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Chalcogen exchange in chalcogen–nitrogen π-heterocycles

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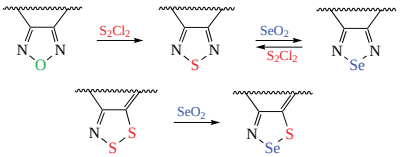
The procedures for synthesizing fused 1,2,5-chalcogenadiazoles and 1,2,3-dithiazoles by direct exchange of one chalcogen atom for another, their scope and reaction pathways are discussed in this focus review.

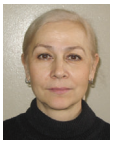


Keywords: 1,2,5-chalcogenadiazoles, 1,2,3-dithiazoles, 1,2,3-thiaselenazoles, exchange of chalcogen atoms, disulfur dichloride, selenium dioxide.

Introduction

The problem of direct transformation of one element into another has been occupying an important place in the minds of people since the emergence of alchemy. In the 20th century, a priority problem for chemists working in the field of heterocyclic chemistry is the replacement of one heteroatom by another one in heteroaromatic cycles, which allows one to obtain analogues of these heterocycles in a single stage, thus modifying the compound structure as desired. It is known that the chemical, physical and biological properties of heterocycles can change fundamentally as just one heteroatom in a molecule changes. The first discovery in this direction was the classical Yuryev reaction,[1] which allows for mutual conversions of simple five-membered oxygen-, sulfur-, nitrogen- and selenium-containing heterocyclic compounds. However, the mechanisms of this reaction seem to be quite different in each particular case, and unfortunately, the scope of its application is limited to heterocycles with a single heteroatom, while high yields were only achieved using furan as the starting material. In addition, the Yuryev reaction occurs under very drastic conditions,[2,3] which did not allow this method to be extended to compounds with labile groups. The reason for such drastic conditions of this reaction apparently lie in the high bond strength between a heteroatom and carbon. It could be assumed that if the heteroatom were located between two heteroatoms, the bond would break much more readily and the reaction would occur under milder conditions. In the course of our research, we found that two classes of heterocycles, 1,2,5-chalcogenadiazoles and 1,2,3-dithiazoles, could undergo this reaction under relatively mild conditions if a chalcogen atom was located at position 2. It should be noted that in most cases (we do not know how the first reaction of this type for Hertz salts was discovered) these reactions were discovered by chance in attempts to obtain completely different compounds.

Due to the rapid progress in the development and studies on the characteristics of functional materials for electronics and spintronics based on individual molecules, there is a constant demand for new compounds that could be used as building blocks for the design of such materials. In this regard, much attention is currently paid to chalcogen–nitrogen heterocycles, the most interesting among them including fused 1,2,5-thiadiazoles, 1,2,3-dithiazoles, and their selenium analogues, *i.e.*, 1,2,5-selenadiazoles and 1,2,3-thiaselenazoles. It was found that these heterocycles were effective electron acceptors and could be used to create many real or potential functional materials for organic electronics and spintronics based on their molecules.[4–7] In the course of our work, we tried to develop new, fast and inexpensive methods for the synthesis of these heterocycles in order to make them readily available for studying the characteristics and for creating new materials based on them. It was found that one of the possible real approaches to these compounds is provided by the direct exchange of one chalcogen atom (oxygen, sulfur or selenium) for another one (sulfur or selenium). This focus review deals with the conversion of the most studied classes of heterocycles, namely, fused 1,2,5-chalcogenadiazoles and 1,2,3-dithiazoles, into other chalcogen-containing heterocycles.



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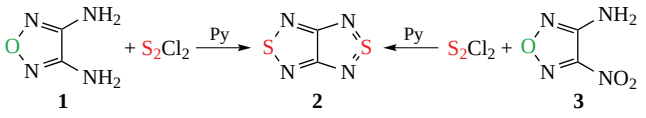
Synthesis of 1,2,5-thiadiazoles from 1,2,5-oxadiazoles

This new transformation was discovered by chance when we were studying the reaction of 3,4-diamino-1,2,5-oxadiazole **1** with disulfur dichloride in an attempt to obtain [1,2,5]oxadiazolo[3,4-*c*][1,2,5]thiadiazole. Contrary to our expectations, this reaction resulted in another bicycle, [1,2,5]thiadiazolo[3,4-*c*][1,2,5]thiadiazole **2**, in a high yield (75%, Scheme 1).[8] The main feature of this reaction was that the oxygen atom in the 1,2,5-oxadiazole ring was exchanged for a sulfur atom under the action of disulfur dichloride. This reaction was the first example of this kind of unusual transformations.

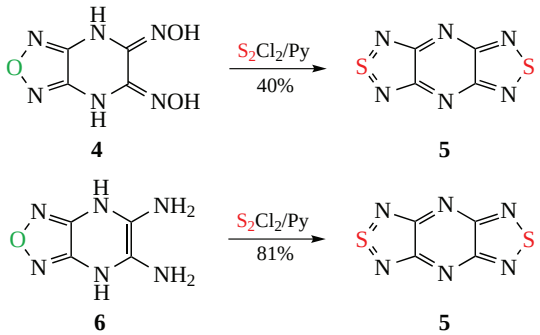


1 **2** **3**

Scheme 1 Synthesis of [1,2,5]thiadiazolo[3,4-*c*][1,2,5]thiadiazole **2** from 4-amino-1,2,5-oxadiazoles **1** and **3**.

Later, it was shown that another oxadiazole derivative, 4-amino-3-nitro-1,2,5-oxadiazole **3**, can also enter a similar reaction with disulfur dichloride, and the reaction product was the same bicyclic thiadiazolothiadiazole **2** in a moderate yield (49%, see Scheme 1).[9] The formation of two thiadiazole rings occurred in this case from two previously unused moieties, *i.e.*, the oxadiazole and the vicinal amino nitro moiety. The second process was no less surprising, since no reactions of this kind were described to date.

Under similar conditions, (5*Z*,6*Z*)-[1,2,5]oxadiazolo[3,4-*b*]pyrazine-5,6(4*H*,7*H*)-dione dioxime **4** and 4,7-dihydro-[1,2,5]oxadiazolo[3,4-*b*]pyrazine-5,6-diamine **6** formed tricyclic bis([1,2,5]thiadiazolo)[3,4-*b*;3′,4′-*e*]pyrazine **5** in 40 and 81% yields, respectively (Scheme 2). In each case, three reactions took place: the formation of a thiadiazole ring from a dioxime or diamine, exchange of an oxygen atom in the 1,2,5-oxadiazole ring for a sulfur atom, and aromatization of the piperazine ring. All the three processes occurred under the action of a single reagent, disulfur dichloride.

