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TRANSFORMATIONS OF 1,2,3-SELENADIAZOLES. (REVIEW)

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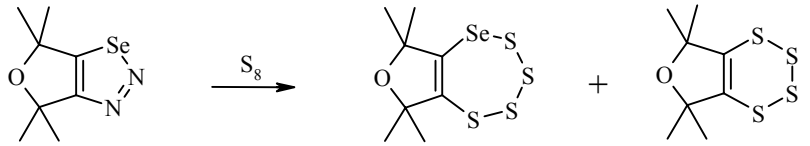
Published data of the last 15 years and the results of the authors' own investigations on the chemical properties of selenadiazoles are reviewed.

Keywords: selenium, selenadiazole.

1,2,3-Selenadiazole and its derivatives play a significant role in the solution of many theoretical and practical problems of organic chemistry [1], and this explains the interest of researchers in these compounds. Compounds containing the selenadiazole ring exhibit aromatic character and also have the very important ability to eliminate a molecule of nitrogen and selenium with ring opening to form both products of the acyclic series and new heterocycles [2, 3]. Consequently, they are promising subjects for studying the mechanisms of certain reactions and the synthesis of numerous compounds of practical interest [4].

1. SYNTHESIS OF POLYSULFUR AND POLYSELENIUM COMPOUNDS

The synthesis of cyclic polysulfides and selenides has attracted the attention of researchers on account of not only the unique physicochemical properties but also of the biological activity of these compounds [5-8]. The fusion of 4,4,6,6-tetramethyl-4,6-dihydrofuro[3,4-*d*]-1,2,3-selenadiazole (**1**) with elemental sulfur at 120°C for 10 min leads to the formation of 1,2,3,4-tetrathia-5-selenepin **2** (22%) and 1,2,3,4-tetrathiin **3** (39%) [9].



1 **2** **3**

When 1,2,3-selenadiazole **4** is heated with an excess of elemental sulfur at 140°C for 4 days a mixture of 1,2,3-trithiole **5** (25%) and 1,2,3,4,5-pentathiepin **6** (11%) is formed. The polysulfide is not formed directly from selenadiazole but in the reaction of the 1,2,3-trithiole **5** with sulfur. The equilibrium begins at a **5**:**6** ratio of 3:1 [10]. The selenadiazole **4** is absolutely inert toward elemental sulfur in the usual solvents, such as DMF. In a mixture of DMF and tributylamine (1:1), however, the reaction with selenium leads to a mixture of products: 4,4,9,9-tetramethyl-4,9-dihydro-1,2,3-triselenacyclopenta[*b*]naphthalene (**7**) (17%) and the diselenide **8** (15%). Moreover, the reaction in pure tributylamine gives **7** exclusively with a yield of 25%.

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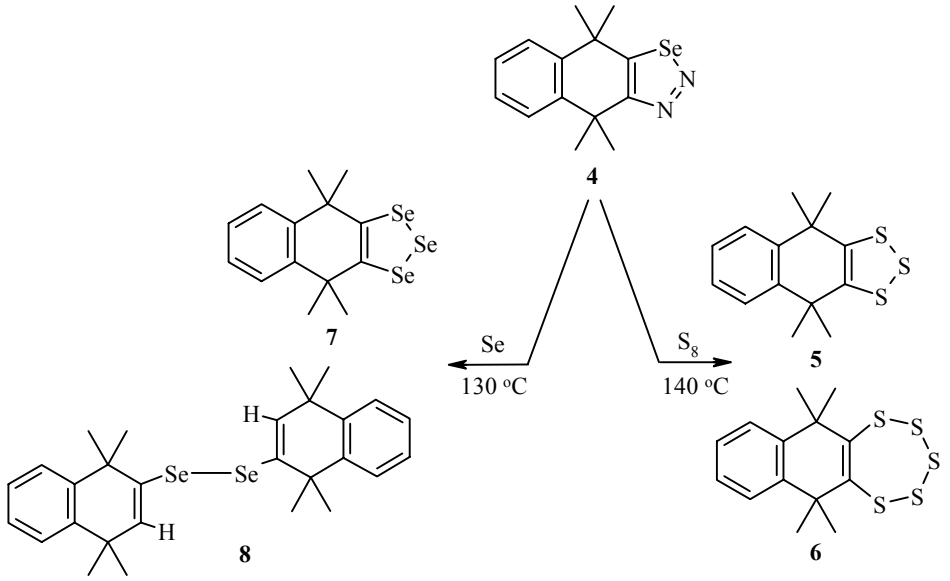
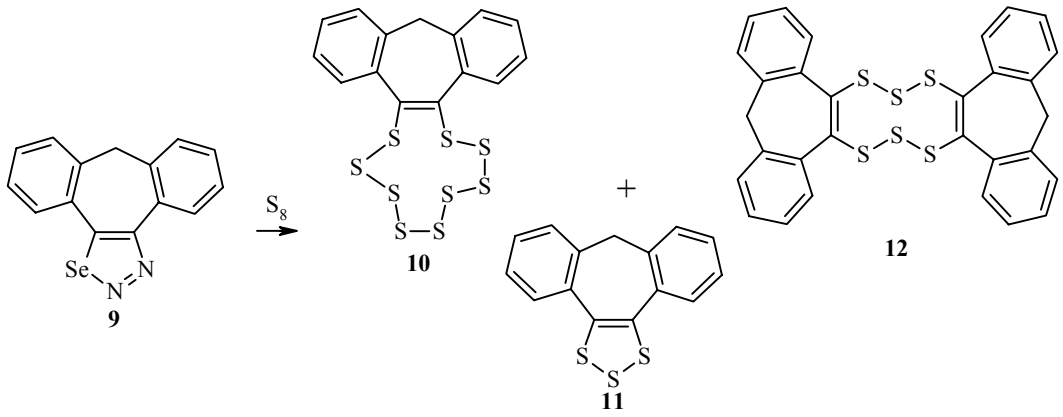


