Review

Recent Approaches in Transition Metal-Catalyzed Chalcogenative Heteroannulation of Alkenes and Alkynes

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Abstract: Organochalcogen-bearing heterocycles are important scaffolds in compounds under the spotlight of scientific interest in optoelectronic fields and for biological applications. The use of transition metals has been a versatile and reliable way to carry out the synthesis of these molecules efficiently, delivering products in high yields and with a wide functional diversity. In the last 10 years, many classes of heterocycles have been synthesized under the cyclization reaction of acyclic alkenes and alkynes with the incorporation of a chalcogen atom on its structure. Transition metal catalysts including Cu, Co, Pd, Ni, In, Ag, and Fe salts have been used in the development of new methodologies, the expansion of substrate scope, and mechanistic studies. This review provides an overview of these recent approaches with the aim of being a useful resource for interested researchers in this area.

Keywords: catalysis; cyclization reaction; heterocycles; organochalcogen; transition metal

1. Introduction

The use of transition metal-catalyzed carbon-carbon and carbon-heteroatom bonds has long been considered a powerful and efficient tool in heterocycle synthesis. This strategy enables the efficient construction from simple to complex heterocyclic structures starting from acyclic materials [1,2]. In this context, the use of cheap, clean, and efficient catalytic systems to access heterocyclic compounds is always desired to design new bioactive compounds, functional materials, agrochemicals, or to synthesize naturally occurring molecules [3,4]. Transition metals have enabled the preparation of heterocyclic structures bearing a broad range of functionalities, in high selectivity and high yields [5–7]. Conventional metals used for this purpose include palladium, copper, iron, and ruthenium, which facilitate key transformations, including C-H or C-heteroatom bond activation, coordination to double and triple bond facilitating cyclization, and functional group manipulations [8–10]. The earliest traditional methods involving metals for the construction of new chemical bonds experienced several drawbacks, such as the need for stoichiometric amounts, low selectivity and efficiency, limited scope, and many side reactions. Over the past years, several advances have been reached to overcome these problems, further expanding the synthetic utility of catalytic systems. The development and use of innovative ligands, optimization of the reaction conditions, and the use of continuous methods or alternative energy sources are recent contributions in this area [11,12].

The preparation of organic chalcogenide compounds has experienced considerable breakthroughs in recent years. These compounds exhibit interesting physical, chemical, and biological properties which motivate studies from synthetic organic chemists and the pharmaceutical industry [13]. In addition, due to their unique physical and chemical...
properties, many of these compounds have been used as versatile building blocks in the synthesis of complex organic molecules, biologically active compounds, pharmaceuticals, and natural products [14–16]. From the viewpoint of biological activities, organochalcogen compounds are known by their antioxidant [17,18], antitumoral [19–21], antimicrobial [22,23], and anti-inflammatory activities [24]. Several are heterocyclic systems containing sulfur on its structure available as FDA-approved drugs [25,26]. On the other hand, organoselenium and organotellurium derivatives display unique reactivity profiles, making them valuable as catalysts, ligands, and intermediates in synthetic methodologies [27–29]. In sum, the interesting properties presented by organochalcogen compounds offer wide research opportunities, considering the design of small molecules presenting pharmacological activity and toxicological safety to new materials.

The heterocyclization of alkenes and alkynes by using halogen- [30–33] or chalcogen-based electrophiles [34,35], or under photocatalysis and electrochemistry conditions involving radical intermediates, has been well documented [36,37]. Traditionally, these cyclization reactions are conducted for alkenes and alkynes neighboring nucleophilic substituents at an appropriate position, which can limit the applicability as most of them are not readily available starting materials, owing to its obtaining of a transition-metal catalysis in at least one reaction step. Although most of them are reliable methodologies, the unique reactivity and capacity of transition-metals to form C-C and C-Heteroatom bonds have not yet been overcome by the metal-free approaches. So, this review article intends to provide the readers with a comprehensive overview on the recent approaches to transition metal-catalyzed chalcogenative heterocyclization reactions, covering research articles published in the last ten years. The most common chalcogen-containing heterocycles explored in this review belong to five, six, and seven membered rings including N-, O-, S-, and Se-heterocycles (Scheme 1). This manuscript is organized into reactions catalyzed by transition metals, including copper, cobalt, iron, palladium, silver, indium, and nickel. Synthetic methodologies for the chalcogenative cyclization of alkenes and alkynes carried out with stoichiometric amounts of these substances are not covered in this review.

