 25.

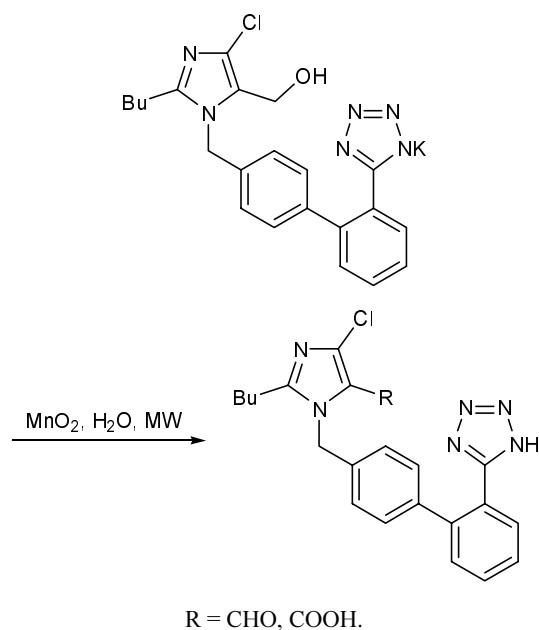


Scheme 26.



Finally, tetrazoles having polyfunctionalized substituents in the 5-position may be obtained by modification of the side-chain in a tetrazole-containing substrate. An example of such transformation is illustrated by Scheme 27. Depending on the reaction time, treatment of Losartan with manganese dioxide under microwave irradiation could lead to formation of the corresponding aldehyde or carboxylic acid [29].

Scheme 27.



3. DISUBSTITUTED TETRAZOLES

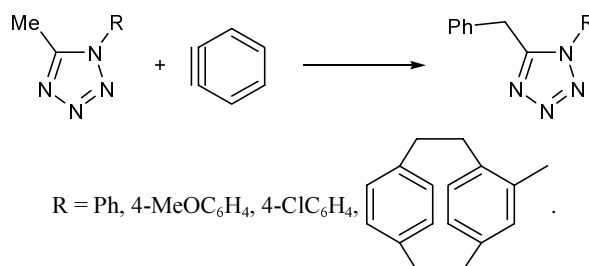
Among a variety of methods for the preparation of 1,5- and 2,5-disubstituted tetrazoles [40–42], only those applicable to the synthesis of functionally substituted derivatives are considered in the present review. Just these trends are typical of searching for new synthetic routes to disubstituted tetrazoles in the past decade.

3.1. 1,5-Disubstituted Tetrazoles

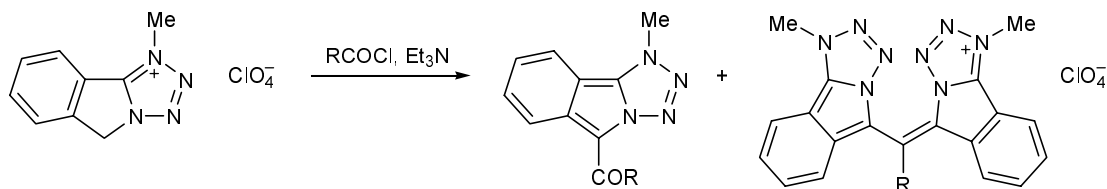
The most promising route to functionalized 1,5-disubstituted tetrazoles implies modification of side chain in the corresponding heterocyclic substrates. Typical examples utilizing this approach are given below. A new simple procedure for the synthesis of 1,5-disubstituted tetrazoles was proposed by Aly and Shaker [87]. It is based on the reaction of 1-aryl-5-methyltetrazoles with dehydrobenzene generated from benzenediazonium carboxylate (Scheme 28). The reaction is carried out by heating the reactants in boiling acetonitrile for 12–18 h, and the yield of the corresponding tetrazoles attains 60–78%.

Polyfunctional 1,5-disubstituted tetrazoles can also be prepared by acylation of 1-methyltetrazolo[5,1-*a*]-isoindolium perchlorate in the presence of triethylamine [88] (Scheme 29). One more procedure involves reaction of tetrazolo[1,5-*a*]quinoline-4-carbaldehyde with substituted acetophenone, followed by treatment

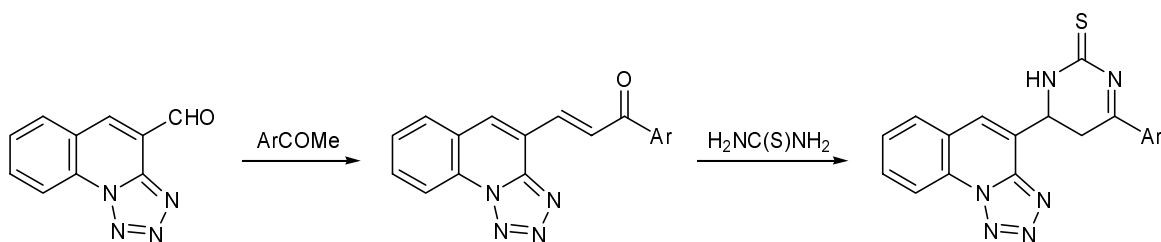
Scheme 28.



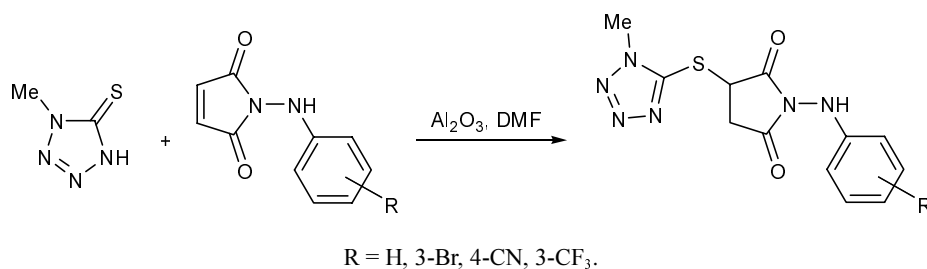
Scheme 29.



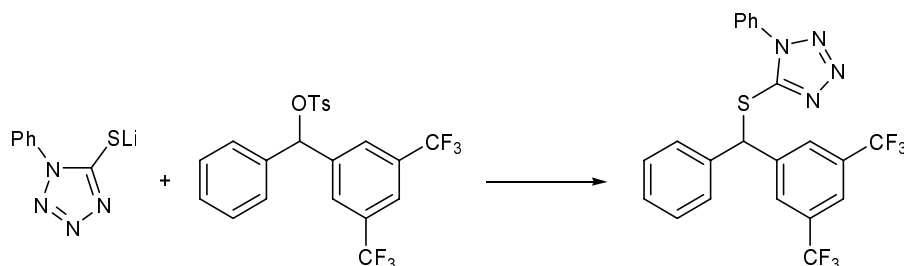
Scheme 30.



Scheme 31.



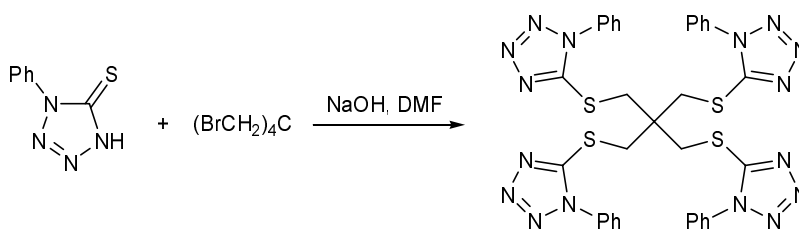
Scheme 32.



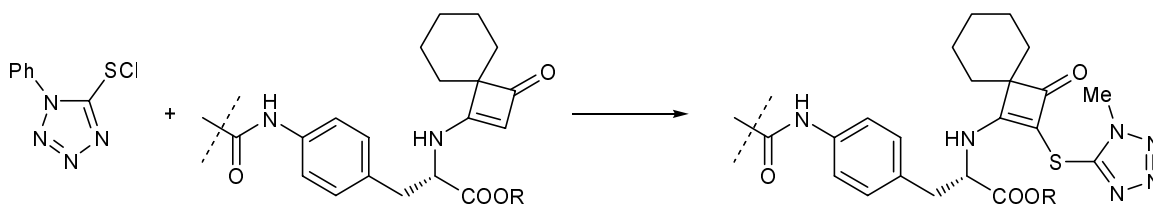
of the α,β -unsaturated ketone thus formed with thio-urea [31] (Scheme 30). In the recent years, interesting studies were performed on the use of 1-alkyl(aryl)-tetrazole-5-thiones in the synthesis of 1,5-disubstituted

tetrazoles. Michael addition of 1-methyltetrazole-5-thione to compounds having an activated double C=C bond [89] (Scheme 31), alkylation of 1-phenyltetrazole-5-thione with diphenylmethyl *p*-toluenesulfonate

Scheme 33.