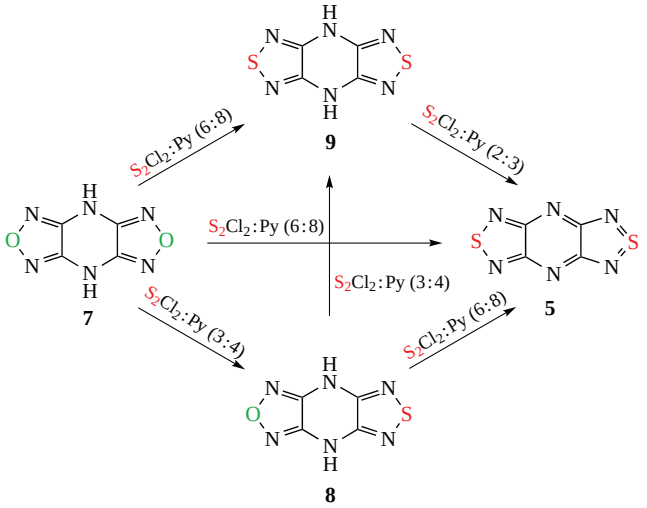


4 **5** **6** **5**

Scheme 2 Synthesis of bis([1,2,5]thiadiazolo)[3,4-*b*;3′,4′-*e*]pyrazine **5**.

In order to find new examples of the conversion of the 1,2,5-oxadiazole ring to the 1,2,5-thiadiazole one, the reaction of 4*H*,8*H*-bis[1,2,5]oxadiazolo[3,4-*b*:3′,4′-*e*]pyrazine **7** containing two oxadiazole rings and two NH groups with disulfur dichloride was studied in detail (Scheme 3).[10]

In fact, refluxing compound **7** with excess S_2Cl_2 (6 equiv.) and pyridine (8 equiv.) in MeCN resulted in a heteroaromatic tricycle, *viz.*, bis(1,2,5-thiadiazolo)pyrazine **5**, in a 76% yield (see Scheme 3). The formation of thiadiazoles **8** and **9** from bis(1,2,5-oxadiazole) **7** at room temperature indicated that the sequential formation of two thiadiazole rings preceded the final aromatization of the piperazine cycle to pyrazine in boiling MeCN. This was also confirmed by treatment of oxadiazolothiadiazole **8** with the same mixture at room temperature

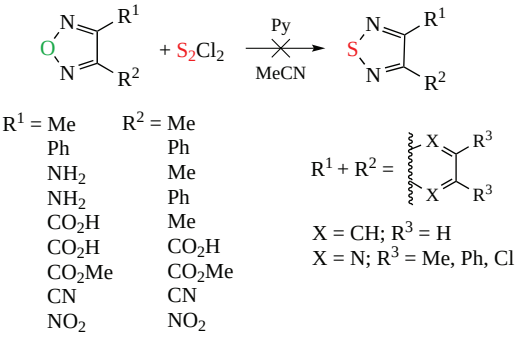


9 **7** **5** **8**

Scheme 3 Reaction of 4*H*,8*H*-bis[1,2,5]oxadiazolo[3,4-*b*:3′,4′-*e*]pyrazine **7** with S_2Cl_2.

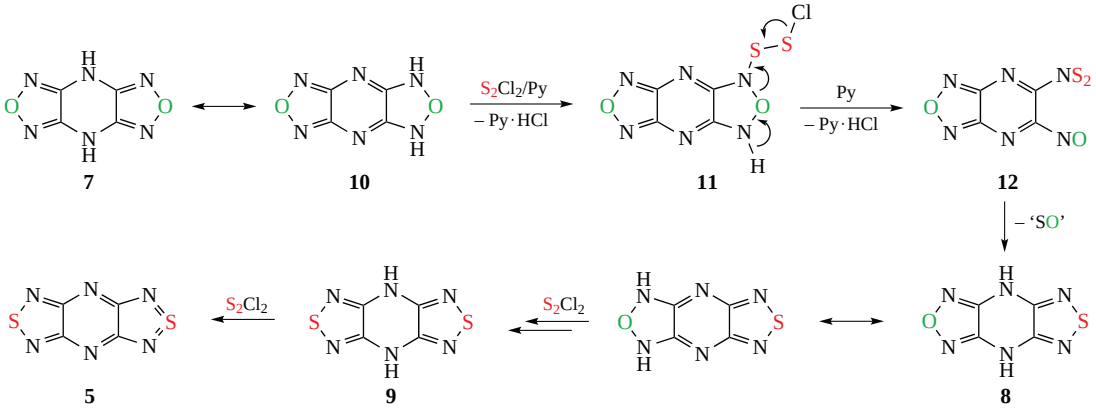
that resulted in bis(1,2,5-thiadiazole) **9** in a good yield, followed by conversion of **9** to aromatic tricycle **5** at high temperature.[10]

We tried to extend the reaction with disulfur dichloride and pyridine in acetonitrile to other monocyclic, fused benzo- and pyrido-1,2,5-oxadiazoles and found that the non-fused 1,2,5-oxadiazoles, 2,1,3-benzooxadiazole and 5,6-disubstituted [1,2,5]oxadiazolo[3,4-*b*]pyrazines (Scheme 4) did not react with S_2Cl_2 in nearly all the cases under the conditions studied. The use of 1,4-diazabicyclo[2.2.2]octane or triethylamine as bases and replacement of the solvent with chloroform or dimethylformamide at temperatures from –25 to 100 °C did not contribute to the formation of 1,2,5-thiadiazole derivatives in these cases, either. Analysis of these results let us to conclude that the successful conversion of 1,2,5-oxadiazoles to 1,2,5-thiadiazoles required the presence of one or two NH_2 or NH groups attached to the oxadiazole cycle.



Scheme 4 1,2,5-Oxadiazoles which did not react with S_2Cl_2.

