SELENIUM-CONTAINING HIGHLY FUNCTIONALIZED 1,2,3-TRIAZOLES

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Abstract: *1,2,3-Triazoles are an interesting class of compounds, either to use as an intermediate in the synthesis of complex molecules or for the exploitation of their biological properties. Especially, the selenium-containing highly functionalized 1,2,3-triazoles have received considerable attention, because of their widespread application as bioactive compounds and building blocks in organic synthesis. Their preparation has been realized through two main synthetic strategies: copper catalysis and organocatalysis. Here we describe methodologies for the preparation of the different selenium-containing functionalized 1,2,3-triazoles, covering the last ten years, and involving copper catalysis and organocatalysis.*

Contents

1. Introduction

1,2,3-Triazoles are five-membered aromatic heterocycles, containing three consecutives nitrogen atoms besides being the major pharmacophore system among nitrogen-containing heterocycles.[1,2] Their versatility and biological activities are well documented in a few reviews articles[3,4] and books;[1] for example, antifungal,[5] anticancer,[6] anti-inflammatory,[7] antitubercular[8] and antiviral[9] activity. Because of this, there are some drugs containing the 1,2,3-triazolic unit in their structure.[10,11] One of those examples is cefatrizine (Figure 1A),[11] which is a first-generation cephalosporin-type molecule with antibacterial activity used as a broad-spectrum antibiotic in several countries.

The chemistry of organic compounds containing selenium has been developed largely in recent years.[12,13,14,15] The interest in this class of compounds is due to the important biological activities that are associated to them, for examples, relevant antioxidant,[16] anti-inflammatory[17] and antitumor[18] activities. In organic synthesis, these compounds are also extremely versatile and can be used as synthons in the building of more complex molecules,[19] in organocatalysis,[20] among others.

The search for methods to prepare highly functionalized 1,2,3-triazole-containing organoselenium compounds started with Back's[21] and Tiecco's[22] research groups, independently, around the 2000s (Figure 1). While Back and co-workers employed the 1-phenylseleno-2-(*p*-toluenesulfonyl)ethyne **1** and the (azidomethyl)trimethylsilane **2** to obtain a mixture of 1,2,3-triazole regioisomers **3** and **4** (Figure 1B), Tiecco and his group described the synthesis of 1,2,3-triazole **5** by the reaction between asymmetrical selenoazides **6** with dimethyl acetylenedicarboxylate **7** (Figure 1C). These works gave rise to studies involving the chemistry of triazoles and selenium compounds and from there general and selective methods have been developed.

Considering the significant number of contributions from our research group to this chemistry in the last decade, this chapter aims to review the copper- and organocatalyzed methodologies towards the synthesis of highly substituted selenium-containing 1,2,3-triazoles. From the number of works collected, to better discuss, this chapter was divided in two main sections: 2. Copper catalysis and 3. Organocatalysis.

2. Copper catalysis

The copper-catalyzed reactions were reported simultaneously and independently by the groups of Meldal[23] and Sharpless,[24] who were laureated with the Nobel Prize in Chemistry in 2022. This strategy converts terminal alkynes **8** and organic azides **9** exclusively into the corresponding 1,4-disubstituted

1,2,3-triazoles **10** (Scheme 1). It is important to highlight that the uncatalyzed reaction to the preparation of 1,2,3-triazoles affords mixtures of 1,4- and 1,5-triazole regioisomers and requires much higher temperatures.

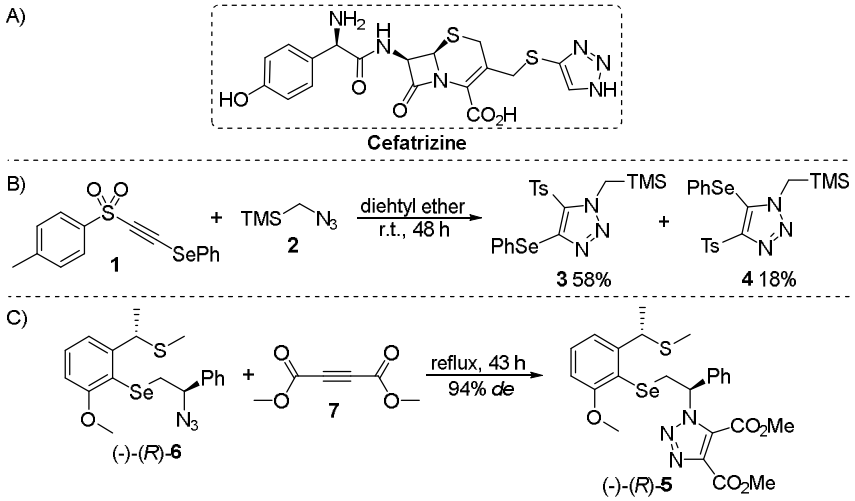
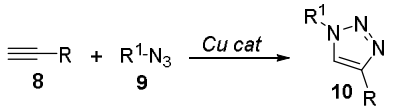


Figure 1. A) Structure of Cefatrizine;[11] B) Synthesis of organoseleno-triazoles **3-5** related by B) Back in 1999[21] and C) Tiecco in 2003.[22]



R, R^1=Organic groups or organoselenyl groups

Scheme 1. General strategy to copper-catalyzed azide-alkyne cycloaddition (CuAAC).

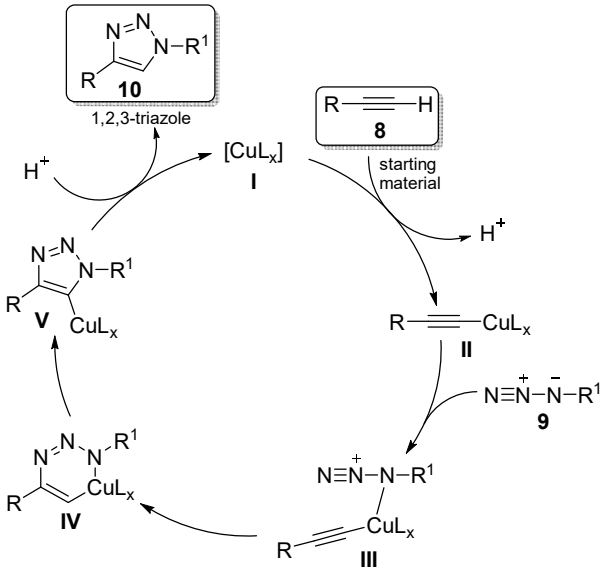
A general mechanism for the copper-catalyzed preparation of 1,2,3-triazole is depicted on Scheme 2.[25,26] The catalytic cycle starts with the interaction of alkyne **8** and copper catalyst **I**, followed by the formation of copper acetylide intermediate **II**. Then the coordination of azide **9** to intermediate **II** generates the unusual six-membered copper metallacycle **IV**. The resulting six-membered copper metallacycle is not stable and immediately undergoes reductive elimination to furnish the copper triazolide complex **V**. Finally, the action of H^+ leads to the product 1,2,3-triazole **10** and regeneration of the copper catalyst **I**.

In the last decade, there was a significant increase in the number of different synthetic strategies to obtain highly functionalized triazoles using copper catalysis. The works described in this section involve the use of $Cu(OAc)_2.H_2O$, CuI or $CuSO_4.5H_2O$ as catalyst; azides, alkynes, or other sources of selenium such as PhSeBr, diorganyl diselenides and elemental selenium as starting materials to afford 1,2,3-triazoles.

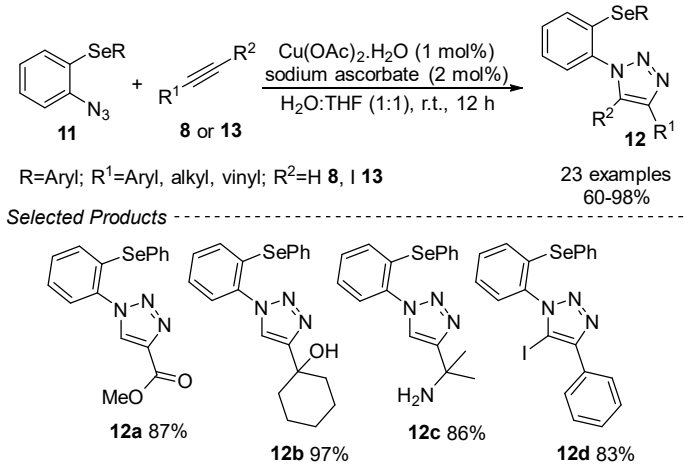
A series of methods to access 1,2,3-triazoles starts from azides bearing an organoselenium substituent. In this line, Braga, Alves and co-workers[27] described in 2011, the reaction of different azido arylselenides with alkynes through a copper-catalyzed Huisgen 1,3-dipolar cycloaddition for the synthesis of different arylseleno-1,2,3-triazoles. In this work, the authors started by preparing the azido arylselenides **11**, which are important intermediates for the synthesis of the desired products.

After some preliminary tests, the authors found the best conditions for the synthesis of the arylseleno-1,2,3-triazoles **12**. It was found that the copper(II) acetate monohydrated [$Cu(OAc)_2.H_2O$] in quantity of 1 mol% was the best copper species catalyst and 2 mol% of sodium ascorbate as co-catalyst. As solvent, the best option was a mixture of H_2O/THF (1:1), in this point, the water was necessary as co-solvent to increase the solubility of the catalysts. The desired products were obtained in good to excellent yields after 12 h of reaction at room temperature (Scheme 3). With the optimized conditions, the authors were able to

synthesize fourteen examples of arylseleno-1,2,3-triazoles **12**, through the reaction of the 2-azido arylselenide **11** with different alkynes **8** and **13**. Many alkynes were tolerated in the 1,3-dipolar cycloaddition, such as alkynes with aryl, alkyl and vinyl as substituents and, in addition, alkynes containing esters, amine and alcohol as functional groups (Scheme 3).



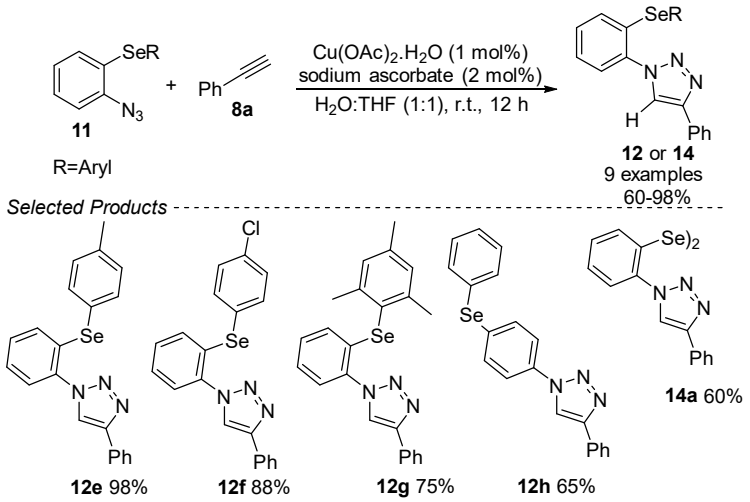
Scheme 2. General mechanism for the synthesis of 1,2,3-triazoles **10** *via* copper catalysis.



Scheme 3. Reaction of the 2-azido arylselenide **11** with different alkynes **8** or **13**.