Scheme 34.

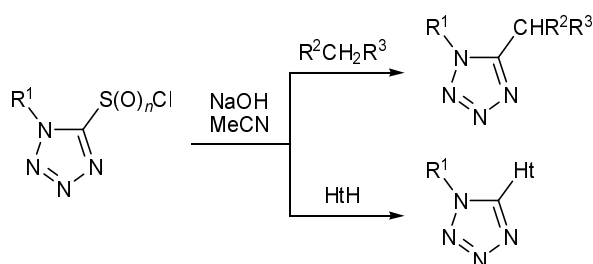


[90] (Scheme 32) and 1,3-dibromo-2,2-bis(bromomethyl)propane [91] (Scheme 33), and reactions of 1-methyltetrazole-5-sulfonyl chloride as electrophile with substrates having a complex structure [92] (Scheme 34) were reported.

Replacement of the methylsulfinyl or methylsulfonyl group in 1-aryl-5-methylsulfinyl- and 1-aryl-5-methylsulfonyltetrazoles by the action of carbon-, nitrogen-, and oxygen-centered nucleophiles [49, 91, 93, 94] (Schemes 35, 36) may be regarded as a simple and promising method for the preparation of functional 1,5-disubstituted tetrazole derivatives. The chlorine atom in 5-chloro-1-phenyltetrazole is replaced by the action of C- and N-nucleophiles [95, 96] (Scheme 37).

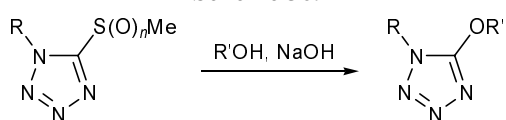
It should be emphasized that the methylsulfinyl or methylsulfonyl group in 5-methylsulfinyl-1-phenyl- and 5-methylsulfonyl-1-phenyltetrazoles is replaced by nucleophiles under considerably milder conditions than the chlorine atom in 5-chloro-1-phenyltetrazole. Furthermore, tetrazole-5-thione derivatives are much more accessible (from the preparative viewpoint) than the corresponding 5-chlorotetrazoles. Chlorine atom in the side chain of tetrazole-containing substrates is also smoothly replaced in reactions with nitrogen-centered nucleophiles [97] (Scheme 38). Electrophilic substitution in the side chain of 1,5-disubstituted tetrazoles

Scheme 35.



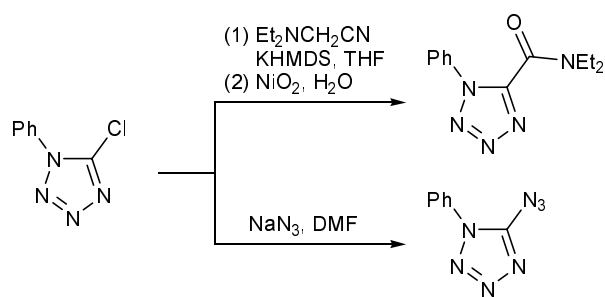
$\text{R}^1 = \text{Ph}, 4\text{-O}_2\text{NC}_6\text{H}_4$; $\text{R}^2 = \text{R}^3 = \text{CN}$; $\text{R}^2 = \text{CN}, \text{R}^3 = \text{COOEt}$;
 $\text{Ht} = \text{piperidinobenzimidazol-1-yl}$; $n = 1, 2$.

Scheme 36.

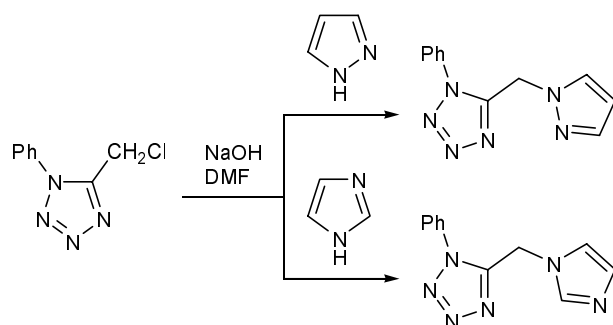


$\text{R} = \text{Ph}, 4\text{-O}_2\text{NC}_6\text{H}_4$; $\text{R}' = \text{Me}, \text{Et}, \text{Pr}, \text{Ph}, 4\text{-O}_2\text{NC}_6\text{H}_4$;
 $n = 1, 2$.

Scheme 37.



Scheme 38.



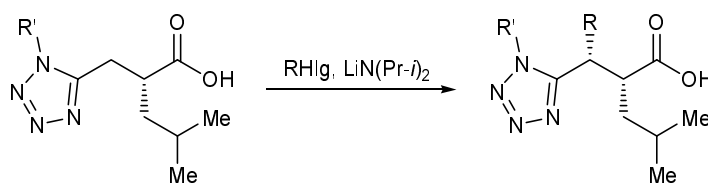
provides one more method for functionalization of these compounds [98] (Scheme 39). A promising method for modification of substituents in 1,5-disubstituted tetrazoles was recently demonstrated using 5-R-tetrazol-1-ylacetamides as examples; their treatment with sodium azide and tetrachlorosilane afforded the corresponding polytetrazoles in a good yield [99] (Scheme 40).

As previously, N-monosubstituted amides and thioamides are widely used in the synthesis of 1,5-disubstituted tetrazoles [33, 37, 100–102]. In the recent years, the procedure was essentially improved to avoid the use of unsafe and hazardous hydrazoic acid (which was used previously in the synthesis of tetrazoles from amides); instead, convenient and effective trimethylsilyl azide in the presence of diisopropyl azodicarboxylate (DIAD) [33, 100] (Scheme 41) and sodium azide in combination with trifluoromethanesulfonic an-

hydride [37] or mercury(I) chloride [101] (Scheme 42) have been proposed.

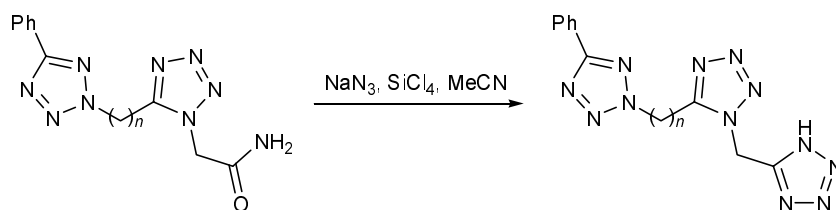
Alkylation of 5-substituted tetrazoles provides a fairly frequently used method for the preparation of 1,5-disubstituted tetrazoles. Despite certain intrinsic disadvantages (see above), the procedure attracts researchers' attention due to its simplicity and the possibility of using functionalized alkylating agents. Here, the common problem is separation of isomeric 1,5- and 2,5-disubstituted tetrazoles which are formed in most alkylation reactions. Nevertheless, numerous examples of successful application of this reaction to the synthesis of functionally substituted tetrazoles have been reported in a few past years. One of these is the alkylation of *tert*-butyl [2-(tetrazol-5-yl)benzyl]carbamate with methyl iodide; the reaction gave a 1:1.5 mixture of isomeric 1,5- and 2,5-disubstituted tetrazoles which were separated by HPLC [51] (Scheme 43). A more

Scheme 39.



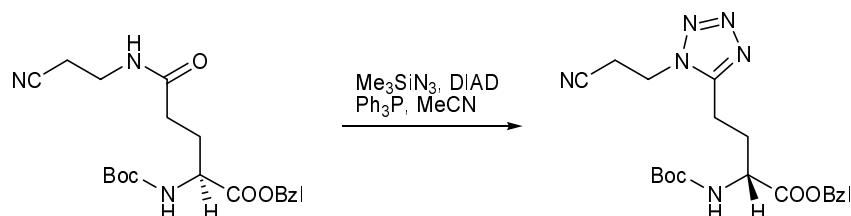
R = Me, Et, *i*-Pr, Bu; R' = Me, Pr; Hlg = I, Br.