The reactions described above opened a completely new synthetic pathway to the synthesis of 1,2,5-thiadiazoles from the corresponding 1,2,5-oxadiazoles. The key steps of this process can be explained by sulfurization of the tautomeric form **10** of tricycle **7** with disulfur dichloride in the presence of a base to give chlorodithiole derivative **11**, followed by removal of a hydrogen chloride molecule with a pyridine base and formation of *N*-thiosulfinylamine **12** (Scheme 5). Further cyclization of compound **12** into 1,2,5-thiadiazole **8** occurs *via* cycloaddition/retrocycloaddition with extrusion of a sulfur monoxide (SO) molecule, which is thermodynamically unstable and decomposes very quickly;[11] the possibility of formation of a 1,2,5-thiadiazole ring from *N*-thiosulfinylamine and nitro groups was established recently.[12] Repetition of this reaction results in bis(1,2,5-



Scheme 5 Suggested consequent transformations for the formation of bis([1,2,5]thiadiazolo)[3,4-*b*;3′,4′-*e*]pyrazine **5** from 4*H*,8*H*-bis[1,2,5]oxadiazolo[3,4-*b*:3′,4′-*e*]pyrazine **7**.

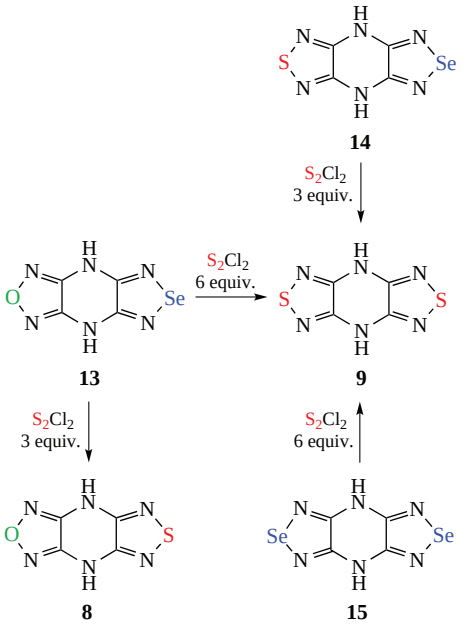
thiadiazole) **9**, which can be further oxidized to form aromatic tricycle **5**. Bis([1,2,5]thiadiazolo)[3,4-*b*;3′,4′-*e*]pyrazine **5** is of interest as a promising precursor of stable radical anions.[13]

The use of disulfur dichloride (S_2Cl_2) as a sulfurizing agent in this reaction is not accidental. The main feature of disulfur dichloride is its diverse reactivity.[14–17] Although S_2Cl_2 is a strong chlorinating agent, it is rarely used in this capacity, as there are many other chlorinating agents that provide higher yields of reaction products. The oxidative capacity of S_2Cl_2 has been studied to a much lesser extent, since the products of formal oxidation reactions are generally formed in complex multi-stage processes, including chlorination, dehydrochlorination, sulfurization, *etc*. The most valuable and frequently used property of this reagent is its pronounced sulfurizing ability. The direct replacement of a chalcogen atom by a sulfur atom in chalcogen–nitrogen heterocycles in the reaction with disulfur dichloride was not known before our work.

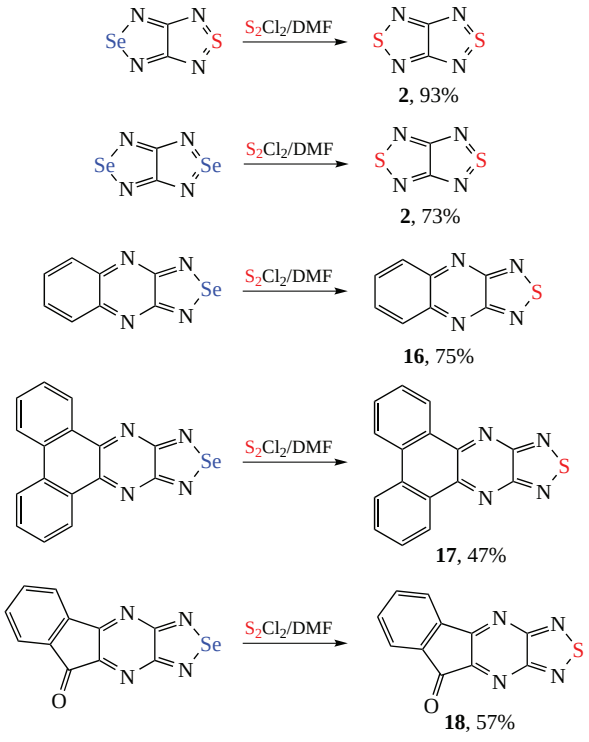
Synthesis of 1,2,5-thiadiazoles from 1,2,5-selenadiazoles

The reaction of 4,8-dihydro[1,2,5]oxadiazolo[3,4-*b*][1,2,5]-selenadiazolo[3,4-*e*]pyrazine **13** with S_2Cl_2 was investigated to further study the ability of disulfur dichloride to replace the oxygen atom in 1,2,5-oxadiazoles with a sulfur atom (Scheme 6). This reaction did not occur in MeCN, possibly due to the low solubility of tricycle **13**. Replacing MeCN with DMF unexpectedly resulted in 4,8-dihydro[1,2,5]oxadiazolo[3,4-*b*]-[1,2,5]thiadiazolo[3,4-*e*]pyrazine **8** in a high yield (91%). This means that the reaction resulted in selective exchange of the selenium atom in the 1,2,5-selenadiazole ring of compound **13** for a sulfur atom. The use of excess disulfur dichloride in this reaction led to replacement of not only the selenium atom but also the oxygen atom in the 1,2,5-oxadiazole ring of compound **13** for sulfur to give bis(1,2,5-thiadiazole) **9** in 78% yield. It was shown that mono- and bis(1,2,5-selenadiazoles) **14** and **15** could be involved into a similar reaction to produce bis(1,2,5-thiadiazole) **9** in 83–85% yields (see Scheme 6).[10]

In an attempt to develop a general method for synthesizing 1,2,5-thiadiazoles from the corresponding selenadiazoles, the latter were studied in the reaction with S_2Cl_2. Treatment of 1,2,5-selenadiazoles fused with electron-withdrawing heterocycles such as 1,2,5-thiadiazole, 1,2,5-selenadiazole, quinoxaline, and others with disulfur dichloride in DMF afforded the corresponding mono- and bis(1,2,5-thiadiazoles) **2**, **16**–**18** in good yields (Scheme 7). It should be noted that in all cases the formation of a characteristic red amorphous precipitate of elemental selenium occurred, which was isolated in almost quantitative yields.