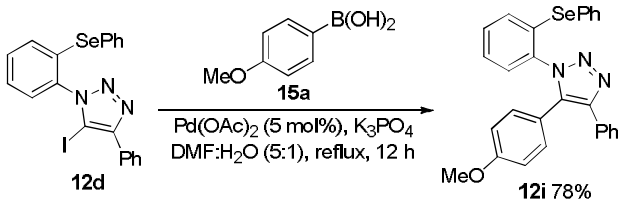
To extend the range of this synthesis, phenylacetylene **8a** was reacted with different azido arylselenides **11**, and the desired products **12** were synthesized in good to excellent yields (Scheme 4). With this protocol, 2-azido arylselenides containing electron-donating or electron-withdrawing groups on the arylselenium moiety produced in good to excellent yields the corresponding arylseleno-1,2,3-triazoles. When a diselenide containing an azide group was utilized as the substrate, an acceptable yield of diaryl-diseleno-1,2,3-triazole

14a was obtained, suggesting that the Se-Se bond was not compromised under these copper-catalyzed azide-alkyne cycloaddition conditions.



Scheme 4. Reaction of phenylacetylene **8a** with different azido arylselenides **11.**

Furthermore, the product **12d** obtained through the cycloaddition was reacted in a Suzuki-Miyaura cross-coupling with 4-methoxyphenylboronic acid **15a**, yielding the corresponding 4,5-disubstituted arylseleno-1,2,3-triazole **12i** in 78% yield (Scheme 5). Compound **12d** seems promising as an intermediary in the synthesis of more highly substituted 1,2,3-triazoles.

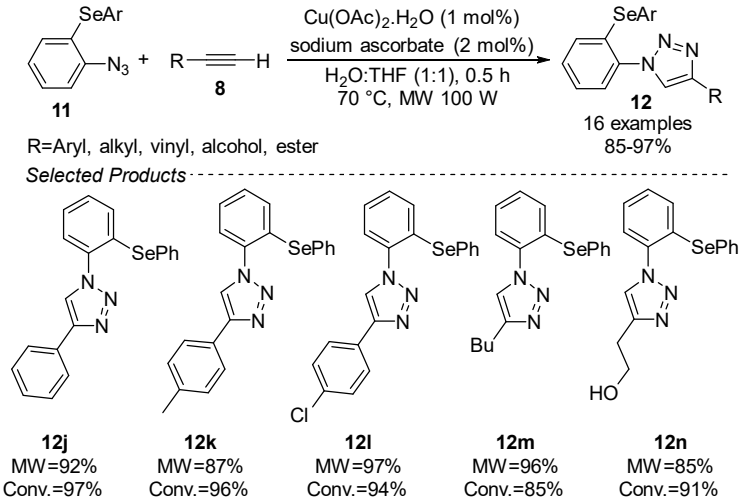


Scheme 5. Suzuki-Miyaura cross-coupling of **12d** with 4-methoxyphenylboronic acid **15a**.

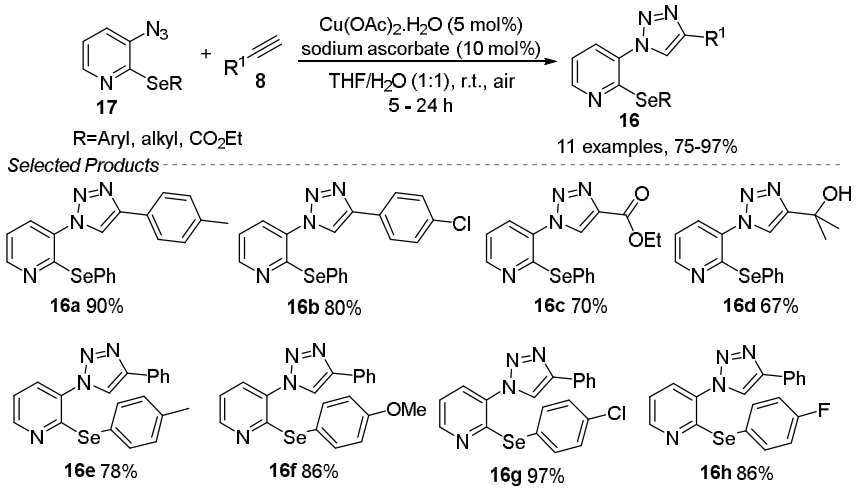
A few years later, in 2016, Alves and co-workers[28] presented a procedure for a fast synthesis of a variety of (arylselanyl)phenyl-*1H*-1,2,3-triazoles **12** by copper catalyzed 1,3-dipolar cycloaddition employing microwave irradiation. In this work, the authors applied under microwave irradiation the previously mentioned method, using copper(II) acetate monohydrate and sodium ascorbate as catalysts in a 1:1 mixture of THF and H_2O as solvent. The study revealed that the reactions done with focused microwave irradiation are quicker than the conventional procedure, yielding the corresponding selanyl 1,2,3-triazoles **12** in relatively short reaction times (Scheme 6). The developed reaction demonstrates tolerance for complex functional groups, terminal alkynes **8** containing a range of substituents, such as substituted aryl, alkyl, vinyl, ester, and alcohols, were efficiently applied. In addition, expanding this microwave approach for the cycloaddition reaction of azidophenyl alkoxyarylselenides with terminal arylalkynes with short and long alkoxyphenyl chains, synthesizing methoxylated selenyl-1,2,3-triazoles in good yields.

In 2015, Alves and co-workers[29] described the synthesis of eleven novel 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines **16** through a copper-catalyzed cycloaddition reaction. Applying the copper-catalyzed cycloaddition reaction, the authors found as the best reaction conditions for the synthesis of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines **16** the presence of 5 mol% $Cu(OAc)_2.H_2O$ and 10 mol% sodium

ascorbate as catalysts, employing a solvent system of H_2O/THF (1:1) for 6 h at room temperature. The scope of this procedure was developed by reacting several 2-(arylselanyl)-3-azido-pyridines **17** with a variety of readily available terminal alkynes **8**, yielding the desired products **16** in good to excellent yields (Scheme 7). The reaction was tolerant to several functional groups, including substituted-benzene rings, alcohol and ester, also, none electronic or steric hindrance influence was observed during the synthesis of the products.

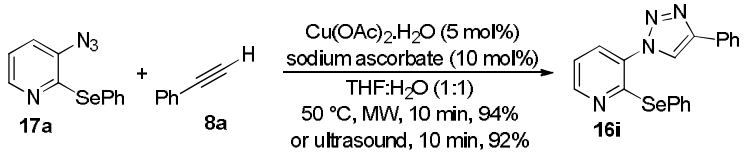


Scheme 6. Synthesis of (arylselanyl)phenyl-*1H*-1,2,3-triazoles **12** under microwave irradiation.



Scheme 7. Synthesis of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines **16a-h**.

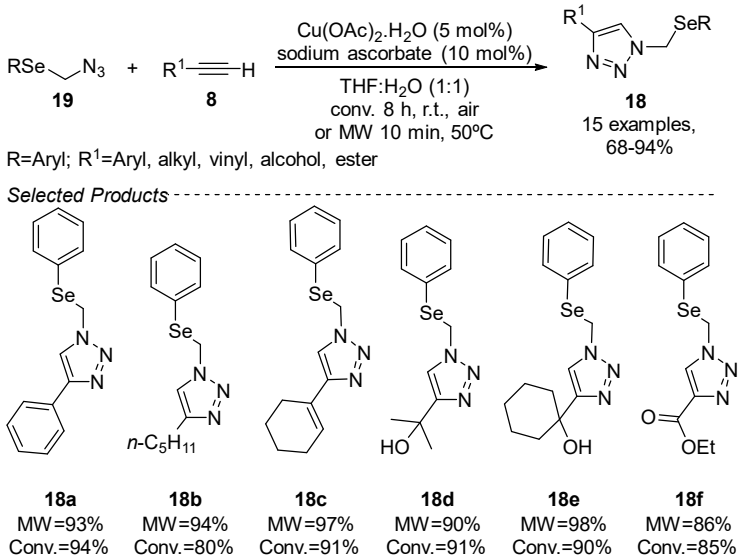
In addition, to investigate this copper-catalyzed cycloaddition reaction between phenyl acetylene **8a** and the 2-(phenylselanyl)-3-azido-pyridine **17a** to obtain the corresponding product **16i** in a shorter reaction time and using greener methods, the authors performed the reaction under focused microwave irradiation (using a power of 100 W) and ultrasound conditions (60% amplitude) (Scheme 8). This last study showed that the product **16i** could be synthesized in excellent yields after only 10 minutes using both non-classical techniques, illustrating the effective utilization of alternative sources of energy in this synthesis.



Scheme 8. Ultrasound and microwave irradiation synthesis of **16i**.

In 2012, Alves and co-workers[30] developed an efficient protocol for the synthesis of various 1-(arylseleno-methyl)-1,2,3-triazoles **18** through a copper catalyzed 1,3-dipolar cycloaddition of azidomethyl arylselenides **19** with terminal alkynes **8** (Scheme 9). Firstly, the authors investigated the solvent effects and the role of the copper salt in the copper catalyzed 1,3-dipolar cycloaddition. The optimal reaction parameters consisted of the reaction of azidomethyl arylselenide **19** with terminal alkyne **8** in the presence of 5 mol% of $Cu(OAc)_2.H_2O$ and 10 mol% of sodium ascorbate in a mixture of THF/H_2O (1:1, 2 mL) at room temperature under air for 8 h (Scheme 9).

Applying the developed protocol, a variety of terminal alkynes containing a range of substituents, such as aryl, alkyl, vinyl, alcohol, and ester, were effectively applied in this method, and high yields (68-94%) of the fifteen 1-(arylseleno-methyl)-1,2,3-triazoles **18** were produced. In addition, they have executed this copper catalyzed 1,3-dipolar cycloaddition reactions with focused microwave irradiation to get an efficient strategy in terms of energy efficiency. Microwave irradiation significantly decreased the reaction time (from 8 h to 10 min), yielding similar yields of six of the corresponding 1-(arylselenomethyl)-1,2,3-triazoles **18**. A comparation between the yields obtained with conventional heating and microwave irradiation are shown on Scheme 9.

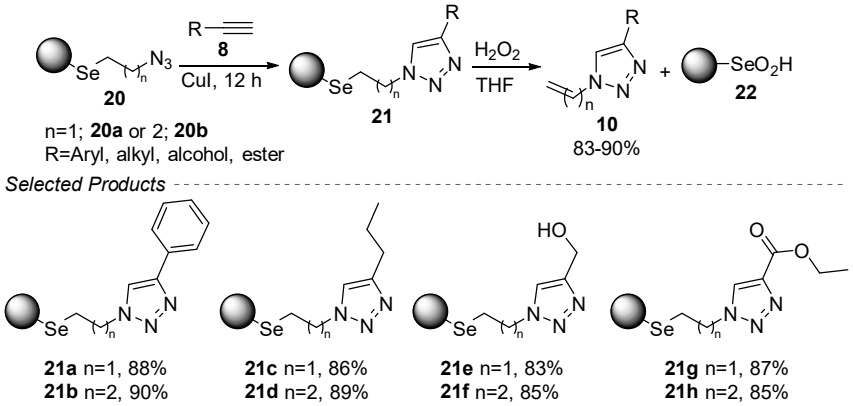


Scheme 9. Comparation between the conventional synthesis and under microwave irradiation.