Scheme 40.

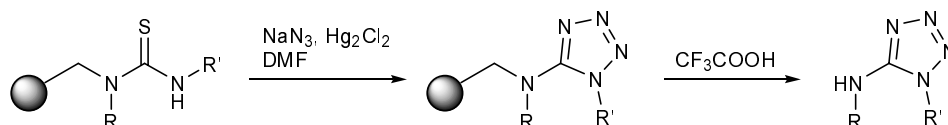


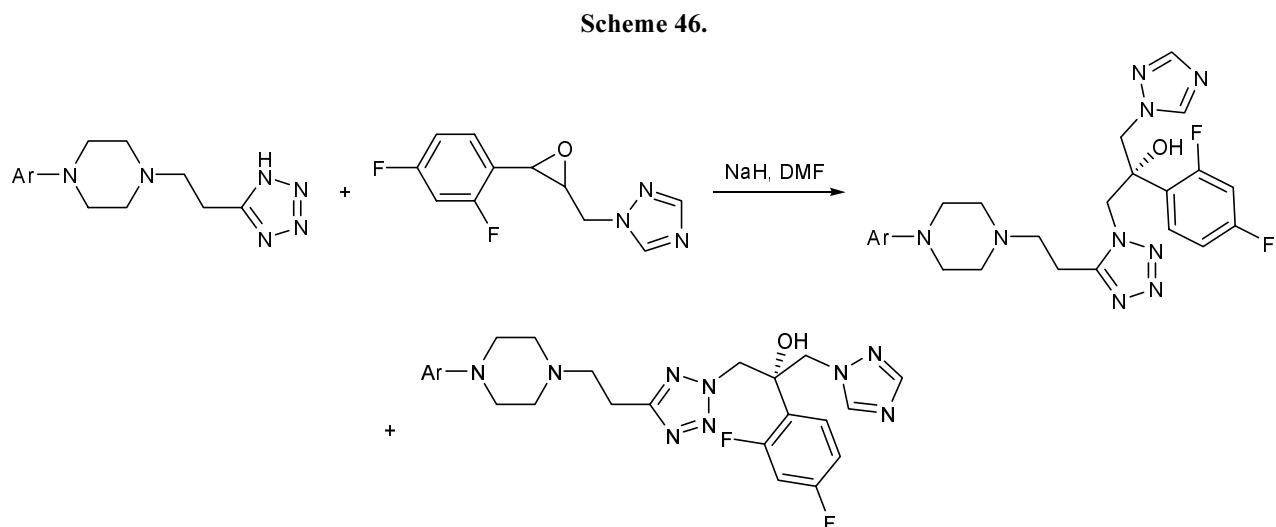
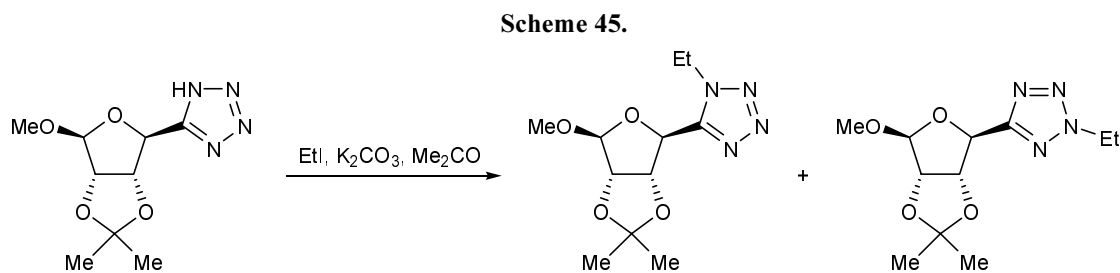
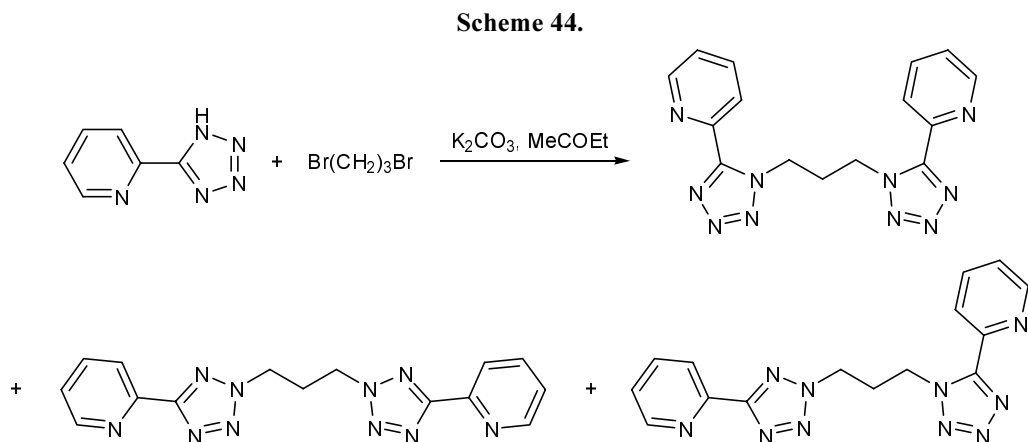
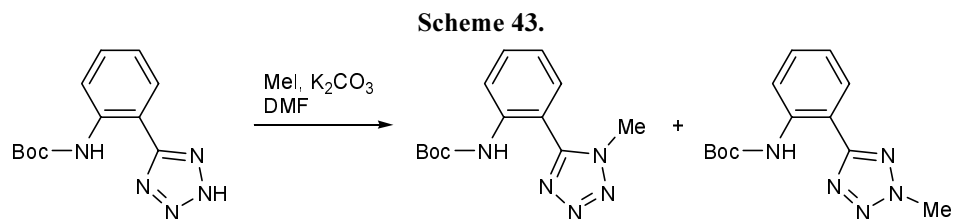
$n = 1, 2.$

Scheme 41.



Scheme 42.





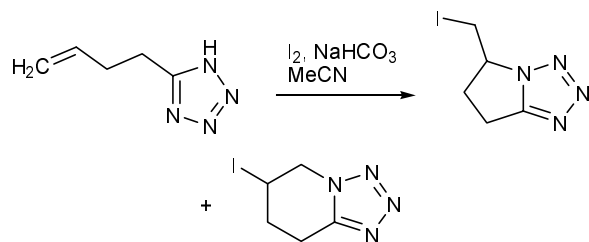
complex mixture of products was obtained in the alkylation of 5-(pyridin-2-yl)tetrazole with 1,3-dibromopropane (Scheme 44); it contained three isomeric bis-tetrazole derivatives at a ratio of 1:1:1; the isomers were separated by column chromatography on silica

gel [103]. Column chromatography was successfully used by Balle *et al.* [68] to separate isomeric 1,5- and 2,5-disubstituted tetrazoles formed in the alkylation with methyl iodide of 5-substituted tetrazoles having a complicated structure.

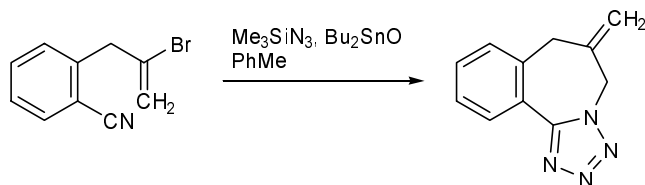
In some cases, 1,5-disubstituted tetrazole may be isolated from the isomer mixture by fractional crystallization, even when 2,5-disubstituted isomer strongly predominates [104] (Scheme 45). 1,5-Disubstituted tetrazoles were also synthesized by alkylation of 5-substituted tetrazoles with complex oxiranes [34, 63] (Scheme 46).

Ek *et al.* [105] proposed one more procedure for the synthesis of 1,5-disubstituted tetrazoles by cyclization of tetrazoles having an unsaturated alkyl chain in the 5-position. The reaction was called iodocyclization by the authors; it may be regarded as regioselective intramolecular alkylation (Scheme 47). Scheme 48 illustrates a modification of this procedure [106].

Scheme 47.