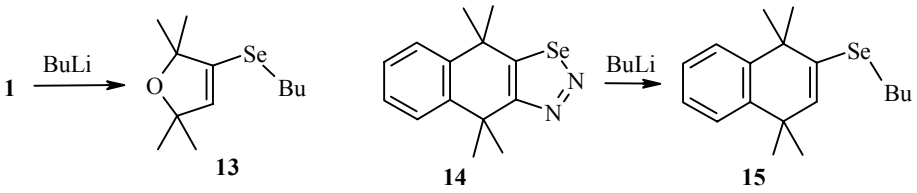
Somewhat different products are formed during the fusion of sulfur with 8,8-dibenzo[3,4:6,7]cyclohepta[1,2-*d*]-1,2,3-selenadiazole (**9**). The reaction was conducted in an atmosphere of nitrogen at 120-125°C for 10 h. The products were identified by NMR and X-ray crystallographic analysis. Together with the 1,2,3-trithiole **11** (37%) and hexathiecin **12** (7%) the new type of polysulfide **1**) was obtained with a yield of 12%.



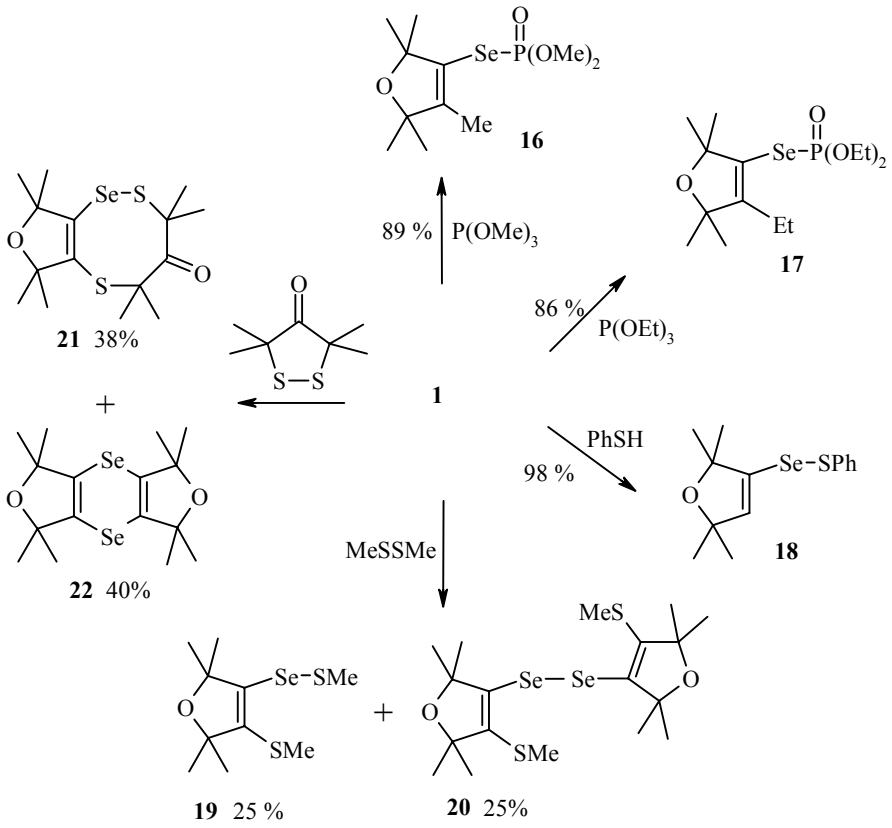
Compounds **11** and **12** are thermally stable, but the nonathiacycloundecene **10** decomposes into a mixture of various polysulfides when heated at 130°C. The mechanism of the thermolysis of the selenadiazole **9** can be represented as attack on the selenium atom by the activated sulfur radical followed by elimination of a molecule of nitrogen and cyclization [11].