Cai and co-workers,[31] presented in 2014 a simple procedure for the traceless solid-phase synthesis of 1-vinyl- and 1-allyl-1,2,3-triazoles **10** through a 1,3-dipolar cycloaddition reaction of polystyrene-supported 2-azidoethyl phenyl selenide **20a** or 3-azidopropyl phenyl selenide **20b** with terminal alkynes **8**, followed by an elimination reaction.

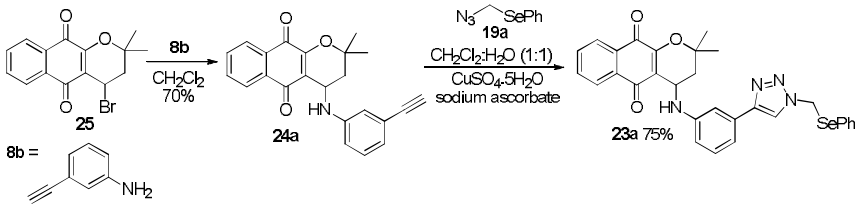
The 1,3-dipolar cycloaddition of polymer **20** with phenyl acetylene **8a** was reported to be mild in DMF/THF with 5 mol% CuI and 1.5 equivalent of diisopropylethylamine (DIPEA) at room temperature for

12 h, resulting in the polymer-supported 2-triazolylethyl phenyl selenide **21a** and 2-triazolylpropyl phenyl selenide **21b**. The polymer-supported 2-triazolylalkyl phenyl selenides **21** were subsequently treated with 30% H_2O_2 at 0 °C, followed by an oxidation-elimination process at room temperature to obtain the corresponding deselenylated 1,2,3-triazoles **10** in excellent yields, and the residual polystyrene supported phenylseleninic acid **22** was obtained as a by-product (Scheme 10). Moreover, several alkynes containing phenyl, alkyl, alcohol, ether and ester groups successfully reacted affording the desired products with high yields.



Scheme 10. Synthesis of 1-vinyl- and 1-allyl-1,2,3-triazoles **21**.

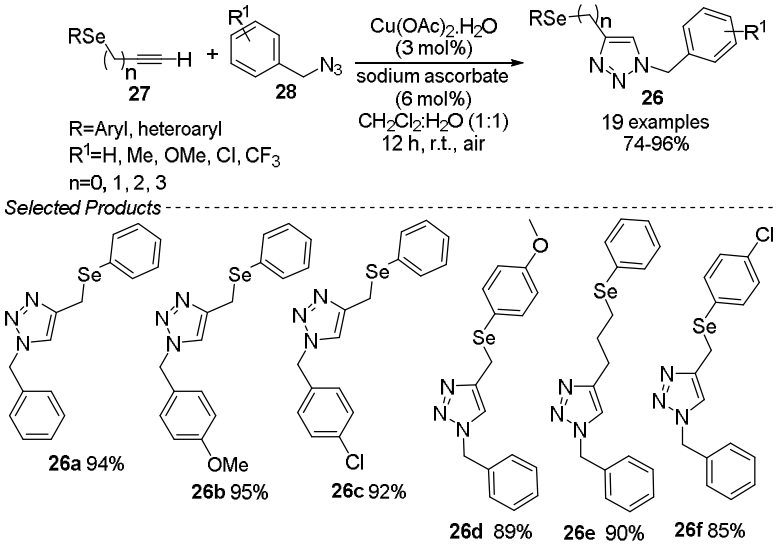
In 2015, da Silva Júnior and co-workers applied a copper catalyzed azide-alkyne 1,3-dipolar cycloaddition to the synthesis of new selenium-containing quinone-based 1,2,3-triazoles **23**, which were posteriorly tested against six different cancer cell lines.[32] Firstly, the alkynyl lapachone **24a** was synthesized through the reaction between 3-ethylaniline **8b** and the bromo derivative **25a**. Afterwards, employing azidomethyl phenylselenide **19a** as a substrate, the first class of selenium-containing quinone-based 1,2,3-triazoles **23** was synthesized. The copper catalyzed azide-alkyne 1,3-dipolar cycloaddition reaction among alkynyl α-lapachone derivative **24** and azidomethyl phenylselenide **19a** produced the compound of interest **23** in 75% yield (Scheme 11). The reaction was evaluated with TLC, and no reaction time was mentioned by the authors.



Scheme 11. Synthesis of compound **23a**.

Another strategy to afford 1,2,3-triazoles is to start from alkynes bearing an organoselenium substituent. Thus, Alves and co-workers, in 2012,[33] developed the synthesis of several [(arylselanyl)alkyl]-1,2,3-triazoles **26** from (arylselanyl)alkynes **27** under click type 1,3-dipolar cycloaddition reactions with a plethora of benzyl azides **28** in the presence of catalytic quantities of copper salts and sodium ascorbate. In this work, the reactions were performed in the presence of $Cu(OAc)_2.H_2O$ (3 mol%) and sodium ascorbate (6 mol%) using as solvent a combination of CH_2Cl_2/H_2O (1:1), and the expected products **26** were synthesized in good to excellent yields (74-96%) (Scheme 12). The protocol has shown to be effective for a wide range of substituted benzylic and alkyl azides, affording high yields of the expected [(arylselanyl)alkyl]-1,2,3-triazoles **26**. Overall, substituents with electronic effects in the aromatic ring of the azide structure had no influence on the reactions. In addition,

the possibility of developing the reaction with aryl azides **28** and different (arylselanyl)alkynes **27** was evaluated, affording the desired products in high to excellent yields (Scheme 12).



Scheme 12. Scope variation of [(arylselanyl)alkyl]-1,2,3-triazoles **26**.

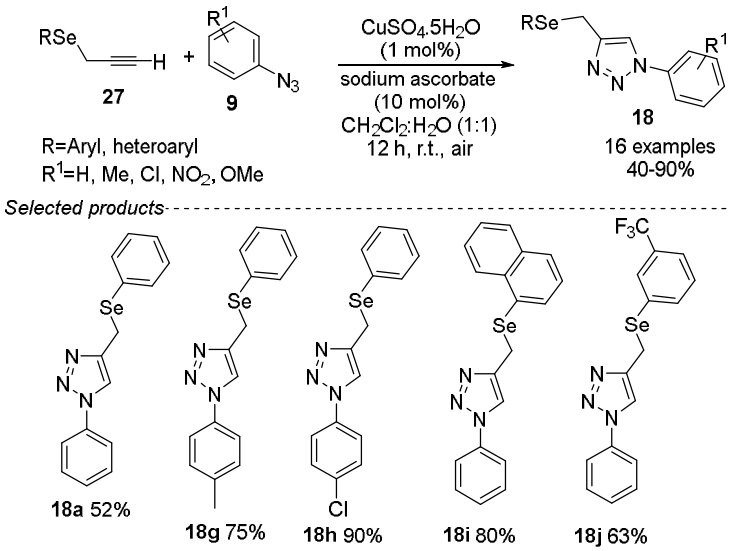
The synthesis of novel 1,2,3-triazole-selenide hybrids **18** and their investigation of the trypanocidal potential was structured by Nascimento and co-workers.[34] The 1,2,3-triazoles were obtained through a 1,3-dipolar cycle addition reaction. With a catalytic system of copper(II) and sodium ascorbate in a mixture of CH_2Cl_2:H_2O (1:1) as solvent after 12 h, sixteen examples were obtained in 40-90% yields. In this reaction, different aryl azides **9** and propargylic selenides **27** were utilized, giving the desired products with good to excellent yields (Scheme 13). In addition, the trypanocide assays demonstrated that the compounds **18i** and **18j** have a low toxicity and good potential against *T. cruzi* when compared to the positive control benznidazole.

In the same work of da Silva Júnior,[32] published in 2015, which developed a copper catalyzed azide-alkyne 1,3-dipolar cycloaddition to the synthesis of new selenium-containing quinone-based 1,2,3-triazoles, it was synthesized a second group of selenium-containing quinone-based 1,2,3-triazoles **29**, through cycloaddition with (prop-2-yn-1-ylselanyl) benzene **27a**. Firstly, the 4-azide-α-lapachone **30a** could be simply synthesized by reacting **25a** with sodium azide in dichloromethane as solvent. Then, the cycloaddition through **30a** and the propargyl selenide **27a** afforded the desired product **29a** with 70% yield, after the consumption of the substrates (Scheme 14).

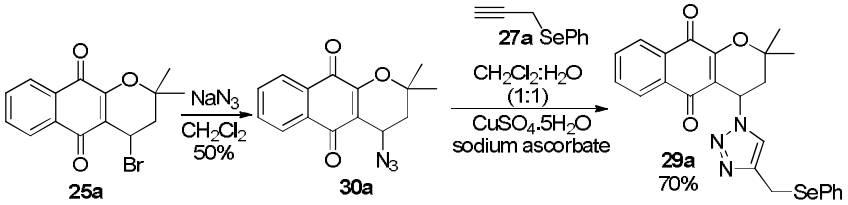
In general, this method was effective for synthesizing a variety of selenium-functionalized 1,2,3-triazoles, with some of them exhibiting intriguing pharmacological activities, with IC_{50} values in antiproliferative assays below 0.3 mM, which were more significant than the derived β-lapachone or doxorubicin, a conventional clinically used anticancer agent.

Sridhar and co-workers,[35] in 2016, proposed the synthesis and characterization of a variety of chalcogenyl triazoles bridging ferrocene-carbohydrate moiety **31**, as well as their cytotoxicity towards five cancer cell lines. The alkyne **32a** was allowed to react with the appropriate azides **9**, yielding the selanyl 1,2,3-triazole derivatives **31** in 65% to 81% yields. The reaction time was not monitored, and the authors evaluated the reaction from HPLC analysis. This approach yielded three intriguing products, compounds **31b-c** having a sugar group in the structure (Scheme 15).

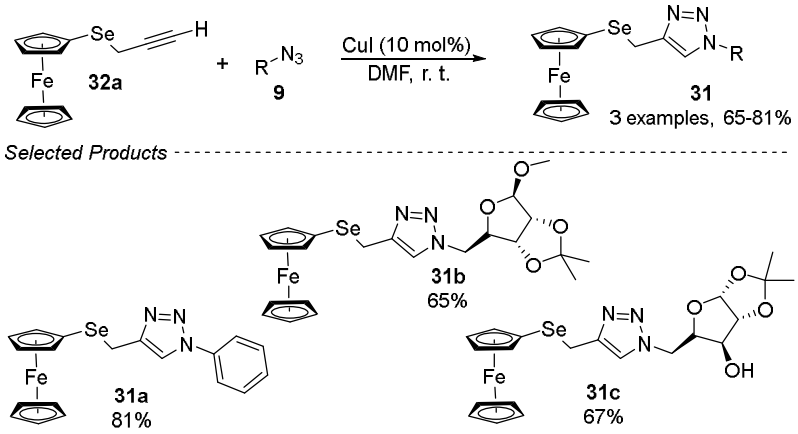
The cytotoxicity of ferrocenyl selanyl 1,2,3-triazoles **31a-c** was tested using in vitro cellular growth assays. Cytotoxicity against many cancer cell lines was observed, with IC_{50} values less than 20 mM. The ferrocenyl seleno ribose triazole conjugate **31c** has the lowest IC_{50} value (2.9 mM).