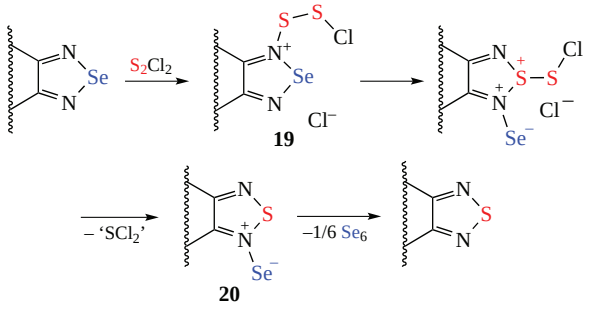
Scheme 6 Reactions of [1,2,5]selenadiazolo[3,4-*b*]pyrazines **13**–**15** with S_2Cl_2 in DMF.



Scheme 7 Reactions of fused 1,2,5-selenadiazoles with S_2Cl_2.

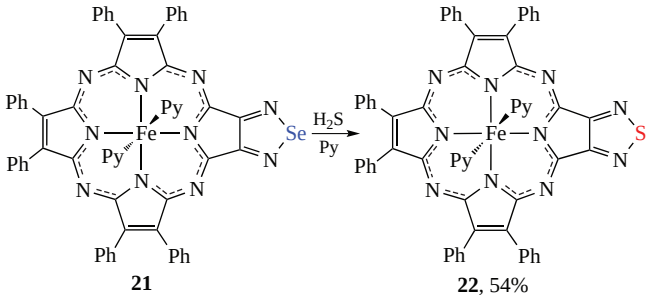
Attempts to extend this reaction to monocyclic and benzo-fused 1,2,5-selenadiazoles failed: 2,1,3-benzoselenadiazole and 3,4-diphenyl-1,2,5-selenadiazole did not react with disulfur dichloride in organic solvents even under drastic conditions (reflux in MeCN or heating in DMF at 100 °C for 10 h) and were recovered almost quantitatively from the reaction mixtures.

Based on an analysis of the results of the reaction of 1,2,5-oxadiazoles and 1,2,5-selenadiazoles with disulfur dichloride, it can be concluded that in both cases the successful exchange of oxygen or selenium atoms for sulfur requires the presence of a nitrogen-containing heterocycle fused with the initial chalcogenadiazole. The most plausible mechanism for the conversion of 1,2,5-selenadiazoles to 1,2,5-thiadiazoles is shown in Scheme 8. The key steps may include the sulfurization of the selenadiazole ring with disulfur dichloride to give the chlorodithio derivative **19**, followed by recyclization of the selenadiazole ring and release of sulfur dichloride to furnish 1,2,5-selenadiazole *N*-selenide **20**. The subsequent extrusion of elementary selenium gives the final 1,2,5-thiadiazole.



Scheme 8 Proposed consequent transformations of hetareno-fused 1,2,5-selenadiazoles to 1,2,5-thiadiazoles.

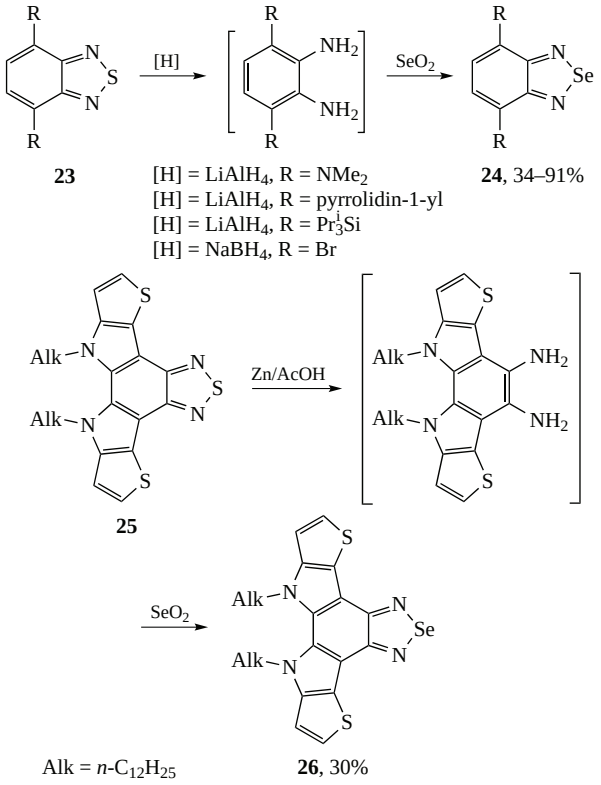
Hydrogen sulfide is another reagent that can directly convert fused 1,2,5-selenadiazoles to the corresponding thiadiazoles. Stuzhin *et al.* showed that hexaphenyl(1,2,5-selenadiazolo)-porphyrazine **21** was converted to the corresponding thiadiazole **22** upon treatment with hydrogen sulfide in pyridine (Scheme 9).[18] It should be noted that this is so far the only example of the use of hydrogen sulfide in this reaction.



Scheme 9 Formation of hexaphenyl(1,2,5-thiadiazolo)porphyrazine **22** from selenium analogue **21**.

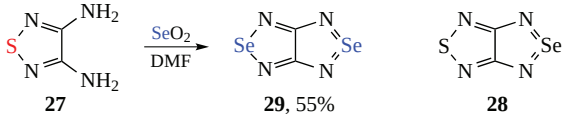
Synthesis of 1,2,5-selenadiazoles from 1,2,5-thiadiazoles

The most common method for the preparation of 1,2,5-selenadiazoles involves the reaction of vicinal diamines with selenium-containing reagents, often with selenium dioxide (SeO_2) that is commercially available and easy to use.[4,19–21] This method is well developed for 2,1,3-benzoselenadiazoles, however there are still no methods for the synthesis of 1,2,5-selenadiazoles fused with other heterocycles, especially electron-withdrawing nitrogen-containing ones. Sulfur-containing analogues of 1,2,5-selenadiazoles, 1,2,5-thiadiazoles, are much more readily available, and the methods for their preparation are numerous and have been developed very well.[19,20,22–26] Benzo-fused 1,2,5-thiadiazoles, *i.e.* 2,1,3-benzothiadiazoles **23**, can serve as starting materials for the preparation of the corresponding 2,1,3-benzoselenadiazoles **24** in a two-stage synthesis involving their reduction into *o*-phenylenediamines (often unstable and air-sensitive) with lithium aluminum hydride,[27,28] sodium borohydride,[29,30] or zinc in acetic acid,[31] followed by treatment with SeO_2 or, more rarely, with selenium tetrachloride ($SeCl_4$),[32,33] or oxochloride ($SeOCl_2$).[34,35] Some examples of such reactions are shown in Scheme 10.