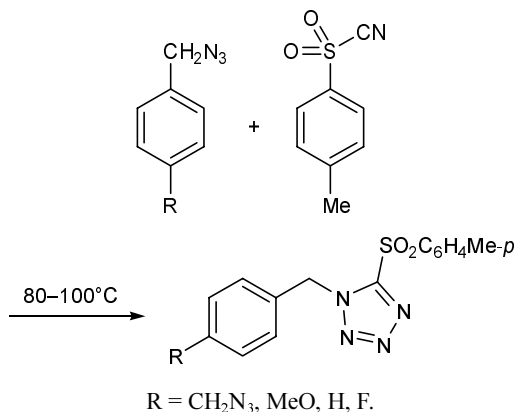


Scheme 48.

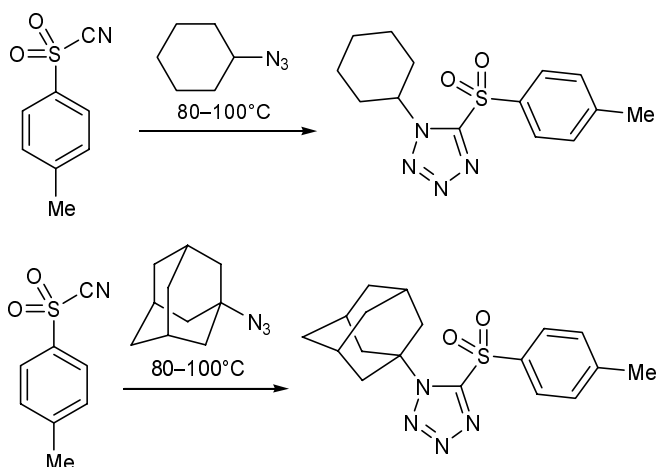


Inter- and intramolecular [2+3]-cycloaddition of nitriles to alkyl or aryl azides is known to afford 1,5-disubstituted tetrazoles [40–42]. In the recent years, this method was developed mainly via extension of a series of reagents which may be used for the syn-

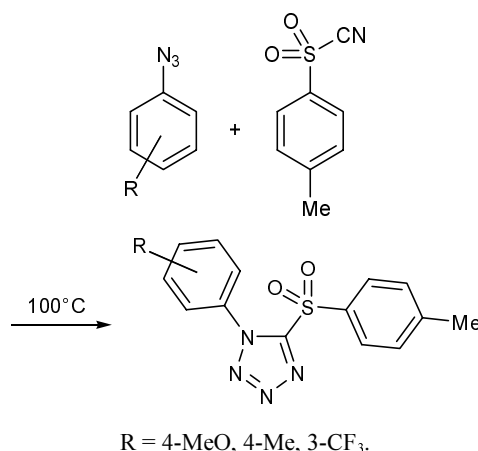
Scheme 49.



Scheme 50.

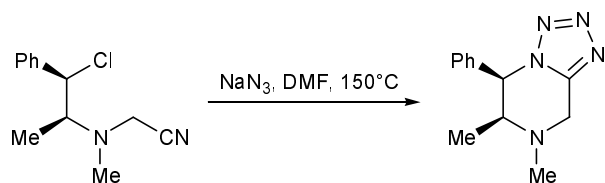


Scheme 51.



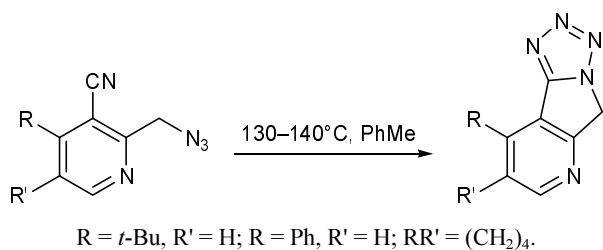
thesis of functionally substituted tetrazoles. The most typical example is the formation of 1,5-disubstituted tetrazoles by [2+3]-cycloaddition of *p*-toluenesulfonyl cyanide to various alkyl and aryl azides [107] (Schemes 49–51). Elevated temperature (130–150°C) promotes intramolecular [2+3]-cycloaddition, presumably due to steric effects in the substrate molecule [108–110] (Schemes 52, 53).

Scheme 52.



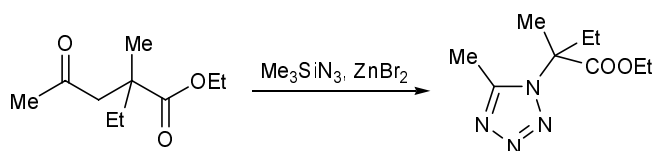
The Schmidt reaction of ketones with excess hydrazoic acid underlies one of the first methods used for the synthesis of 1,5-disubstituted tetrazoles at the early stage of the development of tetrazole chemistry.

Scheme 53.

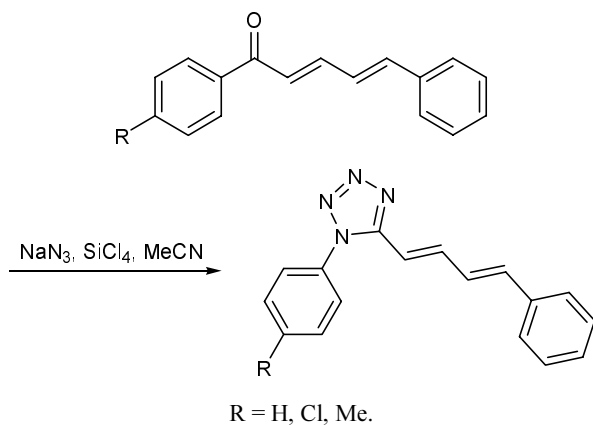


However, this procedure gradually lost its original significance because of the necessity of working with hydrazoic acid which is unsafe to handle with. Considerably increased interest in the Schmidt reaction as a promising method for the preparation of 1,5-disubstituted tetrazoles was observed as a result of replacement of HN_3 by trimethylsilyl azide in combination with ZnBr_2 [111] (Scheme 54) or by sodium azide and TiCl_4 [60] or SiCl_4 [112] (Scheme 55).

Scheme 54.



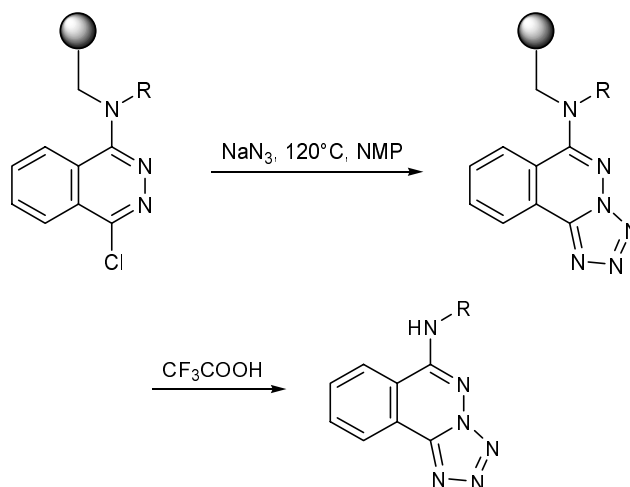
Scheme 55.



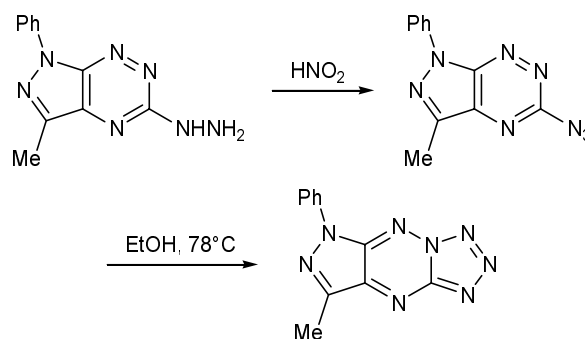
Another well known way of building up tetrazole derivatives implies reaction of cyclic imidoyl chlorides or bromides with sodium azide [113, 114]. The reaction smoothly occurs at 120°C in such solvent as 1-methylpyrrolidin-2-one (NMP) [115] (Scheme 56). Intermediate azide can also be generated from the corresponding hetarylhydrazine [116] (Scheme 57).