Scheme 13. Synthesis of novel 1,2,3-triazole-selenide hybrids **18**.



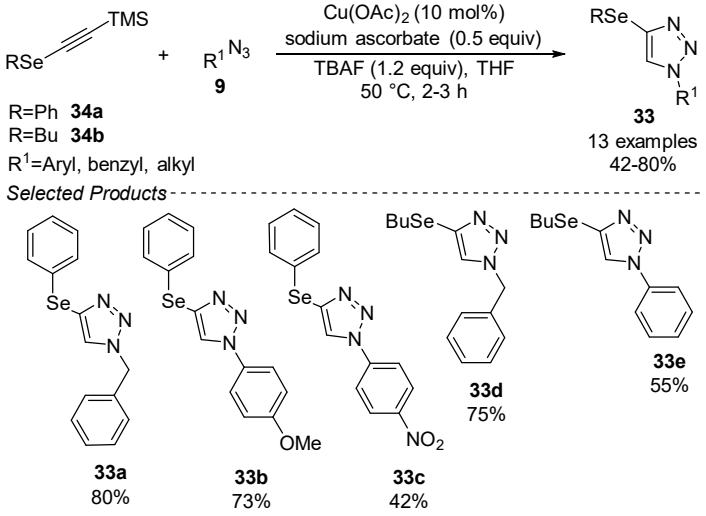
Scheme 14. Synthesis of compound **29a**.



Scheme 15. Synthesis of the triazoles **31**.

Manarin and co-workers,[36] proposed a method for the synthesis of triazoles **33** with the selenium atom straight attached to the heterocycle *via* a CuAAC reaction among a variety of organic azides **9** and a terminal alkynyl selenide formed *in situ* by deprotection of the trimethylsilyl group in the alkyne **34** (Scheme 16). The

authors investigated the protocol applicability employing other organic azides **9** and alkynes **34a-b**. As substrates, aliphatic and aromatic azide analogues were effectively employed. When compared to those with neutral (H) and electron withdrawing (NO_2) substituents in the aromatic ring, the aryl azide with an electron-donating group (*p*-MeO) produced the highest yields. In addition, some examples employing a SeBu group were synthesized with lower yields. (Scheme 16).

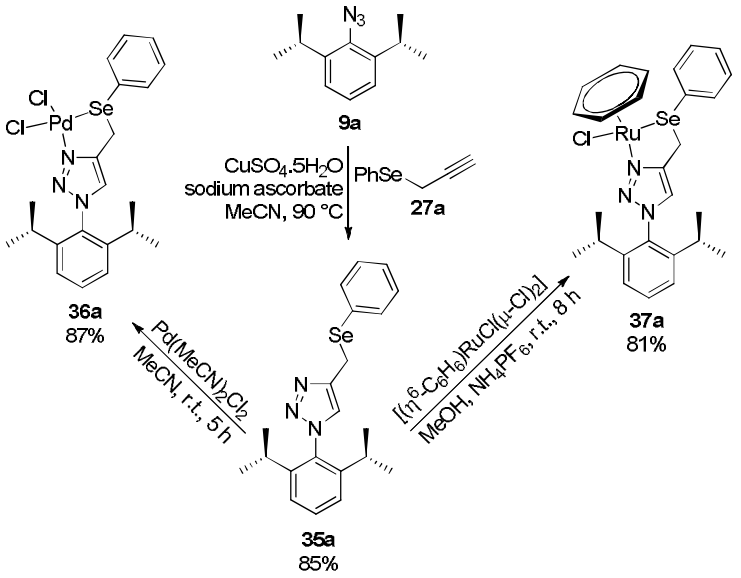


Scheme 16. Synthesis of the triazoles **33a-e**.

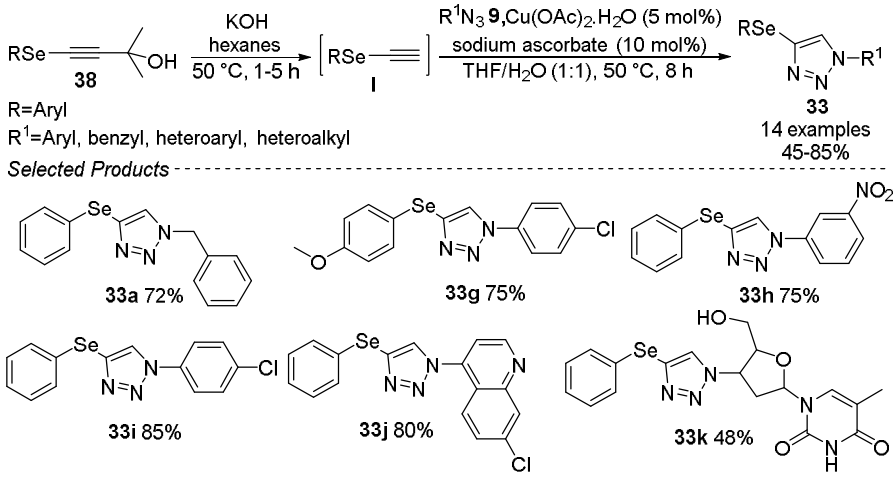
By employing copper-catalyzed azide-alkyne cycloaddition conditions, Singh and co-workers,[37] developed the synthesis of the [(phenylselanyl)methyl]-1,2,3-triazole **35a** and its Pd(II) and Ru(II) complexes. The triazole **35a** was synthesized in 85% yield through the reaction of phenylpropargyl selenide **27a** and 2-azido-1,3-diisopropylbenzene **9a** at 90 °C for 24 h in the presence of $CuSO_4.5H_2O$, sodium ascorbate, and a combination of CH_3CN/H_2O (10:1) as solvent (Scheme 17). The treatment of the triazole **35a** at room temperature with the respective metal complexes, $[Pd(CH_3CN)_2Cl_2]$ or with $[(\eta^6\text{-}C_6H_6)RuCl(\mu\text{-}Cl)]_2$, resulted in the triazole complexes $[Pd(L)Cl_2]$ **36a** or $[(\eta^6\text{-}C_6H_6)Ru(L)Cl]PF_6$ **37a** in 87% and 81% yields, respectively (Scheme 17).

Selenium-containing carbinols **38** and organic azides **9** were used to access 4-arylselanyl-1*H*-1,2,3-triazoles **33** in 45-85% yield in presence of $Cu(OAc)_2.H_2O$ (5 mol%), sodium ascorbate (10 mol%), a mixture of THF and H_2O as solvent, at 50 °C for 8 h (Scheme 18).[38] The method involves initially the reaction of arylselanyl carbinol **38** with KOH in hexanes, and then the appropriate azide **9**, copper catalyst, sodium ascorbate and THF/H_2O were added to the reaction flask. Various arylalkynes were reacted however, arylselanyl carbinols with electron-withdrawing groups showed to be less reactive than those containing electron-donating ones. The azides were little sensible to electronic factors and the reaction performed well with aryl, benzyl and heteroaryl azides. Still, the azido-derivative of Zidovudine was converted to the respective triazole **33k** in 48% yield.

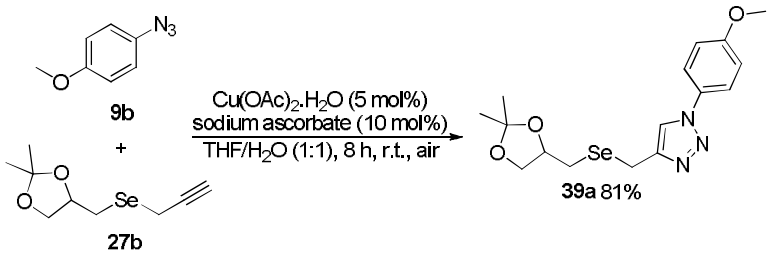
Perin, Wilhelm and co-workers[39] reported the synthesis and pharmacological evaluation of novel selenoethers glycerol derivatives for the treatment of pain and inflammation. The system $NaBH_4$/PEG-400 was employed to access new selenoethers from benzyl halides and bis(2,2-dimethyl-1,3-dioxolanylmethyl) diselenide as well as new pyridylselenides glycerol derivatives from bis(3-amino-2-pyridyl) diselenide and tosyl carbonate or solketal. In order to demonstrate the versatility of selenoethers synthesized, the authors applied copper(II) acetate (5 mol%) and sodium ascorbate (10 mol%) in the reaction between selenoether **27b** and 1-azido-4-methoxybenzene **9b**. Under this condition, the corresponding triazole **39a** could be obtained in 81% yield after 8 h of reaction (Scheme 19).



Scheme 17. Synthesis of **35a** and its derivatization to Pd(II) and Ru(II) complexes.

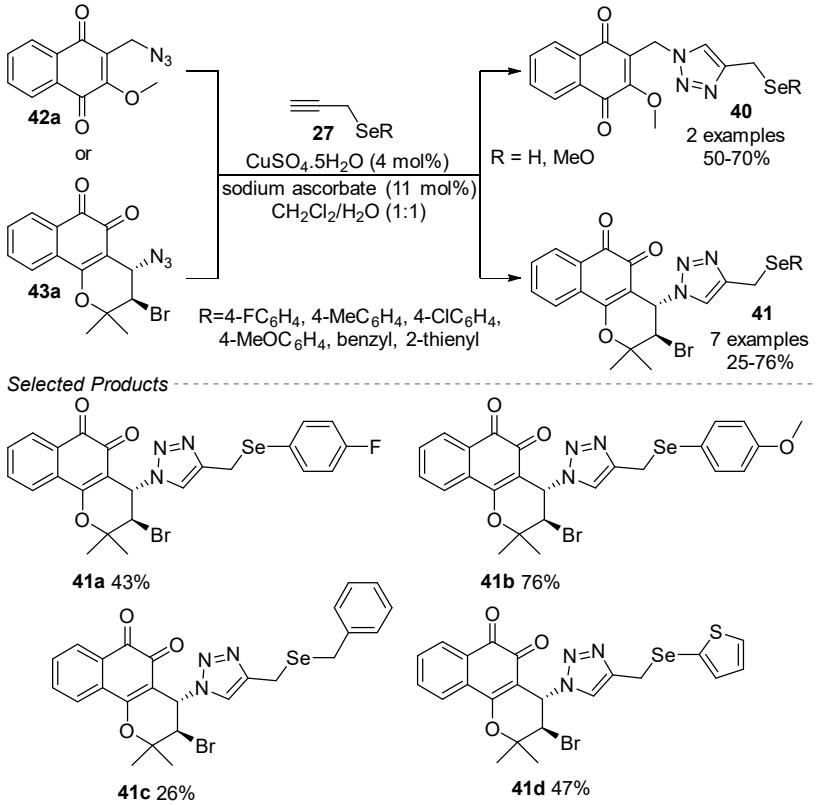


Scheme 18. Synthesis of 4-arylselanyl-1*H*-1,2,3-triazoles **33** from arylselanyl carbinols **38**.