2. REACTIONS WITH NUCLEOPHILIC AND ELECTROPHILIC REAGENTS

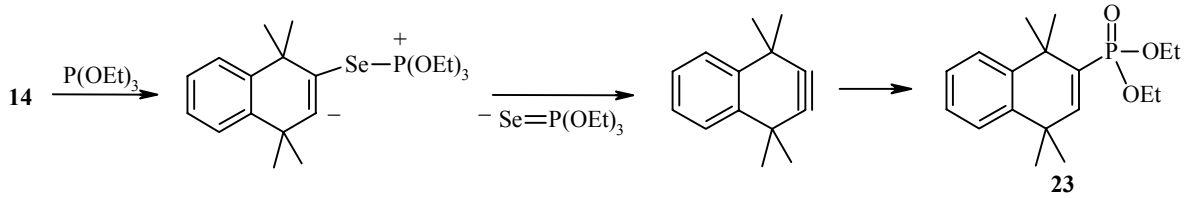
The product of the reaction of dihydrofuro[3,4-*d*]-1,2,3-selenadiazole **1** with butyllithium in THF at -70°C was butyl vinyl selenide **13** and was obtained with a yield of 53%. 2-Butylselanyl-1,1,4,4-tetramethyl-1,4-dihydronaphthalene (**15**) was obtained similarly with a yield of 47% from 4,4,9,9-tetramethyl-2,3-diaza-1-selena-2-cyclopenta[*b*]naphthalene (**14**) [12].



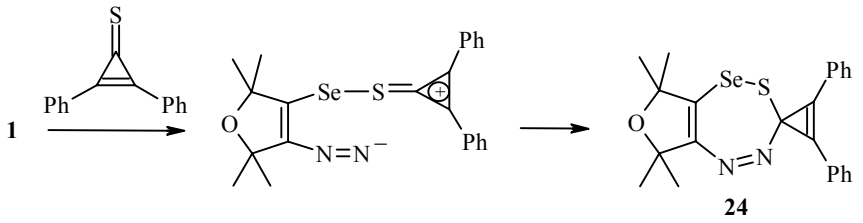
With milder nucleophilic agents, trialkyl phosphites, thiols, and disulfides, the reactions lead to opening of the selenadiazole ring and the formation of the selenium-containing products **16-18**. In the reaction of the selenadiazole **1** with dimethyl disulfide compounds **19** and **20** and also a small amount of the product from dimerization of the intermediate **22** are formed. The diselenide **22** is probably formed as a result of cleavage of the weak S–Se bond followed by recombination under the reaction conditions [12].



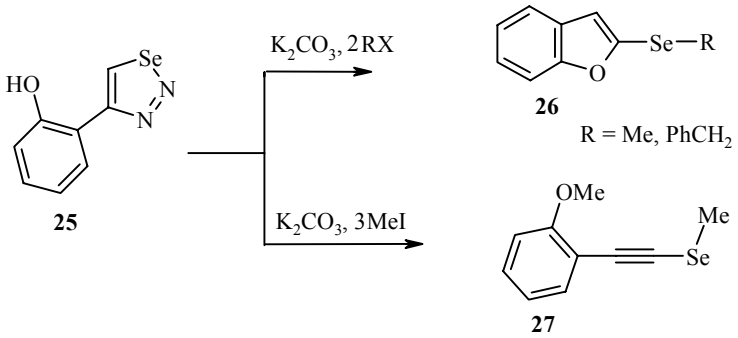
At the same time the reaction of compound **14** with triethyl phosphite takes place in a different way. The data from the NMR spectra indicate the absence of selenium in the reaction product. The quantitative formation of the organophosphorus derivative **23** results from the increased stability of the cyclohexyne intermediate compared with cyclopentyne.



The treatment of the selenadiazole **1** with an equimolar amount of diphenylcyclopropenethione also leads to the formation of an interesting cyclization product with a yield of 90%. The process begins with cleavage of the Se–N bond but without subsequent elimination of a molecule of nitrogen. The intermediate is then transformed into the new seven-membered heterocycle **24** [12].



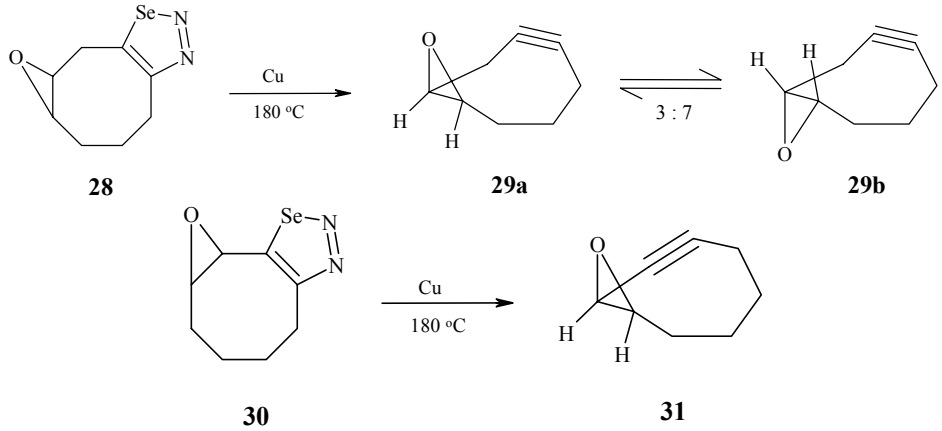
An attempt to treat 2-(1,2,3-selenadiazol-4-yl)phenol (**25**) with two equivalents of methyl iodide or benzyl chloride in the presence of potassium carbonate in boiling acetone led to cleavage of the selenadiazole ring and the formation of the benzofuran derivative **26**.