Scheme 10 Synthesis of fused 1,2,5-selenadiazoles from the corresponding 1,2,5-thiadiazoles *via* intermediate 1,2-diamines.

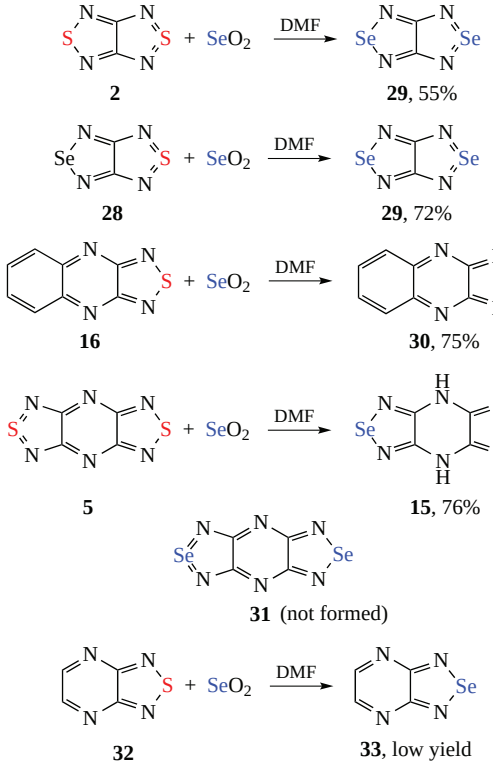
A study on the reaction of 3,4-diamino-1,2,5-thiadiazole **27** with selenium dioxide in an attempt to improve the method for synthesizing the known [1,2,5]selenadiazolo[3,4-*c*][1,2,5]-thiadiazole **28**[36] showed that heating compound **27** at 100 °C in DMF gave [1,2,5]selenadiazolo[3,4-*c*][1,2,5]selenadiazole **29** in a moderate yield (Scheme 11).[37] The main feature of this reaction is that two processes occurred simultaneously: the formation of the 1,2,5-selenadiazole ring by condensation of vicinal diamine with SeO_2 and the replacement of the sulfur atom in the 1,2,5-thiadiazole ring with a selenium atom.



Scheme 11 Synthesis of [1,2,5]selenadiazolo[3,4-*c*][1,2,5]selenadiazole **29** from 3,4-diamino-1,2,5-thiadiazole **27**.

In an attempt to develop a general method for the synthesis of 1,2,5-selenadiazoles from the corresponding thiadiazoles by direct replacement of the sulfur atom in the ring with a selenium atom, the reactions of a wide range of 1,2,5-thiadiazoles with SeO_2 were studied. Treatment of 1,2,5-thiadiazoles fused with electron-withdrawing heterocycles (such as 1,2,5-thiadiazole, 1,2,5-selenadiazole, quinoxaline and thiadiazolopyrazine) with

selenium dioxide under reflux in organic solvents (such as chloroform, benzene, THF, ethanol, or 1,4-dioxane) failed to produce 1,2,5-selenadiazoles; the starting compounds were recovered in almost quantitative yields. Only heating of 1,2,5-thiadiazoles with SeO_2 in DMF at 80–110 °C gave the corresponding mono- **30** and bis-1,2,5-selenadiazoles **15**, **29** in good yields (Scheme 12).

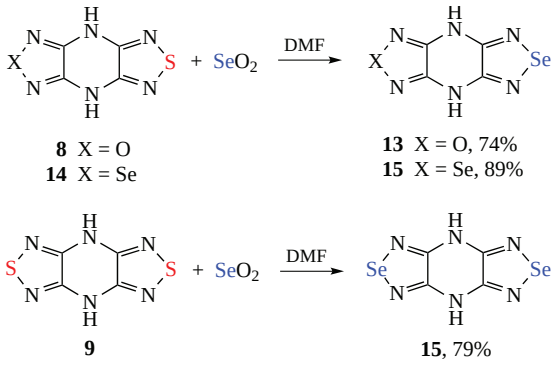


Scheme 12 Synthesis of fused 1,2,5-selenadiazoles from the corresponding thiadiazoles.

The same product, bis(selenadiazole) **29**, was formed from bicycles **2** and **28** upon replacement of two or one sulfur atoms, respectively, with selenium atoms (see Scheme 12). It should be noted that it is not possible to convert selectively only one 1,2,5-thiadiazole ring to 1,2,5-selenadiazole in compound **2** to obtain product **28**; according to the mass spectrometric data, even with an equimolar amount of selenium dioxide in the reaction mixture, the presence of mono- and disubstitution products as well as unreacted starting compound **2** is observed. This fact may indicate that replacement of sulfur atoms by selenium atoms in both rings of compound **2** occurs almost simultaneously and, apparently, at a rate comparable to the rate of a similar replacement of one sulfur atom in bicycle **28**.

The formation of dihydro product, 4*H*,8*H*-bis[1,2,5]-selenadiazolo[3,4-*b*:3′,4′-*e*]pyrazine **15**, instead of the expected fully aromatic bis-selenadiazolopyrazine **31**, was explained by the reduction of **31** with water released upon decomposition of SeO_2 in DMF (see Scheme 12). Importantly, when [1,2,5]-thiadiazolo[3,4-*b*]pyrazine **32** was heated with SeO_2 at 100 °C in DMF, [1,2,5]selenadiazolo[3,4-*b*]pyrazine **33** was formed in a low yield along with a number of side products, obviously due to its instability at the reaction temperature in DMF. Later, compound **33** was obtained in a good yield by condensation of 3,4-diamino-1,2,5-selenadiazole with glyoxal at room temperature.[38]

4*H*,8*H*-[1,2,5]Oxadiazolo[3,4-*b*][1,2,5]thiadiazolo[3,4-*e*]-pyrazine **8** and its selenium analogue **14** react with SeO_2 similarly to give selenadiazoles **13** and **15**, respectively, in high yields (Scheme 13). The formation of compound **13** in this case indicates that the 1,2,5-oxadiazole ring remains unchanged under the reaction conditions whereas the thiadiazole ring is converted to the selenadiazole ring. When 4*H*,8*H*-bis[1,2,5]-thiadiazolo[3,4-*b*:3′,4′-*e*] pyrazine **9** was treated with selenium dioxide, both sulfur atoms were exchanged for selenium atoms, like in the case of other bis-thiadiazoles **2** and **5**. These data indicate that this reaction of bisdithiazoles in DMF cannot be interrupted at the stage of substitution of just one sulfur atom.