Scheme 19. Preparation of 1,2,3-triazole glycerol derivative **39a**.

The synthesis of selenium-quinone hybrid compounds with potential antitumor activity *via* Rh-catalyzed C-H bond activation and click reactions was reported in 2018.[40] In this work, the authors prepared nine selenium containing-1,2,3-triazole **40** and **41** derivatives from quinones **42a** and **43a** and phenyl(prop-2-yn-1-yl)selenides **27** substituted in presence of $CuSO_4.5H_2O$ (4 mol%), sodium ascorbate (11 mol%), a mixture of CH_2Cl_2 and H_2O (1:1) as solvent at room temperature (Scheme 20). The reaction time was not mentioned but the reactions were monitored by TLC until total consumption of starting material. All compounds were evaluated against five types of cancer cell lines: HL-60 (human promyelocytic leukemia cells), HCT-116 (human colon carcinoma cells), SF295 (human glioblastoma cells), NCIH-460 (human lung cells) and PC3 (human prostate cancer cells). Some compounds showed good activity with IC50 values below 1 μM.

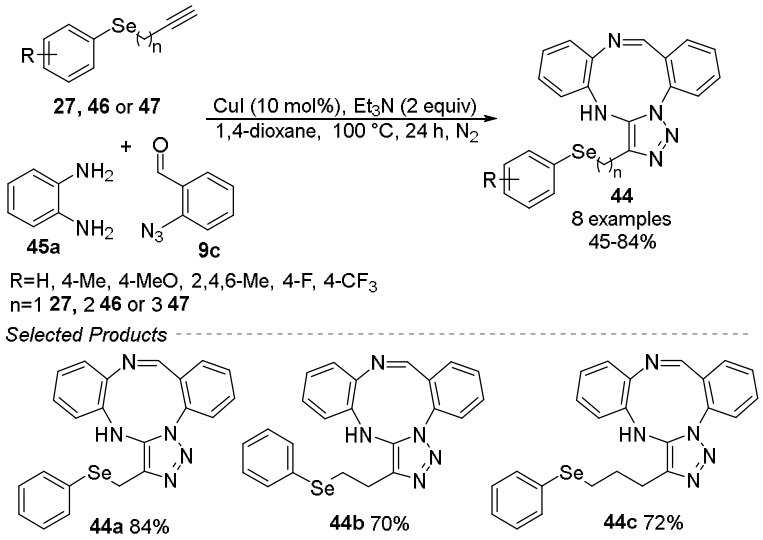


Scheme 20. Synthesis of selenium containing-1,2,3-triazole derivatives from quinone and substituted phenyl(prop-2-yn-1-yl)selenides.

Jacob and co-workers published the synthesis of (arylselanyl)- and (arylsulfenyl)-alkyl-1,2,3-triazolo-1,3,6-triazonines *via* a copper-catalyzed multicomponent reaction.[41] For the synthesis of arylselanylalkyl-1,2,3-triazolo-1,3,6-triazonines **44**, *o*-phenylenediamine **45a** was reacted with 2-azidobenzaldehyde **9c** and different arylchalcogenyl alkynes **27**, **46** or **47** using catalytic copper iodide (10 mol%), triethylamine (2 equiv) in 1,4-dioxane at 100 °C by 24 h (Scheme 21). Eight triazoles were obtained in 45-85% yield and some examples are demonstrated in Scheme 21.

The copper-catalyzed three-component reaction of ethynylstibanes **48**, organic azides **28**, and elemental selenium was described to afford novel selenides **49** and diselenides **50** containing 1,2,3-triazole rings. The reactions are performed in presence of CuI (10 mol%) as catalyst and 1,10-phenantroline (10 mol%) as a ligand in DMSO, at 40 °C to give nine different selenides **49** and for 1-5 h to give seven novel diselenides **50** (Scheme

22).[42] By using an antimony reagent, this one-pot reaction provides regioselective double Se-arylation under simple reaction conditions. The method was compatible with a series of aryl, alkyl and vinyl alkynes as well as differently functionalized azides and some of the compounds isolated are shown in Scheme 22.



Scheme 21. Synthesis of arylselanylalkyl-1,2,3-triazolo-1,3,6-triazonines **44** *via* multicomponent reaction.

In 2009, Benhida and co-workers[43] used an external selenium source to develop a method for preparing 4,5-functionalized triazoyl-nucleosides **51**. The azide-alkyne [1,3]-cycloaddition/electrophilic addition tandem reactions are the key procedure used in this efficient approach. Surprisingly, when PhSeBr **52a** was employed as the electrophile source in the reaction between alkyne **53a** and azido-nucleoside **54a**, a moderate yield of the expected 5-phenylselanyl-substituted triazole **51a** was attained. The authors related the poor reactivity of the electrophilic selenium species to the limited yield (Scheme 23).

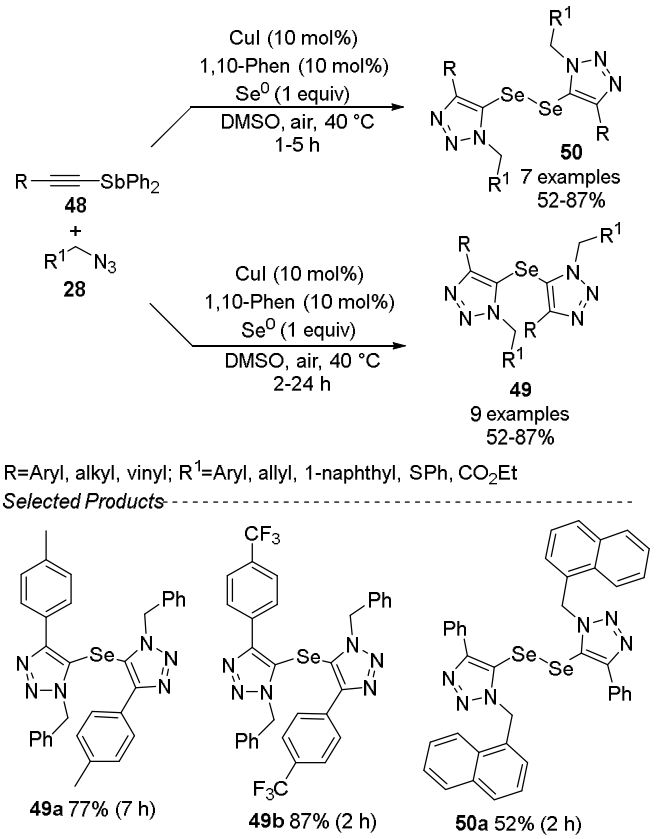
In 2018, Xu and co-workers[44] reported the copper-catalyzed decarboxylative/Click Cascade Reaction between propiolic acids **55**, diselenides **56**, and azides **28**, for the preparation of 1,4-disubstituted 5-arylselanyl-1,2,3-triazoles **57** (Scheme 24). This protocol affords thirtythree products from moderate to good yields and excellent regioselectivity by using $Cu(OAc)_2 \cdot H_2O$ (10 mol %), 1,10-Phen (20 mol %), K_2CO_3 (1.2 equiv), toluene, at 120 °C for 6 h. These reactions show the versatility of application of this protocol to various propiolic acids containing aromatic, heteroaromatic and aliphatic groups, as well as benzyl and alkyl azides. Additionally, the synthesized multisubstituted 5-seleno-1,2,3-triazoles **57a**, **57b**, and **57e** (Scheme 24) exhibited potent anticancer activities *in vitro*.

Wu and co-workers[45] described in 2019 the synthesis of diverse 5-thio- or 5-selenotriazoles under one-pot multicomponent reaction from elemental sulfur or selenium. This mild process involves reactions between alkynes **8**, benzyl and alkyl azides **28**, differently functionalized arylboronic acids, organohalide **58** or tosylate **59** and elemental sulfur to afford forty-one 5-thiotriazoles in 21-91% yield, or elemental selenium to afford thirteen 5-selenotriazoles **60** in 20-85% yield (Scheme 25). For the synthesis of the 5-selenotriazoles the reactions were carried or at 0 °C for 30 min, or at 25/50/70 °C for 2 h to overnight. It is important to point the good functional group compatibility and by this practical method is viable the functionalization of drugs and bioactive compounds.

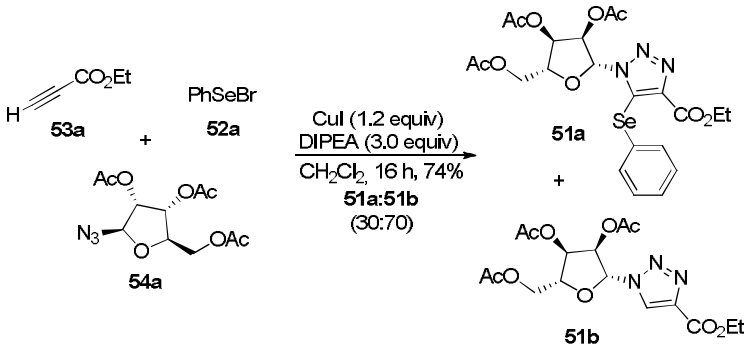
3. Organocatalysis

An alternative methodology to synthesize 1,2,3-triazoles was described by Narayana and co-workers[46] in 2008, employing organocatalysts instead of copper salts. The protocol involves the reaction between azides **9** and carbonyl compounds **61** in presence of catalytic amines to afford the corresponding 1,2,3-tiazole **10**

(Scheme 26). The advantages of this approach consist of minimizing the possible cytotoxicity of the molecules obtained for future pharmacological studies, due to the presence of copper catalyst residues.[47]



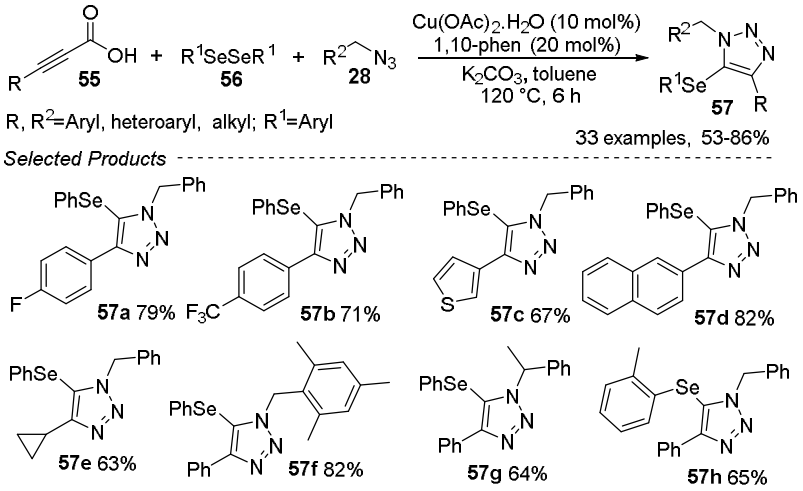
Scheme 22. Synthesis of selenides **49** and diselenides **50** containing 1,2,3-triazole rings.