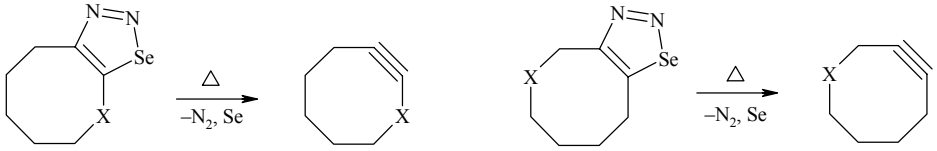
When three equivalents of methyl iodide were used, methyl *o*-methoxyphenylethynyl selenide (**27**) was obtained with a yield of 59% together with traces of the benzofuran **26** [13, 14].

3. PYROLYSIS

Pyrolysis of the tricyclic selenadiazole **28** at copper powder at 180°C leads to the formation of a mixture of isomers of the cyclic acetylene **29a** and **29b** with an overall yield of 25% [15, 16]. The conformational equilibrium for **29a** and **29b** corresponds to 3:7. The ethynyloxirane **31** was obtained with a yield of 17% from the selenadiazole **30**. Only one conformer was formed [17].



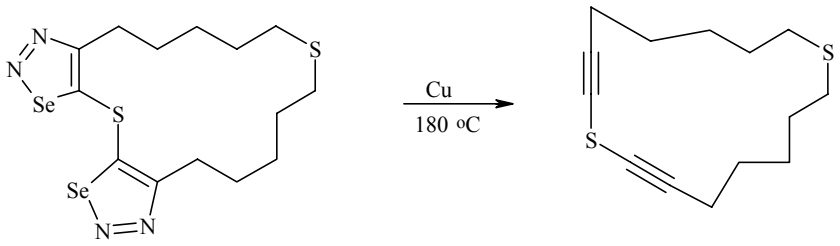
In the case of the thermolysis of 6,7,8,9-tetrahydro-5H-oxocino[3,2-*d*]-1,2,3-selenadiazole (**32**) it was not possible to isolate the cyclic acetylene **34** [18]. Replacement of the oxygen atom in **32** by sulfur (compound **33**) increased the stability of the obtained thiaacetylene **35** (35%) [19]. Thermolysis of the regioisomers of **36** (X = O) and **37** (X = S) led to the elimination of a molecule of nitrogen and elemental selenium with the formation of the cyclic acetylenes **38** (59%) and **39** (67%).



32, **33** **34**, **35** **36**, **37** **38**, **39**

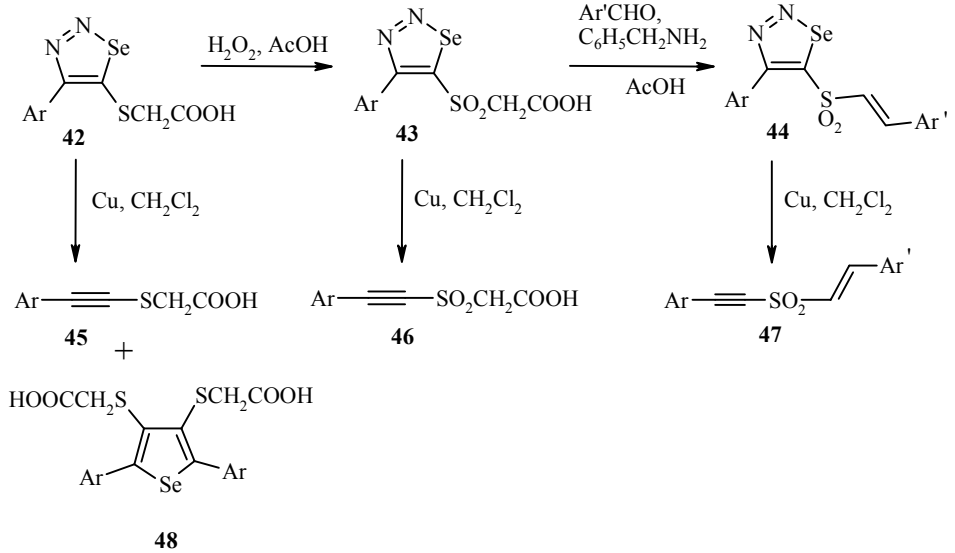
32, 34, 36, 38 X = O; **33, 35, 37, 39** X = S

Pyrolysis of the initial selenadiazole **40** in the presence of copper powder at 180°C and reduced pressure for 20 min was used for the production of the macrocyclic diethynyl sulfide **41**. 1,9-Dithiacyclohexadeca-2,15-diyne (**41**) was formed with a yield of 55% [20].