There are two more methods for the synthesis of 1,5-disubstituted tetrazoles, which have never been discussed in all known reviews on the chemistry of tetrazoles. One of these methods is based on the

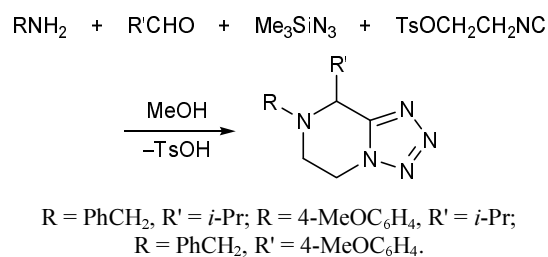
Scheme 56.



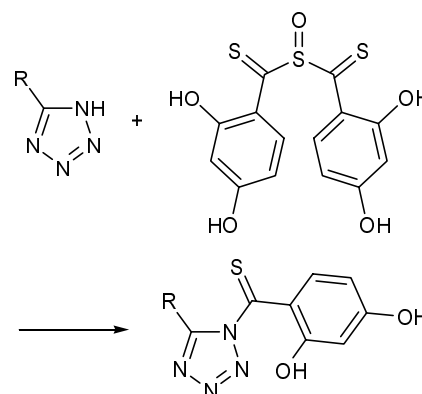
Scheme 57.



Scheme 58.



Scheme 59.

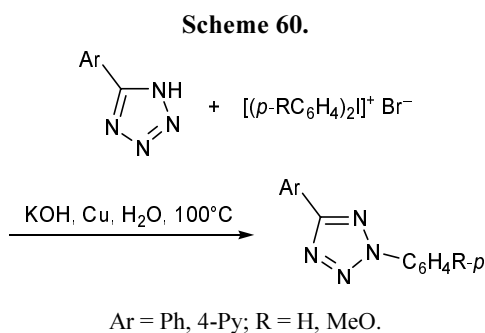


multicomponent Ugi reaction which makes it possible to obtain various tetrazolopiperazines under mild conditions [117] (Scheme 58). Obviously, this is one of the first examples of multicomponent reactions in the chemistry of tetrazoles. After some modification, the procedure can find wide application in the synthesis of functionally substituted tetrazoles. The other method involves treatment of 5-substituted tetrazoles with bis-(2,4-hydroxybenzothioyl) sulfoxide in boiling methanol [118] (Scheme 59).

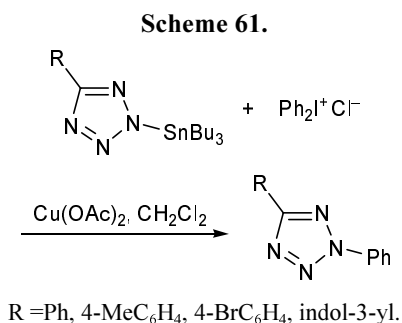
3.2. 2,5-Disubstituted Tetrazoles

This section covers reactions leading to 2,5-disubstituted tetrazoles, which have been reported in the last three years. Early information on this topic has been reviewed in detail in [48].

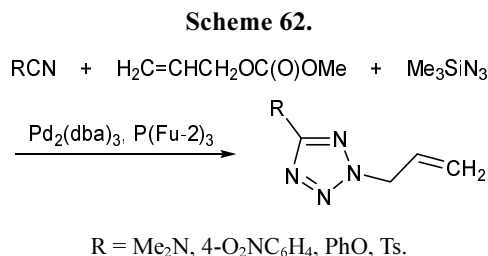
Among methods for the preparation of 2,5-disubstituted tetrazoles, first of all various modifications of arylation of 5-aryltetrazoles with diaryliodonium salts in water [119] or methanol [120] in the presence of copper should be noted (Scheme 60).



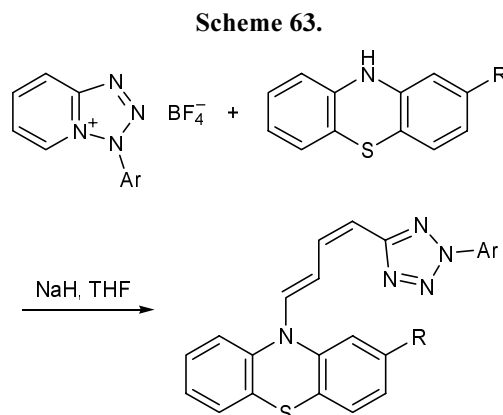
Related methods involve regioselective arylation of 5-aryltetrazoles with diaryliodonium salts in DMF in the presence of palladium and copper catalysts [121] and arylation of 5-aryl-2-tributylstannyltetrazoles in methylene chloride in the presence of copper(II) acetate [122] (Scheme 61). The efficiency of palladium catalysts in the synthesis of 2,5-disubstituted tetrazoles



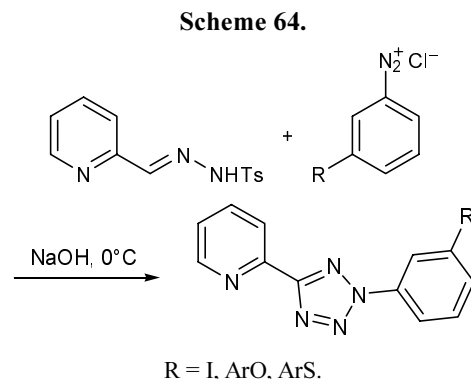
was demonstrated by Kamijo *et al.* [123, 124]. The authors showed that the corresponding 5-substituted 2-allyltetrazoles are formed in high yield from the three-component system nitrile–allyl methyl carbonate–trimethylsilyl azide on heating in the presence of Pd₂(dba)₃ (Scheme 62).



Messmer and co-workers [125, 126] described a novel synthesis of 2,5-disubstituted tetrazoles via reaction of tetrazolopyridinium salts with various nucleophiles (Scheme 63).

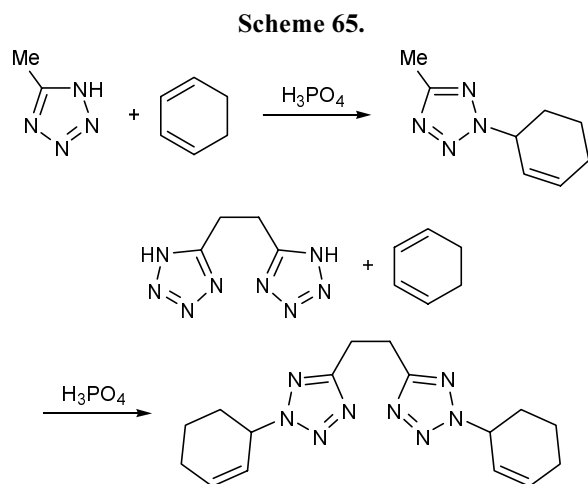


In some cases, well known reactions of *p*-tolylsulfonylhydrazones with arenediazonium salts give good results [127–129] (Scheme 64). Despite known difficulties involving separation of 1,5- and 2,5-disubstituted isomers [44, 48], alkylation of 5-substituted



tetrazoles is frequently used in the synthesis of 2,5-disubstituted tetrazoles containing functional groups [130–132]. This method offers a wide choice of functionally substituted reagents, primarily 5-substituted tetrazoles, simple experimental procedure, and mild reaction conditions. Therefore, it is not surprising that the problem of regioselectivity in the alkylation of tetrazoles has attracted much attention over several past decades. Unfortunately, advances in this field of tetrazole chemistry are not so great as it would be desirable.

An example of successful solution of the regioselectivity problem is the alkylation of 5-substituted tetrazoles with various unsaturated compounds in the presence of mineral acids [48]. Under these conditions, the corresponding 2-substituted derivatives are formed exclusively [131] (Scheme 65).



4. CONCLUSION

While preparing the present review, more than 300 original articles published since 2001 till mid 2005 on various aspects of the tetrazole chemistry (methods of preparation, physical and chemical properties, and applications) were analyzed. No patent information was taken into account. Among the reported data, only those most relevant to the subjects under consideration were selected.

On the basis of detailed analysis of the available experimental data, a conclusion can be drawn that no common approach to solution of the tetrazole functionalization problem exists so far. Two strategies may be proposed for this purpose: functionalization of substituents in substituted tetrazoles and incorporation of tetrazole ring into functionally substituted substrates.