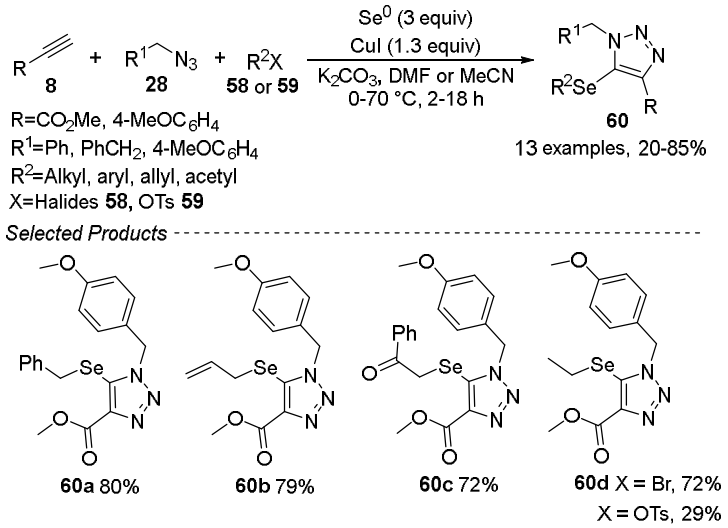
Scheme 23. Synthesis of the compounds **51a** and **51b**.

Based on recently published reports on organocatalytic enamine-azide [3+2]-cycloadditions employing organic azides as dipolarophiles, it is possible to describe a general mechanism for these reactions (Scheme

27). Firstly, the intermediate **I** is formed, after condensation of the amine with the carbonylic starting material **61**. A subsequent 1,3-dipolar cycloaddition between the enamine **I** and the organic azide **9** leads to the triazoline intermediate **II**, which can undergo a plausible 1,3-hydride shift to generate triazoline intermediate **III**. Intermediate **III** is then transformed into the zwitterionic intermediate **IV**, which undergoes an elimination reaction to regenerate organic catalyst (diethylamine, pyrrolidine or *N*,*N*'-dimethylpiperazine) to continue the catalytic cycle and produce the corresponding 1,2,3-triazole **10**.



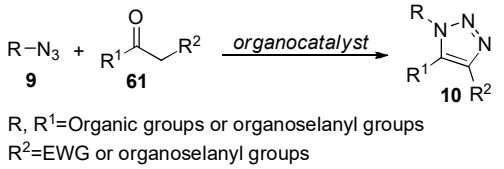
Scheme 24. Preparation of 1,4-disubstituted 5-arylselanyl-1,2,3-triazoles **57a-h**.



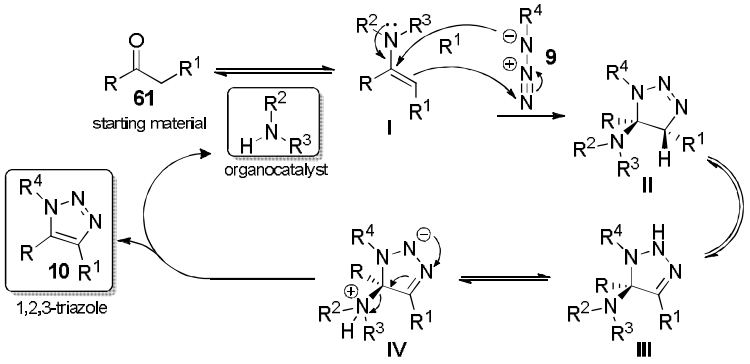
Scheme 25. Synthesis of 5-selenotriazoles **60** from alkynes **8**, azides **28** and differently functionalized organohalides **58**/tosylates **59**.

In this context, a series of new methodologies for the synthesis of 1,2,3-triazoles has been developed by several research groups. The works described in this section involve the use of azides and dicarbonylic

compounds bearing an organoselenium group as starting material to access 1,2,3-triazoles, or the organocatalyzed functionalization of 1,2,3-triazoles with organoselenium groups.



Scheme 26. Cu-catalyzed azido alkyne cycloaddition (CuAAC) reaction.



Scheme 27. General mechanism for the synthesis 1,2,3-triazoles **10** *via* organocatalysis.

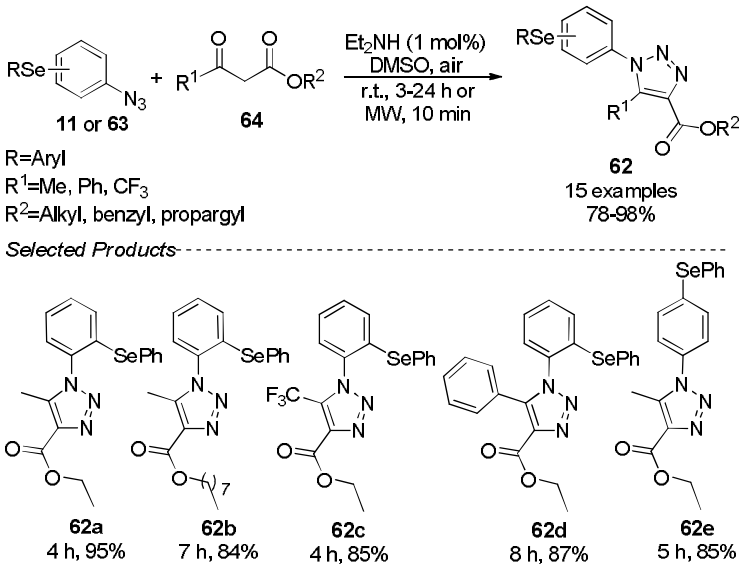
Starting from azides bearing an organoselenium substituent, in 2012, organocatalytic cycloaddition was used to access arylselanyl-1*H*-1,2,3-triazole-4-carboxylate **62**. For this study, azidophenyl arylselanides **11** or **63** were reacted with a range of substituited *β*-ketoesters **64**.[48] The reaction condition is simple, mild and occurs in the presence of 1 mol% of diethylamine as an organocatalyst, DMSO as a solvent, at room temperature from 3 to 24 h (Scheme 28). By this protocol, aromatic azides containing electron-donating and electron-withdrawing groups were successful employed and fourteen 1,2,3-triazoles bearing an organoselenium moiety were isolated after 3-8 h of reaction (78-98% yield). When *tert*-butyl 3-oxobutanoate was reacted, the corresponding product was obtained in 89% yield after 24 h of reaction. It is important to point that when azidophenyl arylselanide was reacted with 3-oxo-3-phenylpropanenitrile, by using 10 mol% of diethylamine, the corresponding 1,2,3-triazole was isolated in 91% yield (18 h). Furthermore, three reactions were performed under microwave irradiation (MW) at 70 °C by 10 min to give the desired products in 90-94% yield.

Later on, a similar condition was developed, but this time using *β*-oxoamide **65** instead of the *β*-keto-esters.[49] The cycloaddition reactions were performed by using 5 mol% of diethylamine to access fourteen different (arylselanyl)phenyl-1*H*-1,2,3-triazole-4-carboxamides **66** in 59-87% yield after 2-5 h (Scheme 29). When *β*-oxo amide **65a**, containing an electron-withdrawing group (-CF_3) adjacent to the oxo group, was reacted with azidophenyl arylselenide **11** or **63**, it was necessary to heat the reaction to 70 °C to produce the 1,2,3-triazole **66a** in 65% yield.

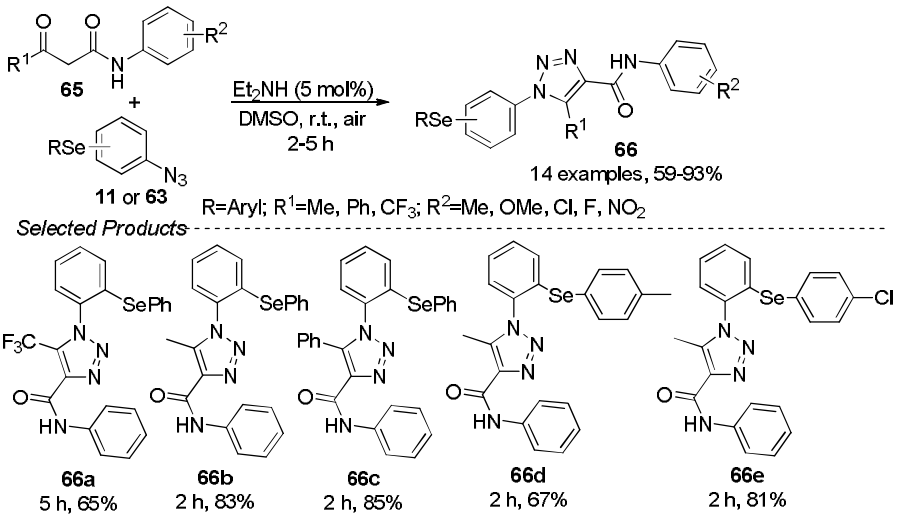
In 2017, the Alves's group[50] described the synthesis of *N*-aryl-1,2,3-triazoyl carboxamides using Et_2NH (5 mol%) as catalyst in DMSO as solvent under US irradiation (40% of amplitude) at room temperature for 15 min. Eighteen 1,2,3-triazoles were prepared in high yields (72-95%) by the reaction between *β*-oxo amides and aryl azides containing neutral, electron-withdrawing and electron-donating groups. Interestingly, under this condition, the selanyl-1,2,3-triazoles was obtained in 91% yield.

Focusing on the development of new 1,2,3-triazoles bearing organoselenium moieties, the sonochemistry was employed in the organocatalytic enamine-azide [3+2]-cycloaddition between 1,3-diketones **67** and aryl azidophenyl selenides **11** or **63**.[51] The condition involved the use of the system

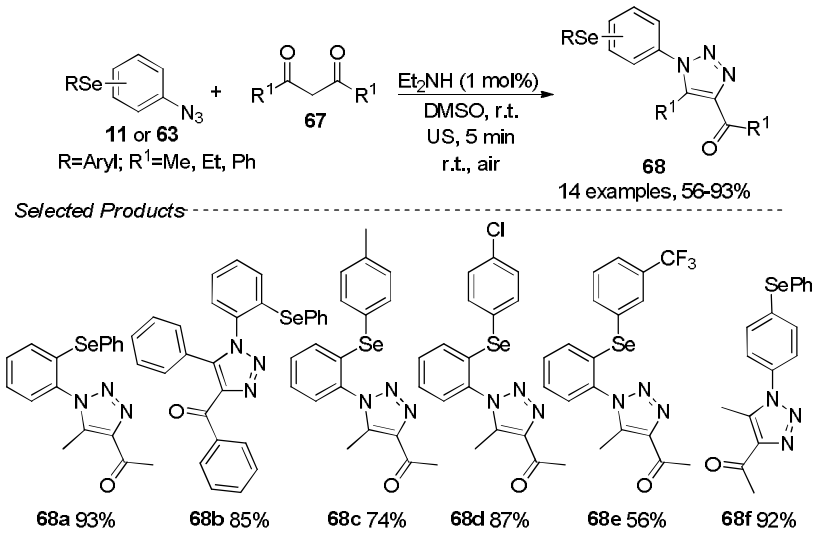
Et_2NH (1 mol%)/DMSO under ultrasound irradiation (US, 40% of amplitude) at room temperature for just 5 min to synthetize 14 selanyl-1,2,3-triazoles **68** in 56-93% yield. This protocol was extended to β-keto-esters, β-ketoamides and α-cyano-ketones, leading to the desired products **68** in 65-90% yield (Scheme 30). As comparison, when the mixture of substrates **11a** and **67a** were reacted at room temperature in the presence of Et_2NH and DMSO, the expected product **68a** was obtained in 98% yield after 2 h under conventional stirring system. The diketones 2,2,6,6-tetramethylheptane-3,5-dione and cyclohexane-1,3-dione did not react using this method.