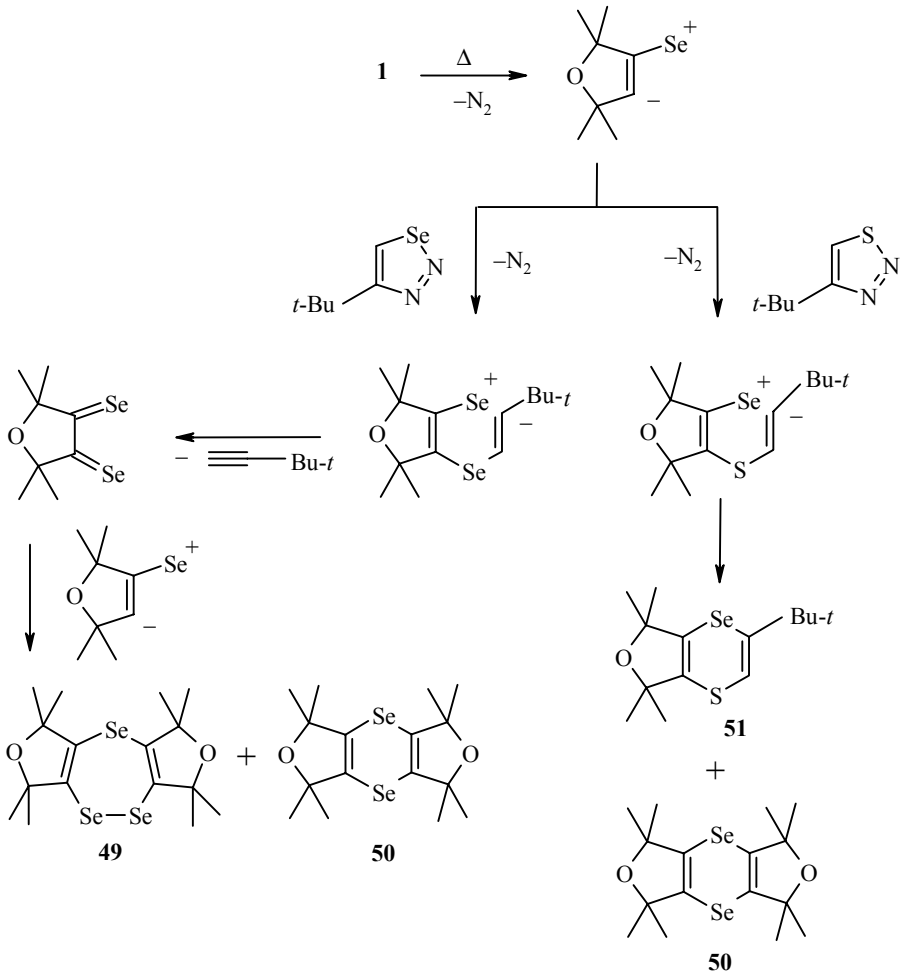
40 **41**

The sulfones **45** and **46** and 2-arylethenyl 2-arylethynyl sulfones **47** can be obtained by pyrolysis of the respective 1,2,3-selenadiazoles **42**-**44** at 200°C in the presence of copper powder. Here 58% of 2-arylethynylthioacetic acid **45** and 18% of the dimerized product 2,5-diarylselenophene-3,4-bis(thioacetic acid) **48** are formed. However, oxidation of the sulfur to sulfone in the initial selenadiazole during pyrolysis led to the exclusive formation of arylethynylsulfonylacetic acid **46** and *E*-2-arylethenyl 2-arylethynyl sulfone **47** [21].



42 **43** **44** **45** **46** **47** **48**

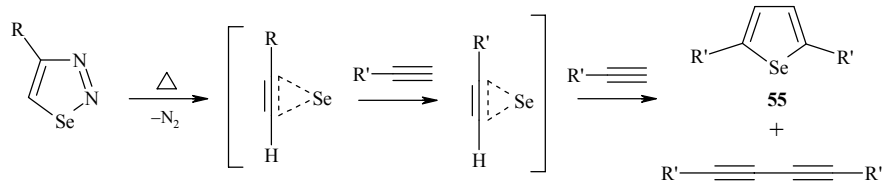
The reaction of compound **1** with 4-*tert*-butyl-1,2,3-selenadiazole for 24 h in boiling benzene led to the formation of 1,2,5-triselenepin **49** (58%) and 1,4-diselenin **50** (30%). In the absence of 4-*tert*-butyl-1,2,3-selenadiazole in the reaction mixture it led to the formation of a high yield of 1,4-diselenin **50**.



Since the selenadiazole **1** is inert in reaction with elemental sulfur, the reaction mechanism can be regarded as nucleophilic attack by the intermediate on the selenium atom of 4-*tert*-butyl-1,2,3-selenadiazole followed by the elimination of 3,3-dimethylbutyne and the formation of 1,2-diselenone. The fact that nucleophilic attack occurs is confirmed by the formation of the 1,4-thiaselenin derivative **51** as a result of the reaction of **1** with the 4-*tert*-butyl-1,2,3-thiadiazole [22].

2,5-Diarylselenophenes were formed with high yields during the prolonged heating of 4-arylselenadiazoles. The thermolysis of 4-phenyl-1,2,3-selenadiazole at 140°C led to the formation of only 2,5-diphenylselenophene. At higher temperatures (240-250°C), however, 2,5-diphenylselenophene was isolated as side product in addition to the 2,5 isomer [23, 24].

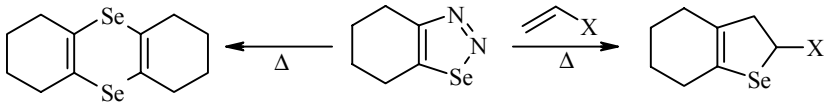
In the case of the thermolysis of 4-phenyl(2-thienyl)selenadiazoles **52** in the presence of arylacetylenes disubstituted selenophenes were formed. A mixture of various symmetrical and unsymmetrical 2,5-disubstituted selenophenes was obtained with a low yield when two equivalents of the arylacetylene were used. The ratio of arylacetylene and selenadiazole was optimized in order to improve the selectivity of the process. It was found that the use of a tenfold excess of the arylacetylene led to the formation of only 2,5-diarylselenophene **55** [25]. In all cases the reaction was accompanied by the formation of 1,4-diaryl-1,3-butadiynes.