Scheme 13 Synthesis of selenadiazolopyrazines from the corresponding thiadiazoles.

Attempts to expand this reaction to other benzene-fused and monocyclic 1,2,5-thiadiazoles failed. Substituted 2,1,3-benzothiadiazoles and non-fused 1,2,5-thiadiazoles (Figure 1) did not react with SeO_2 in various organic solvents even under drastic conditions (reflux in chloroform, benzene, THF, ethanol, 1,4-dioxane, or heating in DMF or DMSO at 100 °C for 10 h).

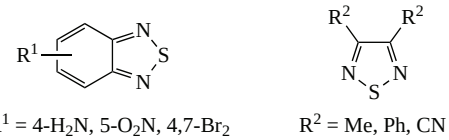
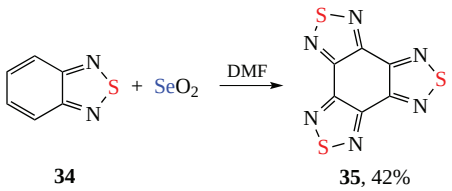


Figure 1 1,2,5-Thiadiazoles that do not react with selenium dioxide.

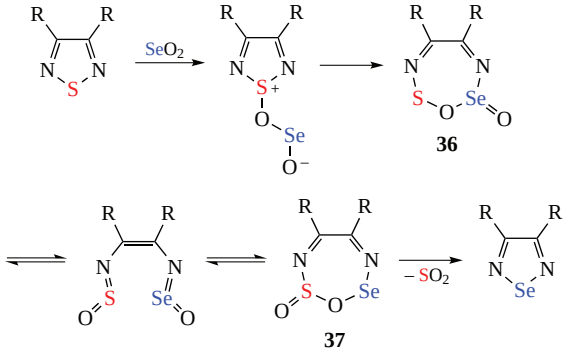
In this context, reaction of the parent of 2,1,3-benzothiadiazole **34** with SeO_2 in DMF looks unexpected. Heating the reaction mixture at 105 °C for 3 h gave benzo[1,2-*c*:3,4-*c*′:5,6-*c*″]-tris[1,2,5]thiadiazole **35** in 42% yield (per three molecules of benzothiadiazole **34**, Scheme 14).[37] The closest formal analogy for the formation of **35** is its isolation as a minor product in the synthesis of 5,6,8-trifluoro-3,1,2,4-benzothiaselenadiazine from of the corresponding Ar^F–Se–N=S=N–$SiMe_3$ derivative upon closure of the heterocyclic ring under the action of CsF.[39] In our experiments, the formation of thiadiazole rings fused with the benzene ring probably occurs with participation of a sulfur–nitrogen reagent formed upon oxidation of the starting benzothiadiazole **34** with selenium dioxide.

Analysis of the positive and negative results obtained in the studies on the conversion of 1,2,5-thiadiazoles to 1,2,5-selenadiazoles in the presence of SeO_2 allowed us to conclude that a success of this reaction requires the direct fusion of 1,2,5-thiadiazole ring in the starting compound to an electron-



Scheme 14 Synthesis of benzo[1,2-*c*:3,4-*c*′:5,6-*c*″]tris[1,2,5]thiadiazole **35** from 2,1,3-benzothiadiazole **34**.

deficient nitrogen-containing heterocycle capable of stabilizing the intermediates formed. Calculation of the stoichiometry of this reaction suggests the formation of a sulfur dioxide (SO_2) molecule in the course of conversion. This assumption is consistent with the inertness of the 1,2,5-oxadiazole ring in similar reactions. A schematic mechanism of the process in question was suggested (Scheme 15). At the first stage, the addition of the SeO_2 molecule to 1,2,5-thiadiazole at the sulfur atom probably occurs. Subsequent cleavage followed by ring closure results in heterocyclic intermediate **36**, which can be converted to intermediate **37** through a series of tautomeric equilibria. The irreversible elimination of volatile SO_2 from intermediate **37** apparently shifts the reaction equilibrium towards 1,2,5-selenadiazole.



Scheme 15 Scheme of the conversion of 1,2,5-thiadiazoles to the corresponding 1,2,5-selenadiazoles in the presence of SeO_2.

The reactions described above open prospects for the development of new efficient ways to synthesize fused 1,2,5-selenadiazoles from 1,2,5-thiadiazoles using selenium dioxide, a cheap and easy-to-use reagent.

Conversion of 1,2,3-dithiazoles to 1,2,3-thiaselenazoles

1,2,3-Thiaselenazoles, close analogues of well-known and fairly widespread 1,2,3-dithiazoles, have been studied much less due to difficulties in their synthesis. To date, only two neutral 1,2,3-thiaselenazole derivatives **38** and **39** were reported,[40,41] as well as a few neutral radicals **40**, **41** (Figure 2).[42–48] It is important to note that 1,2,3-thiaselenazolyls exhibit enhanced conductivity and/or magnetism compared to 1,2,3-dithiazolyl derivatives.[45,49–55] The above results stimulated further studies on 1,2,3-dichalcogenazoles, in particular, towards the synthesis of new derivatives of 1,2,3-thiaselenazoles. Such compounds are typically prepared from *o*-aminothiophenol derivatives by reactions with SeO_2, $SeCl_4$, $SeOCl_2$ or $SeCl_2$.[41,48,56]

The replacement of a sulfur atom for a selenium atom in the 1,2,3-dithiazole ring is a very rare transformation; only a few examples of such reactions were reported. Such a reaction