Scheme 28. Synthesis of arylselanyl-1*H*-1,2,3-triazole-4-carboxylate **62**.



Scheme 29. Preparation of (arylselanyl)phenyl-1*H*-1,2,3-triazole-4-carboxamides **66**.



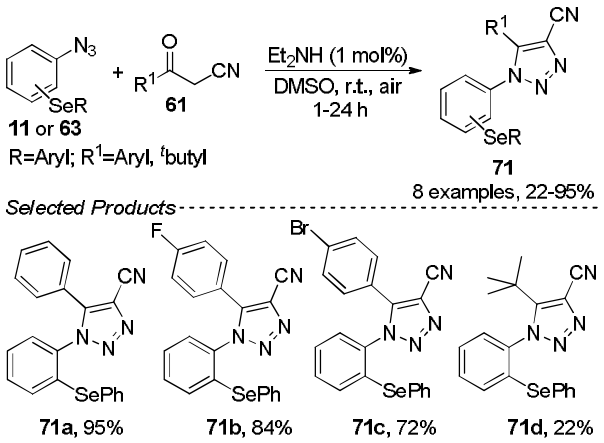
Scheme 30. Synthesis of selanyl-1,2,3-triazoles **68** from 1,3-diketones **67** and aryl azidophenyl selenides **11** or **63**.

In 2015 it was described the use of pyrrolidine in the organocatalytic cycloaddition of azides with *β*-ketosulfones to access twenty-two new sulfonyl-1,2,3-triazoles in presence of DMSO, at room temperature for 24 h.[52] A wide variety of aryl azides was employed and, in particular, the reaction between the 1-phenyl-2-(phenylsulfonyl)ethan-1-one **69a** and the (2-azidophenyl)(phenyl)selenide **11a** to form the triazole **70a** (83% yield) is highlighted (Scheme 31). This reaction was the only example involving an azide containing an organoselanyl group.

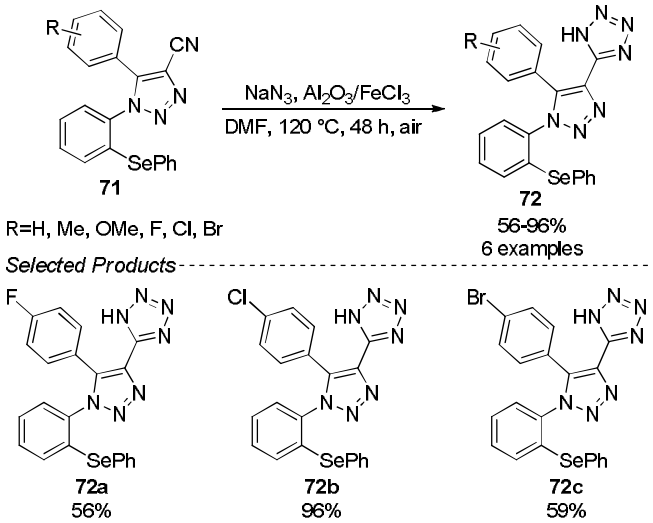
Scheme 31. Use of system pyrrolidine/DMSO in the preparation of the triazole **70a.**

In another study, the same group described the synthesis, antioxidant properties and chemical diversification of phenylselanyl-1*H*-1,2,3-triazole-4-carbonitriles **71** (Scheme 32).[53] Initially eight examples were obtained from 22 to 95% yield using triethylamine (1 mol%) and DMSO as a solvent at room temperature for 1-2 h. Under this condition was performed a series of cycloaddition reactions between 2-azidophenyl phenylselenide **11** or **63** and *α*-ketonitriles **61**. The only reaction performed in presence of a 4-azidophenyl phenylselenide led to a mixture of regioisomers in 5:1 (90% yield). In general, no electronic effects of substituents in the aromatic ring were observed, however, the yield was reduced when 4,4-dimethyl-3-oxopentanenitrile was used (22%) even after 24 h at 70 °C. The synthesized compounds were screened for their *in vitro* antioxidant activity and 5-phenyl-1-[2-(phenylselanyl)phenyl]-1*H*-1,2,3-triazole-4-carbonitrile **71a** exhibited the highest antioxidant effect in different *in vitro* assays.

Lastly, the selanyltriazoyl carbonitriles **71** were readily manipulated to yield bifunctional hybrids selanyl-triazoyl tetrazoles **72** by reaction with NaN_3 in $Al_2O_3/FeCl_3$ as a catalytic system. The reactions were performed in presence of DMF at 120 °C for 48 h to give six new selanyltriazoyl tetrazole **72** in 56-96% yield (Scheme 33).



Scheme 32. Synthesis of phenylselanyl-1*H*-1,2,3-triazole-4-carbonitriles **71**.

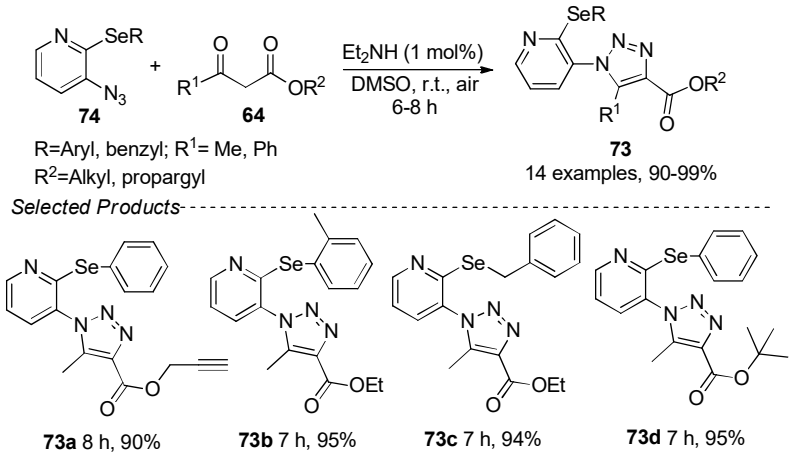


Scheme 33. Synthesis of bifunctional hybrids selanyltriazoyl tetrazoles **72**.

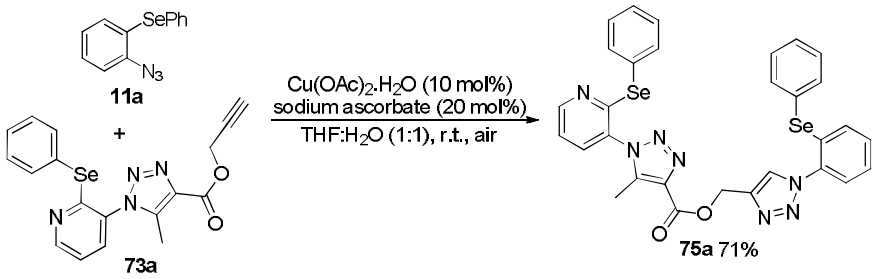
In 2017 the system Et_2NH/DMSO/r.t. was used to access 1-[2-(organylselanyl)pyridin-3-yl]-1*H*-1,2,3-triazole-4-carboxylate derivatives **73** through the reaction between 3-azido-2-organylselanyl-pyridines **74** and 1,3-dicarbonyl compounds **64** (Scheme 34).[54] By this protocol fourteen different substituted 2-(organylselanyl)-3-triazole-pyridines were prepared in 90-99% yield in 6-8 h. The reaction is not sensitive to electronic effects in the aromatic ring of the 3-azido-2-selanylpyridine **74** or in the dicarbonyl substituents **64** and excellent yields were obtained for all performed examples. In addition, to explore their synthetic application, the compound **73d** was used in a Cu-catalyzed azido alkyne cycloaddition (CuAAC) reaction. In this way, **73d** was reacted with (2-azidophenyl)(phenyl)selenide **11a**, using $Cu(OAc)_2.H_2O$ (10 mol%), sodium ascorbate (20 mol%) and a mixture of THF/H_2O (1:1) as solvent. The new triazolic core **75a** was isolated in 71% yield after total consumption of the starting materials monitored by TLC (Scheme 35).

The use of dicarbonylic compounds bearing an organoselenium substituent is other important strategy to access 1,2,3-trtiazoles under organocatalytic conditions. This way, Alves and co-workers[55] demonstrated the synthesis of 7-chloroquinoline-1,2,3-triazoyl carboxylates **76a** with antioxidant properties from

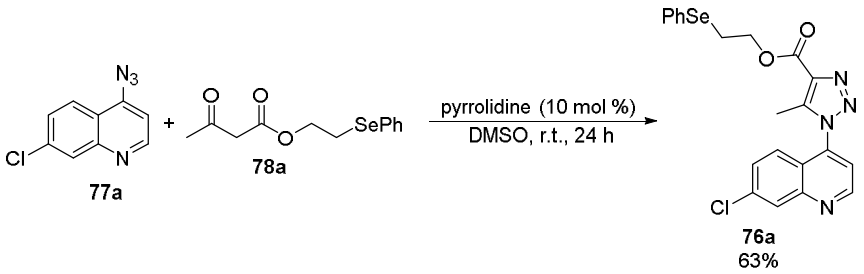
4-azido-7-chloroquinoline **77a** and *β*-ketoester **78a**. By using pyrrolidine (10 mol%) as organic catalyst and DMSO as solvent, eleven products were isolated in 41-98% yield after 24-48 h. When a *β*-ketoester containing an organoselanyl portion **78a** was employed, the corresponding triazole **76a** was obtained in 63% yield after 24 h of reaction time (Scheme 36).



Scheme 34. Use of system Et_2NH/DMSO to access 1-[2-(organylselanyl)pyridin-3-yl]-1*H*-1,2,3-triazole-4-carboxylate derivatives **73**.



Scheme 35. Cu-catalyzed azido alkyne cycloaddition (CuAAC) reaction.



Scheme 36. Synthesis of 7-chloroquinoline-1,2,3-triazoyl carboxylate **76a** under organocatalyst.

4. Conclusion

The number of studies on the synthesis of hybrid selenium-containing compounds has expanded considerably in recent years, due to their pharmacological effects and prospective applications in materials science. In this chapter, we have demonstrated how copper-catalyzed and organocatalyzed cycloadditions may

be used to generate densely functionalized selanyl-1,2,3-triazoles with great molecular variety and complexity. Under mild reaction conditions, the cooper-catalyzed cycloaddition reaction between suitably selenium-functionalized azides and terminal alkynes provides for the construction of a range of hybrid compounds in good to excellent yields. Furthermore, enamino-azide cycloaddition methods were carried out using a variety of carbonyl compounds and substituted organic azides, yielding selenium containing 1,2,3-triazoles with great selectivity and excellent yields. The metal-free methods prove to be an efficient way to synthesize more complexes structures of selenium containing 1,2,3-triazoles.