52 **53** **54** **55**

At the beginning of the process a molecule of nitrogen is eliminated, and the intermediates **53** (R = phenyl, 2-thienyl) are formed, and they are then transformed into compounds **54** [R' = phenyl, 2-pyridyl, 3-(6-methylpyridyl)]. The latter enter into [2+3] cycloaddition with a second molecule of the arylacetylene (R'–C≡CH). The yield of the 2,5-diarylselenophenes **55** amounts to 80%. The synthesis of the diarylselenophenes **55** from 4-phenylselenadiazole **52** is preferred to synthesis from 4-(2-thienyl)selenadiazole.

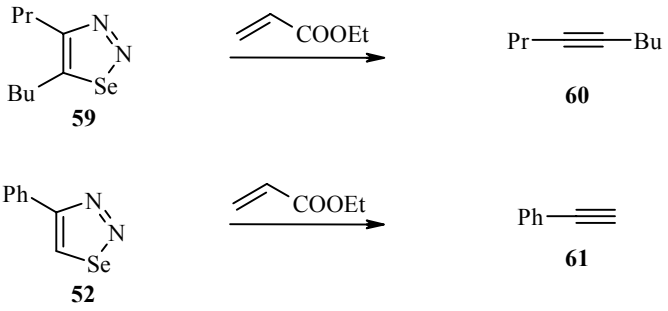
The thermolysis of 4,5,6,7-tetrahydrobenzo-1,2,3-selenadiazole (**56**) at 150°C led to the formation of 1,4-diselenin **57** with a yield of 82%. If the reaction is carried out in the presence of 200 eq. of CH_2=CH–X, the bicyclic dihydroselenophenes **58** (12-76%) are formed [26].



57 **56** **58**

X = COOMe, CN, COMe, OBu, C_6H_{13}

In cycloaddition to vinyl butyl ether (XC = OBu) and 1-octene (X = C_6H_{13}) 1,4-diselenin **57** was isolated as the main reaction product (71-74%). The increased yield of the dihydroselenophene **58** was due to the electron-accepting characteristics of the substituent at the double bond.

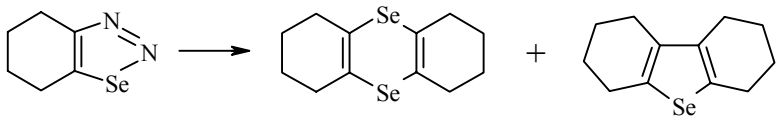


59 **60** **52** **61**

During thermolysis under analogous conditions 5-butyl-4-propylselenadiazole **59** and 4-phenyl-selenadiazole **52** are converted into the acetylenes **60** and **61**, and dihydroselenophenes are not formed.

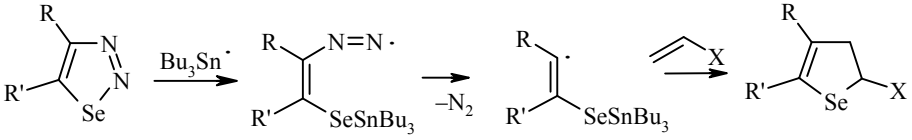
4. RADICAL REACTIONS

Free-radical reactions initiated by the stannyl radical are widely used in organic synthesis [27-29]. When the selenadiazole **56** is heated in benzene for 5 h in the presence of a catalytic amount of stannane (Bu_3SnH, $Bu_3SnCH_2CH=CH_2$) and AIBN, a mixture of 1,4-diselenin **57** (77-81%) and selenophene **62** (7-15%) is formed [30].



56 **57** **62**

The free-radical reaction of selenadiazole **63** with 200 eq. of CH_2=CH–X (benzene, 80°C, 5 h) was used for the production of the dihydroselenophenes **66** [30].