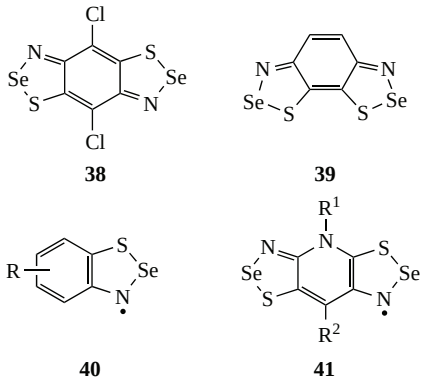
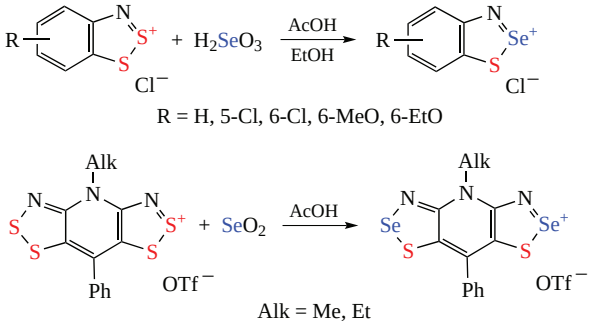


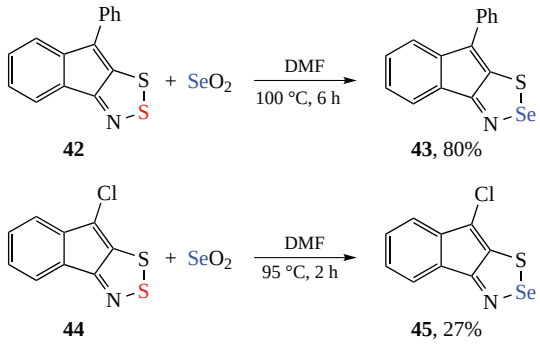
Figure 2 Known compounds of the 1,2,3-thiaselenazole series.

involving selenous acid (H_2SeO_3) in acetic acid was first discovered by Akulinin *et al.* in 1976,[57] and then Oakley used SeO_2 for this purpose[44,46,47] (Scheme 16). It is important to note that in all these examples the reaction was described for dithiazolium salts in which the positive charge on the sulfur atom S(2) facilitated the attack of the selenium dioxide molecule.



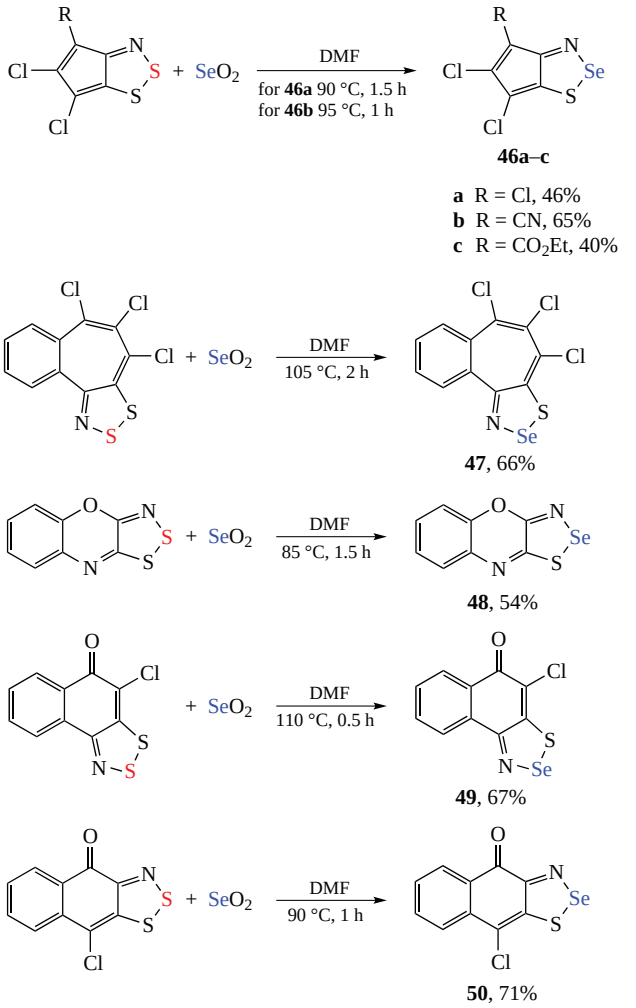
Scheme 16 Replacement of a sulfur atom for a selenium atom in 1,2,3-dithiazolium salts.

The possibility of replacing a sulfur atom with a selenium atom in neutral 1,2,3-dithiazoles using selenium dioxide as a reagent was studied using the example of 8-phenylindeno-[1,2-*d*][1,2,3]dithiazole **42**. Refluxing compound **42** in various organic solvents (chloroform, benzene, THF, methanol, ethanol, 1,4-dioxane, acetonitrile, or DMSO) with excess SeO_2 did not give any reaction products, and the starting compound was almost fully recovered. However, on prolonged heating of dithiazole **42** with excess SeO_2 (10 equiv.) in DMF at 100 °C, the corresponding thiaselenazole **43** was obtained in a high yield (Scheme 17).[58] The application of a significant excess of SeO_2 was dictated by its liability to undergo decomposition in DMF at temperatures required for the reaction to occur successfully. Quite similar results were obtained using *N*,*N*,*N*′,*N*′-tetramethylurea (TMU) as a solvent: the yield of thiaselenazole **43** was 76% in this case. Under similar conditions, 8-chloroindeno[1,2-*d*][1,2,3]dithiazole **44** formed thiaselenazole **45** on heating in DMF, but in a much lower yield (see Scheme 17). The reason for the low yield of product **45** apparently lies in the participation of the Cl atom in the conversion process, which results in the occurrence of side reactions leading to the formation of unidentified products.



Scheme 17 Synthesis of thiaselenazoles **43** and **45** from the corresponding dithiazoles **42** and **44**.

This approach was extended to other fused 1,2,3-dithiazoles.[58] Treatment of 1,2,3-dithiazoles fused with carbo- (cyclopentene, hydronaphthalene) or hetero- (benzoxazine) rings with SeO_2 on heating in DMF gave the corresponding thiaselenazoles **46**–**50** (Scheme 18). The yields of the target products significantly depended on the reaction temperature, and even a 5 °C deviation from the optimal value could play a decisive role. Scheme 18



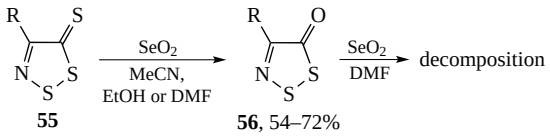
Scheme 18 Synthesis of thiaselenazoles **47**–**50** from the corresponding dithiazoles.

shows the optimal reaction conditions and the yields of the products obtained. Trichloro-substituted thiaselenazole **46a** was obtained from the corresponding polychlorinated dithiazole in the low yield of 46%; however, the yields of products **46b**, **47**, **49**, and **50** from other chlorinated starting materials were much higher and amounted to 65–71%.