Taking into account that new efficient versions of building up tetrazole systems appeared in the recent years, namely microwave activation, multicomponent syntheses, and the use of Me_3SiN_3 or $\text{SiCl}_4\text{-NaN}_3$ instead of hazardous hydrazoic acid, the second strategy seems to be preferred.

At the same time, one more quite promising synthetic route to functionally substituted tetrazoles should be given strong attention, i.e., highly regioselective alkylation of 5-substituted tetrazoles with olefins in the presence of mineral acids and the use of metal complexes as catalysts in the synthesis of 2,5-disubstituted tetrazoles.

One can state with certainty that development of the chemistry of tetrazole in the nearest future will largely involve search for new and improvement of known methods for functionalization of these compounds and their application in the synthesis of complex tetrazole-containing substrates.

I would like to conclude the present review by citing two famous specialists in organic synthesis, L. Tietze and T. Eicher, who accurately noted that just specific reactions of particular functional groups constitute the basis of organic synthesis [133].

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REFERENCES

- Dhaybaran, V.V., Ludia, I.S., Merlin, J.P., and Srenganayaki, P., *Ionics*, 2004, vol. 10, p. 123; *Chem. Abstr.*, 2004, vol. 141, no. 353 205.
- Moskvin, L.B., Bulatov, A.V., Grigorjev, G.L., and Koldobskij, G.I., *Flow Injection Anal.*, 2003, vol. 20, p. 53.
- Energetic Materials. Part 1. Decomposition, Crystal, and Molecular Properties*, Politzer, P. and Murray, J.S., Eds., Amsterdam: Elsevier, 2003.
- Klapotke, T.M., Mayer, P., Schulz, A., and Weigand, J.J., *J. Am. Chem. Soc.*, 2005, vol. 127, p. 2032.
- Xue, H., Gao, Y., Twamley, B., and Shreeve, J.M., *Chem. Mater.*, 2005, vol. 17, p. 191.
- Ogihara, W., Yashizawa, M., and Ohno, H., *Chem. Lett.*, 2004, vol. 33, p. 1022.
- Miyata, Y., Date, S., and Hasue, K., *Propellants, Explos., Pyrotech.*, 2004, vol. 29, p. 247.
- Hatzinger, P.B., Palmer, P., Smith, R.U., Penarrieta, C.T., and Yoshinari, T., *J. Microbiol. Meth.*, 2003, vol. 52, p. 47.
- Gruden, C.L., Fevig, S., Abu-Dalo, M., and Hernandez, M., *J. Microbiol. Meth.*, 2003, vol. 52, p. 59.

10. Bačkor, M. and Fashelt, D., *Environ. Exper. Botany*, 2005, vol. 53, p. 125.
11. Moussa, A., Baranyai, M., Wojnarovits, L., Kovacs, A., and McLaughlin, W.L., *Radiat. Phys. Chem.*, 2003, vol. 68, p. 1011.
12. Welz, R. and Muller, S., *Tetrahedron Lett.*, 2002, vol. 43, p. 795.
13. Nurminen, E.J., Mattinen, J.K., and Lonberg, H., *Helv. Chim. Acta*, 2003, vol. 86, p. 2005.
14. Elmquist, C.E., Stover, J.S., Wang, Z., and Rizzo, C.J., *J. Am. Chem. Soc.*, 2004, vol. 126, p. 11 189.
15. Stepinski, D.C., Nelson, D.W., Zalupski, P.R., and Herlinger, A.W., *Tetrahedron*, 2001, vol. 57, p. 8637.
16. Stepinski, D.C., Hess, J.N., and Herlinger, A.W., *Synth. Commun.*, 2003, vol. 33, p. 3483.
17. Jankowski, P., Pleśniak, K., and Wicha, J., *Org. Lett.*, 2003, vol. 5, p. 2789.
18. Cobb, A.J.A., Shaw, D.M., and Ley, S.V., *Synlett*, 2004, p. 558.
19. Cobb, A.J.A., Longbottom, D.A., Shaw, D.M., and Ley, S.V., *Chem. Commun.*, 2004, p. 1808.
20. Torii, H., Nakadai, M., Ishihara, K., Saito, S., and Yamamoto, H., *Angew. Chem., Int. Ed.*, 2004, vol. 43, p. 1983.
21. Yamamoto, Y., Momiyama, N., and Yamamoto, H., *J. Am. Chem. Soc.*, 2004, vol. 126, p. 5962.
22. Dabbagh, H.A., Noroozi-Pesyan, N., Patrick, B.O., and James, B.R., *Can. J. Chem.*, 2004, vol. 82, p. 1179.
23. Gupta, A.K., Song, C.H., and Oh, C.H., *Tetrahedron Lett.*, 2004, vol. 45, p. 4113.
24. Nikulin, V.V., Artamonova, T.V., and Koldobskii, G.I., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 1525.
25. Denisenko, S.M., Gladkov, E.S., Nenaidenko, V.G., Shishkin, O.V., and Shishkina, S.V., *Khim. Geterotsikl. Soedin.*, 2004, p. 71.
26. Nikulin, V.V., Artamonova, T.V., and Koldobskii, G.I., *Russ. J. Org. Chem.*, 2005, vol. 41, p. 444.
27. Wexler, R.R., Greenlee, W.J., Irvin, J.D., Goldberg, M.R., Prendergast, K., Smith, R.D., and Timmermans, P.B.M.W.M., *J. Med. Chem.*, 1996, vol. 39, p. 625.
28. Schmidt, B. and Schieffer, B., *J. Med. Chem.*, 2003, vol. 46, p. 2261.
29. Santagada, V., Fiorino, F., Perissutti, E., Severino, B., Terracciano, S., Teixeira, C.E., and Caliendo, G., *Tetrahedron Lett.*, 2003, vol. 44, p. 1149.
30. Tanaka, T., Okuda, T., and Yamamoto, Y., *Chem. Pharm. Bull.*, 2004, vol. 52, p. 830.
31. Bekhit, A.A., El-Sayed, O.A., Aboulmagd, E., and Park, J.Y., *Eur. J. Med. Chem.*, 2004, vol. 39, p. 249.
32. Rajasekaran, A. and Thampi, P.P., *Eur. J. Med. Chem.*, 2004, vol. 39, p. 273.
33. Kozikowski, A., Zhang, J., Nan, F., Petukhov, P.A., Grajkowska, E., Wroblewski, J.T., Yamamoto, T., Bzdega, T., Wroblewska, B., and Neale, J., *J. Med. Chem.*, 2004, vol. 47, p. 1729.
34. Upadhayaya, R.S., Jain, S., Sinha, N., Kishore, N., Chandra, R., and Arora, S.K., *Eur. J. Med. Chem.*, 2004, vol. 39, p. 579.
35. Faucher, A.-M., White, P.W., Brochu, C., Grand-Maitre, C., Rancourt, J., and Fazal, G., *J. Med. Chem.*, 2004, vol. 47, p. 18.
36. Balle, T., Haldin, C., Andersen, L., Alifrangis, L.H., Perregaard, J., and Farde, L., *Nucl. Med. Biol.*, 2004, vol. 31, p. 327.
37. Biot, C., Bauer, H., Schirmer, R.H., and Davioud-Charvet, E., *J. Med. Chem.*, 2004, vol. 47, p. 5972.
38. Park, H. and Merz, K.M., Jr., *J. Med. Chem.*, 2005, vol. 48, p. 1630.
39. Bekhit, A.A., El-Sayed, O.A., Al-Allaf, T.A.K., Aboul-Enein, H.Y., Kunhi, M., Pulicat, A.M., Al-Hussain, K., Al-Khodairy, F., and Arif, J., *Eur. J. Med. Chem.*, 2004, vol. 39, p. 499.
40. Koldobskii, G.I. and Ostrovskii, V.A., *Usp. Khim.*, 1994, vol. 63, p. 847.
41. Wittenberger, S.J., *Org. Prep. Proced. Int.*, 1994, vol. 26, p. 499.
42. Butler, R.N., *Comprehensive Heterocyclic Chemistry II*, Katritzky, A.R., Rees, C.W., and Scriven, E.F.V., Eds., Oxford: Pergamon, 1996, vol. 4, p. 621.
43. Zubarev, V.Yu. and Ostrovskii, V.A., *Khim. Geterotsikl. Soedin.*, 2000, p. 867.
44. Ostrovskii, V.A. and Koren, A.O., *Heterocycles*, 2000, vol. 53, p. 1421.
45. Voitekhovich, S.V., Gaponik, P.N., and Ivashkevich, O.A., *Usp. Khim.*, 2002, vol. 71, p. 819.
46. Herr, R.J., *Bioorg. Med. Chem.*, 2002, vol. 10, p. 3379.
47. Kizhnyayev, V.N. and Vereshchagin, L.I., *Usp. Khim.*, 2003, vol. 72, p. 159.
48. Koldobskii, G.I. and Kharbash, R.V., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 453.
49. Koldobskii, G.I., Hrabalek, A., and Esikov, K.A., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 447.
50. Soldatenkov, A.T., Temesgen, A.V., and Kolyadina, N.M., *Khim. Geterotsikl. Soedin.*, 2004, p. 643.
51. Young, M.B., Barrow, J.C., Glass, K.L., Lundell, G.F., Newton, C.L., Pellicore, J.M., Rittle, K.E., Selnick, H.G., Stauffer, K.J., Vacca, J.P., Williams, P.D., Bohn, D., Clayton, F.C., Cook, J.J., Krueger, J.A., Kuo, L.C., Lewis, S.D., Lucas, B.J., McMasters, D.R., Miller-Stein, C., Pietrak, B.L., Wallace, A.A., White, R.B., Wong, B., Yan, Y., and Nantermet, P.G., *J. Med. Chem.*, 2004, vol. 47, p. 2995.
52. Stassen, A.F., Grunert, M., Dova, E., Muller, M., Weinberger, P., Wiesinger, G., Schenk, H., Linert, W., Haas-