Acknowledgements

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References

1. Dehaen, W.; Bakulev, V. A. in *Chemistry of 1,2,3-Triazoles*. Topics in Heterocycle Chemistry 40, Springer Cham Heidelberg New York Dordrecht London **2015**, ISBN 978-3-319-07962-2 (eBook), DOI 10.1007/978-3-319-07962-2.
2. Bozorov, K.; Zhao, J.; Aisa, H. A. *Bioorg. Med. Chem.* **2019**, *27*, 3511-3531.
3. Alves, D.; Goldani, B.; Lenardão, E. J.; Perin, G.; Schumacher, R. F.; Paixão, M. W. *Chem. Rec.* **2018**, *18*, 527-542.
4. Forezi, L. S. M.; Lima, C. G. S.; Amaral, A. A. P.; Ferreira, P. G.; de Souza, M. C. B. V.; Cunha, A. C.; da Silva, F. C.; Ferreira, V. F. *Chem. Rec.* **2021**, *21*, 1-27.
5. Surineni, G.; Yogeeswari, P.; Sriram, D.; Kantevari, S. *Med. Chem. Res.* **2015**, *24*, 1298-1309.
6. Dong, H.-R.; Wu, J.-G. *Heterocycl. Commun.* **2018**, *24*, 109-112.
7. Dasari, S. R.; Tondepu, S.; Vadali, L. R.; Seelam, N. *J. Heterocycl. Chem*. **2019**, *56*, 1318-1329.
8. Keri, R. S.; Patil, S. A.; Budagumpi, S.; Nagaraja, B. M. *Chem. Biol. Drug Des.* **2015**, *86*, 410-423.
9. Gonzaga, D. T. G.; Souza, T. M. L.; Andrade, V. M. M.; Ferreira, V. F.; da Silva, F. C. *Med. Chem.* **2018**, *14*, 242-248.
10. Giacobbe, D. R.; Bassetti, M.; De Rosa, F. G.; Del Bono, V.; Grossi, P. A.; Menichetti, F.; Pea, F.; Rossolini, G. M.; Tumbarello, M.; Viale, P.; Viscoli, C. *Expert Rev. Anti Infect. Ther.* **2018**, *16*, 307-320.
11. Santella, P. J.; Tanrisever, B. *Drugs Exp. Clin. Res.* **1985**, *11*, 441-445.
12. Santi, C. *Organoselenium Chemistry: Between Synthesis and Biochemistry*; Santi, C., Ed.; Bentham Science: Sharjah U. A. E., **2014**.
13. Lenardão, E. J.; Santi, C.; Sancineto, L.; *New Frontiers in Organoselenium Compound*; Springer: Cham, Switzerland, **2018**.
14. Jain, V. K.; Priyadarsini, K. I.; *Organoselenium Compounds in Biology and Medicine Synthesis, Biological and Therapeutic Treatments*; Royal Society of Chemistry: London, UK, **2017**.
15. Lenardão, E. J.; Santi, C.; Perin, G.; Alves, D. *Organochalcogen Compounds: Synthesis, Catalysis and New Protocols with Greener Perspectives*. Elsevier, eBook ISBN: 9780128194508.
16. Orian, L.; Toppo, S. *Free Radical Biol. Med.* **2014**, *66*, 65-74.
17. Parnham, M. J.; Kindt, S. *Biochem. Pharmacol*. **1984**, *33*, 3247-3250.
18. Fu, J.-N.; Wang, J.-Y.; Wang, L.-H.; Wang, L.; Tang, W.-C.; Cai, G.-X.; Liu, M.; Zeng, H.-H. *J. Chin. Pharm. Sci*. **2010**, *19*, 163-168.
19. Wirth, T. *Organoselenium Chemistry: Synthesis and Reactions*. Wiley-VCH Verlag GmbH & Co. KGaA, **2012**.
20. Santi, C.; Santoro, S.; Battistelli, B. *Curr. Org. Chem.* **2010**, *14*, 2442-2462.
21. Back,T. G.; Bethell, R. J.; Parvez, M.; Taylor, J. A.; Wehrli, D. *J. Org. Chem.* **1999**, *64*, 7426-7432.
22. Tiecco, T.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Angew. Chem. Int. Ed.* **2003**, *42*, 3131-3133.
23. Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057-3062.
24. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596-2599.
25. Hin, J. E.; Fokin, V. V. *Chem. Soc. Rev*. **2010**, *39*, 1302-1315.

26. M. Meldal, C. W. Tornøe, *Chem. Rev.* **2008**, *108*, 2952-3015.
27. Deobald, A. M.; Camargo, L. R. S.; Hörner, M.; Rodrigues, O. E. D.; Alves, D.; Braga, A. L. *Synthesis* **2011**, *15*, 2397-2406.
28. Xavier, M. C. D. F.; Xavier, D. M.; Seus, N.; Lenardão, E. J.; Perin, G.; Alves, D. *Curr. Microwave Chem.* **2016**, *3,* 14-23.
29. Schumacher, R. F.; Von Laer, P. B.; Betin, E. S.; Cargnelutti, R.; Perin, G.; Alves, D. *J. Braz. Chem. Soc.* **2015**, *26*, 2298-2306.
30. Seus, N.; Saraiva, M. T.; Alberto, E. E.; Savegnago, L.; Alves, D. *Tetrahedron* **2012**, *68*, 10419-10425.
31. Wang, Q.; Sheng, W.; Sheng, S.; Li, Y.; Cai, M. *Synth. Commun.* **2014**, *44*, 59-67.
32. Cruz, E. H. G.; Silvers, M. A.; G. A. M. Jardim, Resende, J. M.; Cavalcanti, B. C.; Bomfim, I. S.; Pessoa, C.; Simone, C. A.; Botteselle, G. V.; Braga, A. L.; Nair, D. K.; Namboothiri, I. N. N.; Boothman, D. A.; da Silva Júnior, E. N. *Eur. J. Med. Chem.* **2016**, *122*, 1-16.
33. Saraiva, M. T.; Seus, N.; Souza, D.; Rodrigues, O. E. D.; Paixão, M. W.; Jacob, R. G.; Lenardão, E. J.; Perin, G.; Alves, D. *Synthesis* **2012**, *44*, 1997-2004.
34. Chipoline, I. C.; Brasil, B. F. A. B.; Neto, J. S. S.; Valli, M.; Krogh, R.; Cenci, A. R.; Teixeira, K. F.; Zapp, E.; Brondani, D.; Ferreira, L. L. G.; Andricopulo, A. D.; Oliveira, A. S.; Nascimento, V. *Eur. J. Med. Chem.* **2022**, *243*, 114687.
35. Panaka, S.; Trivedi, R.; Jaipal, K.; Giribabu, L.; Sujitha, P.; Kumar, C. G.; Sridhar, B. *J. Organomet. Chem.* **2016**, *813*, 125-130.
36. Stefani, H. A.; Leal, D. M.; Manarin, F. *Tetrahedron Lett.* **2012**, *53*, 6495-6499.
37. Kumar, S.; Saleem, F.; Singh, A. K. *Dalton Trans.* **2016**, *45*, 11445-11458.
38. Begini, F.; Balaguez, R. A.; Larroza, A.; Lopes, E. F.; Lenardão, E. J.; Santi, C.; Alves, D. *Molecules* **2021**, *26*, 2224.
39. Perin, G.; Goulart, H. A.; Soares, L. K.; Peglow, T. J.; Schumacher, R. F.; Pinz, M. P.; Reis, A. S.; Luchese, C.; Wilhelm, E. A. *Appl. Biochem. Biotechnol.* **2019**, *187*, 1398-1423.
40. Jardim, G. A. M.; Cruz, E. H. G.; Valença, W. O.; Lima, D. J. B.; Cavalcanti, B. C.; Pessoa, C.; Rafique, J.; Braga, A. L.; Jacob, C.; Júnior, E. N. S. *Molecules* **2018**, *23*, 83.
41. Aquino, T. B.; Nascimento, J. E. R.; Dias, I. F. C.; Oliveira, D. H.; Barcellos, T.; Lenardão, E. J.; Perin, G.; Alves, D.; Jacob, R. G. *Tetrahedron Lett.* **2018**, *59*, 1080-1083.
42. Yamada, M.; Matsumura, M.; Sakaki, E.; Yen, S.-y.; Kawahata, M.; Hyodo, T.; Yamaguchi, K.; Murata, Y.; Yasuike, S. *Tetrahedron* **2019**, *75*, 1406-1414.
43. Malnuit, V.; Duca, M.; Manout, A.; Bougrin, K.; Benhida, R. *Synlett* **2009**, *13*, 2123-2128.
44. Cui, F. H.; Chen, J.; Mo, Z. -Y.; Su, S. -X.; Chen, Y. -Y.; Ma, X. -L.; Tang, H. -T.; Wang, H. -S.; Pan, Y. -M.; Xu, Y. -L. *Org. Lett.* **2018**, *20*, 925-929.
45. Zhang, L.-L.; Li, Y.-T.; Gao, T.; Guo, S.-S.; Yang, B.; Meng, Z.-h.; Dai, Q.-P.; Xu, Z.-B.; Wu, Q.-P. *Synthesis* **2019**, *51*, 4170-4182.
46. Ramachary, D. B.; Ramakumar, K.; Narayana, V. V. *Chem. Eur. J*. **2008**, *14*, 9143-9147.
47. Yoon, H, Y.; Lee, D.; Lim, D.-K.; Koo, H.; Kim, K. *Adv. Mater*. **2022**, *34*, e2107192.
48. Seus, N.; Gonçalves, L. C.; Deobald, A. M.; Savegnago, L.; Alves, D.; Paixão, M. W. *Tetrahedron* **2012**, *68*, 10456-10463.
49. Seus, N.; Goldani, B.; Lenardão, E. J.; Savegnago, L.; Paixão, M. W.; Alves, D. *Eur. J. Org. Chem*. **2014**, *5*, 1059-1065.
50. Xavier, D. M.; Goldani, B. S.; Seus, N.; Jacob, R. G.; Barcellos, T.; Paixão, M. W.; Luque, R.; Alves, D. *Ultrason. Sonochem.* **2017**, *34*, 107-114.
51. Costa, G. P.; Seus, N.; Roehrs, J. A.; Jacob, R. G.; Schumacher, R. F.; Barcellos, T.; Luque, R.; Alves, D. *Beilstein J. Org. Chem.* **2017**, *13*, 694-702.
52. Saraiva, M. T.; Costa, G. P.; Seus, N.; Schumacher, R. F.; Perin. G.; Paixão, M. W.; Luque, R.; Alves, D. *Org. Lett.* **2015**, *17*, 6206-6209.
53. Savegnago, L.; Sacramento, M.; Brod, L.; Fronza, M. G.; Seus, N.; Lenardão, E. J.; Paixão, M. W.; Alves, D. *RSC Adv.* **2016**, *6*, 8021-8031.
54. Duarte, L. F. B.; Nascimento, J. E.; Perin, G.; Luque, R.; Alves, D.; Schumacher, R. F. *ChemistrySelect* **2017**, *2*, 6645-6649.

55. Saraiva, M. T.; Krüger, R.; Baldinotti, R. S. M.; Lenardão, E. J.; Luchese, C.; Savegnago, L.; Wilhelm, E. A.; Alves, D. *J. Braz. Chem. Soc.* **2016***, 27*,41-53.