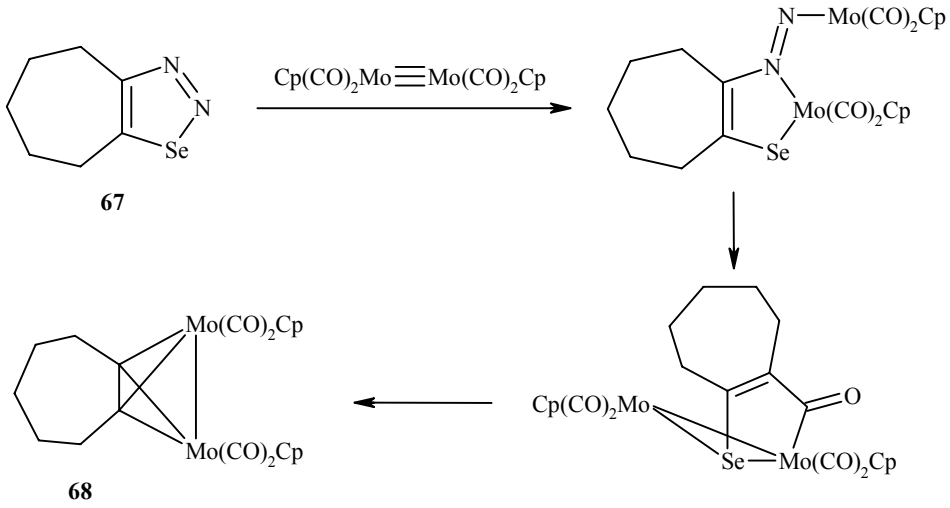


63 **64** **65** **66**

The reaction path is based on attack by the tributylstannyl radical on the initial 1,2,3-selenadiazole **63** with opening of the ring and the formation of the intermediate **64**. The radical **64** is then transformed into the energetically more favorable intermediate **65** by elimination of a molecule of nitrogen. Subsequent reaction with the C=C double bond of the substituted ethylene leads to removal of the tributylstannyl radical and the formation of the dihydroselenophene **66**. Replacement of the selenium in compounds **63** by sulfur leads to total inactivity in free-radical processes.

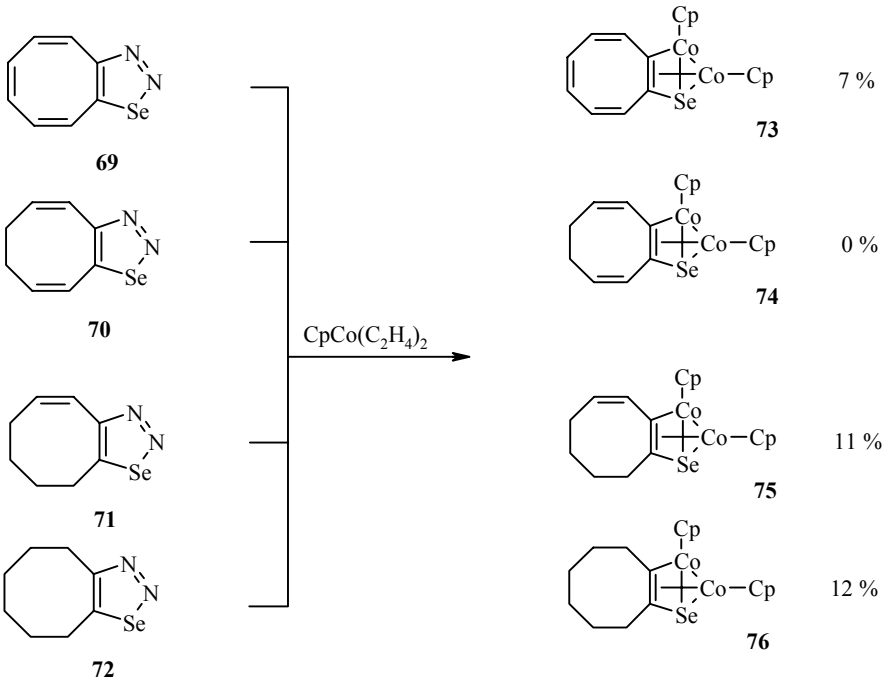
5. REACTIONS WITH COMPLEXES OF TRANSITION METALS

The reaction of cyclohepteno-1,2,3-selenadiazole with a twofold excess of $(\eta^5\text{-}C_5H_5)_2Mo_2(CO)_4$ leads to the formation of a dimolybdenum complex with a yield of 10%. The structure of the complex was confirmed by X-ray crystallographic analysis [31].