- noot, J.G., and Reedijk, J., *Eur. J. Inorg. Chem.*, 2003, p. 2273.
53. Jin, T., Kamijo, S., and Yamamoto, Y., *Tetrahedron Lett.*, 2004, vol. 45, p. 9435.
54. Grunert, C.M., Weinberger, P., Schweifer, J., Hampel, C., Stassen, A.F., Mereiter, K., and Linert, W., *J. Mol. Struct.*, 2005, vol. 733, p. 41.
55. Gupta, A.K., Rim, C.Y., and Oh, C.H., *Synlett*, 2004, p. 2227.
56. Bronisz, R., *Eur. J. Inorg. Chem.*, 2004, p. 3688.
57. Bronisz, R., *Inorg. Chem. Acta*, 2004, vol. 357, p. 396.
58. Gaponik, P.N., *Doctoral (Chem.) Dissertation*, St. Petersburg, 2000.
59. Myznikov, L.V., Artamonova, T.V., Bel'skii, V.K., Stash, A.I., Skvortsov, N.K., and Koldobskii, G.I., *Russ. J. Org. Chem.*, 2002, vol. 38, p. 1360.
60. Furmeier, S. and Metzger, J.O., *Eur. J. Org. Chem.*, 2003, p. 885.
61. Zubarev, V.Yu., Bezklubnaya, E.V., Pyartman, A.K., Trifonov, R.E., and Ostrovskii, V.A., *Khim. Geterotsikl. Soedin.*, 2003, p. 1496.
62. Chien, Y.-Y., Wong, K.-T., Chou, P.-T., and Cheng, Y.-M., *Chem. Commun.*, 2002, p. 2874.
63. Upadhayaya, R.S., Sinha, N., Jain, S., Kishore, N., Chandra, R., and Arora, S.K., *Bioorg. Med. Chem.*, 2004, vol. 12, p. 2225.
64. Facchetti, A., Abbotto, A., Beverina, L., Bradamante, S., Mariani, P., Stern, C.L., Marks, T.J., Vacca, A., and Pagani, G.A., *Chem. Commun.*, 2004, p. 1770.
65. Yu, W., Zhou, Z., Zhao, X., and Yu, C., *J. Chem. Crystallogr.*, 2004, vol. 34, p. 597.
66. Pinkerton, A., Vernier, J.-M., Schaffhauser, H., Rowe, B.A., Campbell, U.C., Rodriguez, D.E., Lorrain, D.S., Baccei, C.S., Daggett, L.P., and Bristow, L.J., *J. Med. Chem.*, 2004, vol. 47, p. 4595.
67. Pinkerton, A.B., Cube, R.V., Hutchinson, J.H., Rowe, B.A., Schaffhauser, H., Zhao, X., Daggett, L.P., and Vernier, J.-M., *Bioorg. Med. Chem. Lett.*, 2004, vol. 14, p. 5329.
68. Balle, T., Perregaard, J., Ramirez, M.T., Larsen, A.K., Soby, K.K., Liljefors, T., and Andersen, K., *J. Med. Chem.*, 2003, vol. 46, p. 265.
69. Kivrakidou, O., Brase, S., Hulshorst, F., and Griebnow, N., *Org. Lett.*, 2004, vol. 6, p. 1143.
70. Huang, M.-R., Li, X.-G., Li, S.-X., and Zhang, W., *React. Funct. Polym.*, 2004, vol. 59, p. 53.
71. Finnegan, W.G., Henry, R.A., and Lofquist, R., *J. Am. Chem. Soc.*, 1958, vol. 80, p. 3908.
72. Demko, Z.P. and Sharpless, K.B., *J. Org. Chem.*, 2001, vol. 66, p. 7945.
73. Himo, F., Demko, Z.P., Noodleman, L., and Sharpless, K.B., *J. Am. Chem. Soc.*, 2002, vol. 124, p. 12210.
74. Himo, F., Demko, Z.P., Noodleman, L., and Sharpless, K.B., *J. Am. Chem. Soc.*, 2003, vol. 125, p. 9983.
75. Qu, Z.-R., Zhao, H., Wang, X.-S., Li, Y.-H., Song, Y.-M., Liu, Y.-J., Ye, Q., Xiong, R.-G., Abrahams, B.F., Xue, Z.-L., and You, X.-Z., *Inorg. Chem.*, 2003, vol. 42, p. 7710.
76. Wang, L.-S., Qu, Z.-R., Zhao, H., Wang, X.-S., Xiong, R.-G., and Xue, Z.-L., *Inorg. Chem.*, 2003, vol. 42, p. 3969.
77. Hartikka, A. and Arvidsson, P.I., *Tetrahedron: Asymmetry*, 2004, vol. 15, p. 1831.
78. Yu, Z., Wang, X., Feng, Y., and Zhong, X., *Inorg. Chem. Commun.*, 2004, vol. 7, p. 492.
79. Tsarevsky, N.V., Bernaerts, K.V., Dufour, B., Du Prez, F.E., and Matyjaszewski, K., *Macromolecules*, 2004, vol. 37, p. 9308.
80. Amantini, D., Beleggia, R., Fringyelli, F., Pizzo, F., and Vaccaro, L., *J. Org. Chem.*, 2004, vol. 69, p. 2896.
81. Xu, Y. and Guo, Q.-X., *Heterocycles*, 2004, vol. 63, p. 903.
82. Alterman, M. and Hallberg, A., *J. Org. Chem.*, 2000, vol. 65, p. 7984.
83. Schulz, M.J., Coats, S.J., and Hlasta, D.J., *Org. Lett.*, 2004, vol. 6, p. 3265.
84. Bliznets, I.V., Vasil'ev, A.A., Shorshnev, S.V., Stepanov, A.E., and Lukyanov, S.M., *Tetrahedron Lett.*, 2004, vol. 45, p. 2571.
85. Shie, J.-J. and Fang, J.-M., *J. Org. Chem.*, 2003, vol. 68, p. 1158.
86. Mo, X.-J., Gao, E.-Q., He, Z., Li, W.-J., and Yan, C.-H., *Inorg. Chem. Commun.*, 2004, vol. 7, p. 353.
87. Aly, A.A. and Shaker, R.M., *Tetrahedron Lett.*, 2005, vol. 46, p. 2679.
88. Voitenko, Z.V., Yegorova, T.V., Kysil', A.I., Andre, C., and Wolf, J.G., *Tetrahedron*, 2004, vol. 60, p. 195.
89. Cheng, S. and Comer, D.D., *Tetrahedron Lett.*, 2002, vol. 43, p. 1179.
90. Bolshan, Y., Chen, C., Chilenski, J.R., Gosselin, F., Mathre, D.J., O'Shea, P.D., Roy, A., and Tillyer, R.D., *Org. Lett.*, 2004, vol. 6, p. 111.
91. Artamonova, T.V., Zatssepina, M.V., and Koldobskii, G.I., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 1318.
92. Brand, S., de Candole, B.C., and Brown, J.A., *Org. Lett.*, 2003, vol. 5, p. 2343.
93. Hrabalek, A., Myznikov, L., Kunes, J., Vavrova, K., and Koldobskii, G., *Tetrahedron Lett.*, 2004, vol. 45, p. 7955.
94. Koreneva, A.P. and Koldobskii, G.I., *Russ. J. Org. Chem.*, 1999, vol. 35, p. 1511.
95. Zhang, Z., Yin, Z., Kadow, J.F., Meanwell, N.A., and Wang, T., *J. Org. Chem.*, 2004, vol. 69, p. 1360.
96. Hammerl, A., Klapotke, T.M., Mayer, P., and Weigand, J.J., *Propellants, Explos., Pyrotech.*, 2005, vol. 30, p. 17.