A quantum-chemical simulation of the reaction pathway showed that two reaction mechanisms were possible. Pathway **A** (Scheme 19) should begin with the addition of a SeO_2 molecule with ring opening at the S–N bond of dithiazole and formation of a seven-membered intermediate **51**. The next step is the transfer of an oxygen atom from a selenium atom to a sulfur one *via* a spirocyclic intermediate to produce a second intermediate compound **52**. At the last stage of formation of the 1,2,3-thiaselenazole ring, a sulfur dioxide SO_2 molecule is eliminated and a new S–Se bond is simultaneously formed.

Reaction pathway **B** (see Scheme 19) also begins with the addition of SeO_2 to the dithiazole ring, but through the S–S bond to form a seven-membered intermediate **53**. In this case, the transition state lies much lower than the transition state for pathway **A**. The further conversion to the final product **46a** occurs in the same way as in the pathway **A** described above. Based on these calculations, pathway **B** seems to be a more likely reaction mechanism. According to quantum-chemical calculations, the substitution of a sulfur atom in the 1,2,3-dithiazole ring for a selenium atom is a thermodynamically advantageous reaction due to the gain from conversion of the less stable SeO_2 into more stable SO_2.[59]

Attempts were made to extend the reaction with selenium dioxide to monocyclic 1,2,3-dithiazole-3-thiones and 1,2,3-dithiazol-3-ones. However, it was found that upon refluxing in acetonitrile and alcohol, as well as upon heating in DMF to 100 °C, thiones **55** were converted to the corresponding ketones **56** without affecting the dithiazole ring (Scheme 20),[60] that is, in all these cases, SeO_2 acted only as an oxidizing agent. Ketones **56** remained inert on heating with SeO_2 in glacial acetic acid and chlorobenzene, while heating to 135 °C in DMF resulted in their decomposition.



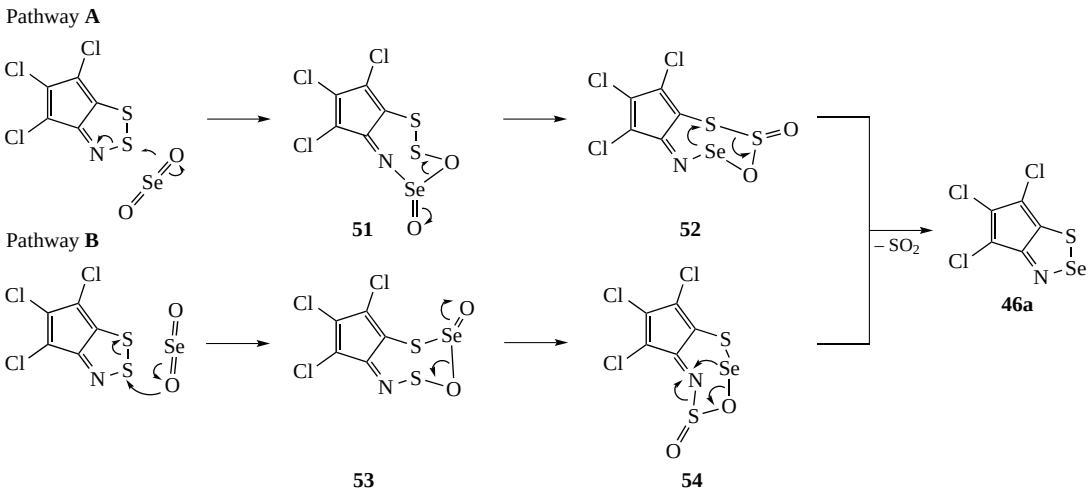
R = Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, 2-thienyl, 4-$O_2NC_6H_4$, Cl

Scheme 20 Reactions of monocyclic 5-thioxo- and 5-oxo-1,2,3-dithiazoles with SeO_2.

Thus, the monocyclic sulfur atoms in 1,2,3-dithiazoles studied were not replaced by selenium atoms in the presence of SeO_2 even under drastic conditions.

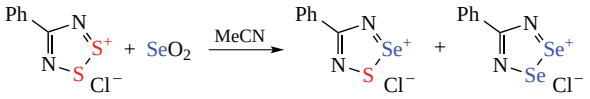
Reactions of direct replacement of a chalcogen atom in other heterocycles

The only example of replacement of a sulfur atom by a selenium atom in 1,2,3,5-dithiadiazolium cations was reported by Rawson *et al.*[61] The reaction of 4-phenyl-1,2,3,5-dithiadiazolium chloride



Scheme 19 Possible pathways for the formation of 1,2,3-thiaselenazole **46a** from the corresponding dithiazole.

with 1 equiv. selenium dioxide results in a mixture of dichalcogenadiazolium salts that were isolated as a mixture with the starting salt (Scheme 21). The structure of these salts was not confirmed in any way, except by mass spectra. Obviously, in this case, the rate of the reaction of the S,S-salt with SeO_2 is comparable to the rate of the similar reaction of the S,Se-salt, and it is difficult or simply impossible to obtain a pure thiaselenadiazole by this method.



Scheme 21 Synthesis of 1,2,3,5-dichalcogenoazolium salts.

On the other hand, diselenadiazoles can be easily obtained from tris(trimethylsilyl) derivatives of amidines and selenium tetrachloride.[62–64] Therefore, this method has no synthetic value and was not developed further.

Conclusions

In conclusion, it should be noted that the new transformations described above are direct and convenient routes for the synthesis of fused 1,2,5-thiadiazoles, 1,2,5-selenadiazoles, and 1,2,3-thiaselenazoles using commercially available and cheap reagents, namely disulfur dichloride and selenium dioxide. Of course, other possible transformations of this type can be envisioned, for example, replacement of sulfur and selenium atoms in chalcogen-containing heterocycles with tellurium, or conversion of chalcogen-containing heterocycles to 1,2,5-oxadiazoles, and the likewise processes. However, we believe that the development of this approach is hindered by the search for appropriate convenient and efficient reagents that appear to have a decisive role in expanding the scope of these reactions. Nevertheless, we believe that this synthetic approach to various chalcogen–nitrogen-containing heterocycles based on the direct replacement of one chalcogen atom in the ring with another one is promising and will undoubtedly be developed further.

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