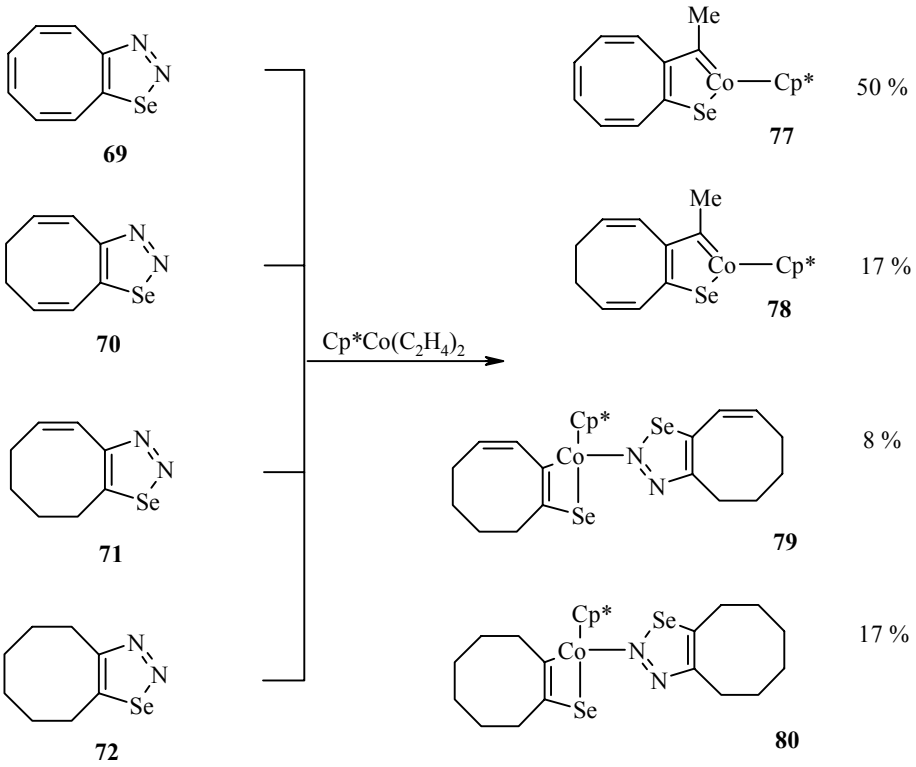


67 **68**

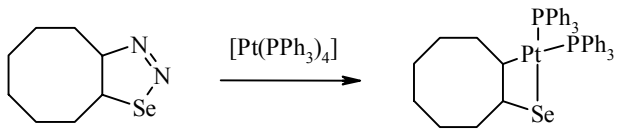
Treatment of the selenadiazoles **69-72** with one equivalent of $(\eta^5\text{-}C_5H_5)_2Co(C_2H_4)_2$ in diethyl ether leads to the release of gas and the separation of a precipitate. The products **73-76** were purified on a chromatographic column, and their structure was confirmed by X-ray crystallographic analysis [32, 33].



Replacement of the cyclopentadienyl substituent by pentamethylcyclopentadienyl [(η^5-$C_5Me_5)_2Co(C_2H_4)_2$] led to a significant change in the reaction path [32, 33]. The five-membered heterocycles **77** and **78**, containing selenium and cobalt atoms, were formed as a result of the elimination of a molecule of nitrogen from the initial selenadiazole followed by the addition of cobalt and a molecule of ethylene. On the other hand, the reaction of $(\eta_5$-$C_5Me_5)_2Co(C_2H_4)_2$ with two equivalents of the selenadiazoles **69**-**72** led to the four-membered heterocycles **79** and **80**.



The selenaketocarbene complex **81** was obtained with a high yield by the reaction of tetrakis(triphenylphosphino)platinum [$Pt(PPh_3)_4$] with 3a,4,5,6,7,8,9,9a-octahydrocycloocta-1,2,3-selenadiazole (**72**) [34].

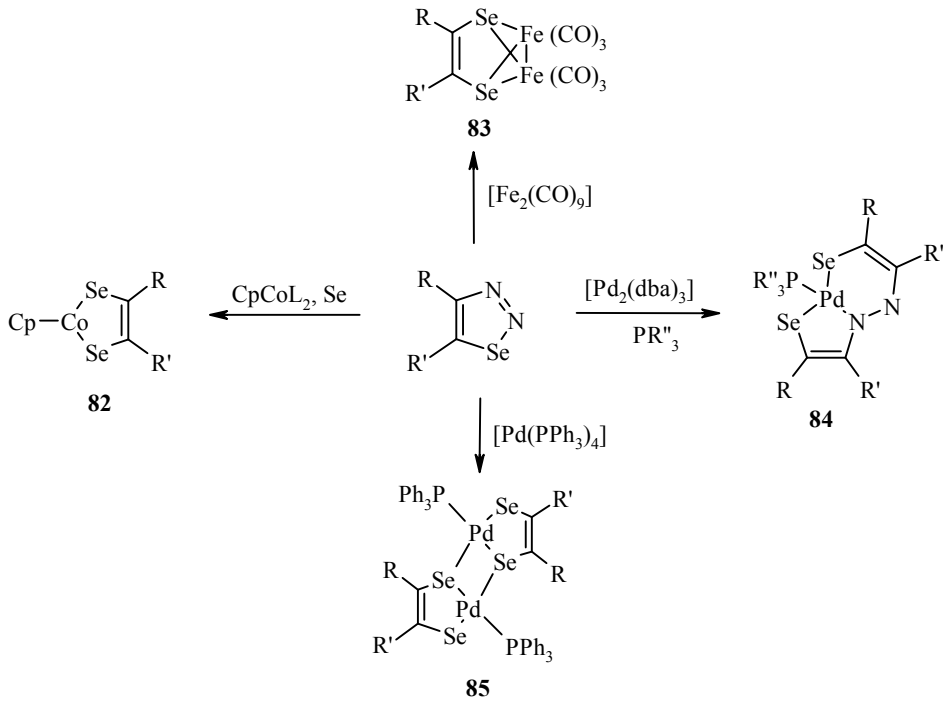


72 **81**

The cyclopentadienylcobaltdiselenones **82** were isolated from the reaction mixture obtained after boiling the initial selenadiazole, selenium powder, and the triphenylphosphine or carbonyl complex of cobalt [35].

The diiron diselenolates **83** were formed during treatment of the initial selenadiazole with one equivalent of nanocarbonyldiiron [$Fe_2(CO)_9$] at room temperature in dry hexane [36].

When a mixture of selenadiazole, dipalladium tris(dibenzylideneacetonate [$Pd_2(dba)_3$], and trialkylphosphine was heated, palladium complexes of a new type with Se,N,Se-tridentate ligands **84** were formed [37].



R, R' = H, Ph, $(CH_2)_4$, $(CH_2)_5$, $(CH_2)_6$; R" = Et, Bu; L = CO, PPh_3

In contrast to the reaction of selenadiazole with $Pt(PPh_3)_4$, products with a different structure were formed in the case of the palladium analog. The dimer of 1,3-diselena-2-palladiumcyclopentene **85** was obtained by heating two equivalents of selenadiazole with [$Pd(PPh_3)_4$] [38].

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