97. Katritzky, A.R., Maimait, R., Xu, Y.-J., and Gyoung, Y.S., *J. Org. Chem.*, 2002, vol. 67, p. 8230.
98. Yang, M.G., Modi, D.P., Wexler, R.R., and Olson, R.E., *Tetrahedron Lett.*, 2004, vol. 45, p. 111.
99. Morozova, S.E., Komissarov, A.V., Esikov, K.A., Zubarev, V.Yu., Malin, A.A., and Ostrovskii, V.A., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 1532.
100. Athanassopoulos, C.M., Garnelis, T., Vahliotis, D., and Papaioannou, D., *Org. Lett.*, 2005, vol. 7, p. 561.
101. Yu, Y., Ostresh, J.M., and Houghten, R.A., *Tetrahedron Lett.*, 2004, vol. 45, p. 7787.
102. Lodyga-Chruścińska, E., Oldziej, S., Micera, G., Sanna, D., Chruściński, L., Olczak, J., and Zaborocki, J., *J. Inorg. Biochem.*, 2004, vol. 98, p. 447.
103. Gallardo, H., Meyer, E., Bortoluzzi, A., Molin, F., and Mangrich, A., *Inorg. Chim. Acta*, 2004, vol. 357, p. 505.
104. Caddell, J.M., Chapman, A.M., Cooley, B.E., Downey, B.P., Le Blanc, M.P., Jeckson, M.M., O'Connell, T.M., Phung, H.-M., Roper, T.D., and Xie, S., *J. Org. Chem.*, 2004, vol. 69, p. 3212.
105. Ek, F., Wistrand, L.-G., and Frejd, T., *Tetrahedron*, 2003, vol. 59, p. 6759.
106. Ek, F., Manner, S., Wistrand, L.-G., and Frejd, T., *J. Org. Chem.*, 2004, vol. 69, p. 1346.
107. Demko, Z.P. and Sharpless, K.B., *Angew. Chem., Int. Ed.*, 2002, vol. 41, p. 2110.
108. Couty, F., Durrat, F., and Prim, D., *Tetrahedron Lett.*, 2004, vol. 45, p. 3725.
109. Bliznets, I.V., Shorshnev, S.V., Aleksandrov, G.G., Stepanov, A.E., and Lukyanov, S.M., *Tetrahedron Lett.*, 2004, vol. 45, p. 9127.
110. Lee, C.H., Song, Y.S., Cho, H.I., Yang, J.W., and Lee, K.-J., *J. Heterocycl. Chem.*, 2003, vol. 40, p. 1103.
111. Cristau, H.-J., Marat, X., Vors, J.-P., and Pirat, J.-L., *Tetrahedron Lett.*, 2003, vol. 44, p. 3179.
112. Salama, T.A., El-Ahl, A.-A.S., Khalil, A.-G.M., Girges, M.M., Lachner, B., Steindl, C., and El-morsy, S.S., *Monatsh. Chem.*, 2003, vol. 134, p. 1241.
113. Cappelli, A., Mohr, G. la P., Gallelli, A., Rizzo, M., Anzini, M., Vomero, S., Mennuni, L., Ferrari, F., Makovec, F., Menziani, C., De Benedetti, P.G., and Giorgi, G., *J. Med. Chem.*, 2004, vol. 47, p. 2574.
114. Allan, R.D., Greenwood, J.R., Hambley, T.W., Hanrahan, J.R., Hibbs, D.E., Itani, S., Tran, H.W., and Turner, P., *Org. Biomol. Chem.*, 2004, vol. 2, p. 1782.
115. Hwang, J.Y., Choi, H.-S., and Gong, Y.-D., *Tetrahedron Lett.*, 2005, vol. 46, p. 3107.
116. Mojzych, M., Karczmarzyk, Z., and Rykowski, A., *J. Chem. Crystallogr.*, 2005, vol. 35, p. 151.
117. Umkehrer, M., Kolb, J., Burdac, K.C., Ross, G., and Hiller, W., *Tetrahedron Lett.*, 2004, vol. 45, p. 6421.
118. Matysiak, J., Niewiadomy, A., Krajewska-Kula, E., and Macik-Niewiadomy, G., *Farmaco*, 2003, vol. 58, p. 455.
119. Reinov, M.V., Yurovskaya, M.A., Davydov, D.V., and Streletskii, A.V., *Khim. Geterotsikl. Soedin.*, 2004, p. 223.
120. Zubarev, V.Yu., Putis, S.M., and Ostrovskii, V.A., *Khim. Geterotsikl. Soedin.*, 2001, p. 400.
121. Davydov, D.V., Beletskaya, I.P., and Gorovoy, M.S., *Tetrahedron Lett.*, 2002, vol. 43, p. 6221.
122. Davydov, D.V., Beletskaya, I.P., Semenov, B.B., and Smushkevich, Y.I., *Tetrahedron Lett.*, 2002, vol. 43, p. 6217.
123. Kamijo, S., Jin, T., and Yamamoto, Y., *J. Org. Chem.*, 2002, vol. 67, p. 7413.
124. Kamijo, S., Jin, T., Huo, Z., Gyoung, Y.S., Shim, J.-G., and Yamamoto, Y., *Mol. Diversity*, 2003, vol. 6, p. 181.
125. Nagy, I., Konya, D., Riedl, Z., Kotschy, A., Timari, G., Messmer, A., and Hajos, G., *Tetrahedron*, 2003, vol. 59, p. 7485.
126. Nagy, I., Riedl, Z., Hajos, G., Messmer, A., Gye-mant, N., and Molnar, J., *Arkivoc*, 2004, part VII, p. 177.
127. Huang, D., Poon, S.F., Chapman, D.F., Chung, J., Gramer, M., Reger, T.S., Roppe, J.R., Tehrani, L., Cosford, N.D.P., and Smith, N.D., *Bioorg. Med. Chem. Lett.*, 2004, vol. 14, p. 5473.
128. Poon, S.F., Eastman, B.W., Chapman, D.F., Chung, J., Cramer, M., Holtz, G., Cosford, N.D.P., and Smith, N.D., *Bioorg. Med. Chem. Lett.*, 2004, vol. 14, p. 5477.
129. Roppe, J., Smith, N.D., Huang, D., Tehrani, L., Wang, B., Anderson, J., Brodtkin, J., Chung, J., Jiang, X., King, C., Munoz, B., Varney, M.A., Prasit, P., and Cosford, N.D.P., *J. Med. Chem.*, 2004, vol. 47, p. 4645.
130. Verkhozina, O.N., Kizhnyayev, V.N., Vereshchagin, L.I., Rokhin, A.V., and Smirnov, A.I., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 1792.
131. Gaponik, P.N., Voitekhovich, S.V., and Klyaus, B.G., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 598.
132. Lenda, F., Guenoun, F., Tazi, B., Iarbi, N.B., Al-louchi, H., Martinez, J., and Lamaty, F., *Eur. J. Org. Chem.*, 2005, p. 326.
133. Tietze, L.-F. and Eicher, T., *Reactions and Syntheses in the Organic Chemistry Laboratory*, Mill Valley, California: University Science Books, 1989.