Scheme 1. Overview of transition metal-catalyzed chalcogenative heterocyclization reactions.

2. Transition Metal-Catalyzing Chalcogenative Heteroannulation

2.1. Using Copper as Catalyst

The chemistry of copper in organic synthesis is extremely rich and abundant, representing a significant field of research that is under constant development. The low cost, high abundance, high functional group tolerance, and capacity of copper to vary its oxidation state may represent attractive aspects involved in the application as a catalyst in cyclization reactions. The synthesis of a plethora of heterocyclic compounds by the copper-catalyzed chalcogen-chalcogen bond cleavage of disulfides or diselenides and the subsequent transfer of the ensuing chalcogen species to activated alkenes or alkynes is described. In this way, the use of copper catalysts represents a powerful synthetic tool to afford different classes of N-, O-, and Chalcogen-based heterocycles bearing an organochalcogen group.

2.1.1. N-Based Heterocycles
The synthesis of spiro[4.5]trienones 1 via sequential C-Chalcogen bond formation, ipso-cyclization, and dearomatization of N-(p-methoxyaryl)propiolamides catalyzed by CuCl₂ (10 mol%) has been reported (Scheme 2) [38]. The optimal conditions still include the use of O₂ atmosphere and H₂O (2 equiv.) in DMF as solvent at 100 °C for 24 h. The substrate scope covered diverse N-arylpropiolamides and diaryldisulfides containing halogen, alkyl, alkoxy, and nitrile as substituents, providing the spirocycles in yields ranging from 41% to 95%. Despite the broad scope and group compatibility, limitations on product formation were observed for alkyl-substituted terminal alkyne and in the presence of a free N-H group.

![Scheme 2. Synthesis of 3-(arylsulfanyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-diones 1.](image)

The synthesis of 2-(chalcogenyl)indolizines 2 by copper-catalyzed chalcogenative cyclization of propargyl pyridines has been reported by Zeni and coworkers (Scheme 3) [39]. This protocol demonstrated the reaction of propargyl pyridines with diorganyl dichalcogenides via copper(I) iodide (20 mol%) catalysis in the presence of Na₂CO₃ as a base, and DMF as a solvent at 60 °C. This strategy was compatible with several propargyl pyridines bearing both acetate and carbonate groups directly bonded to the propargylic carbon, providing 2-chalcogenylindolizines 2 via 5-endo-dig cyclization by copper selenolate species activating the C-C triple bond to the anti-attack of the nitrogen atom of the pyridine nucleus. Moreover, differently substituted diorganyl diselenides and ditellurides were used, which delivered the target products in moderate to excellent yields. Exceptionally, when a terminal propargylpyridine was used to react with diphenyl diselenide, the coupling of two phenylselenyl groups at positions 2 and 3, in the indolizine structure was observed. In addition, the synthetic applicability of the Csp²-tellurium bond on some 2-(butyltellurenyl)indolizines has been successfully evaluated in palladium-catalyzed Suzuki-type cross-coupling reactions.

![Scheme 3. Synthesis of 2-(chalcogenyl)indolizines 2.](image)
A novel copper-catalyzed oxidative alkene chalcogenofunctionalization starting from alkenyl N-Ts-protected amines and diorganyldichalcogenides in the presence of CuBr₂ (10 mol%) as a catalyst was reported by Zhong and co-workers (Scheme 4) [40]. The substrate scope covered the synthesis of diverse indolines, tetrahydroquinolines, pyrrolines, and piperidines highly functionalized 3 in good to excellent yields. Furthermore, diorganyldisulfides and diselenides were used as a stable and highly available chalcogen source, which were well tolerated under optimal conditions and produced N-heterocycles 3 by exo-trig cyclization form. Still, the highlight of this methodology is the use of an inexpensive catalytic system based on copper(II) bromide and air oxygen as the oxidant.

![Scheme 4. Chalcogenative cyclization of alkenyl amines catalyzed by CuBr₂.](image)

In 2019, Reddy and co-workers described the open-air synthesis of organochalcogenylated nicotinate derivatives by Cu-catalyzed intramolecular chalcogenamination reaction [41]. The one-pot aza-annulation of (E)-2-en-4-ynyl azides—which are readily prepared from the corresponding Morita–Baylis–Hillman acetate of acetylenic aldehydes—in the presence of diorganyldiselenides or disulfides and CuCl₂ (5 mol %) as the Cu(II) catalyst source provided direct access to a series of twenty-three structurally diverse 5-selenyl/sulfenyl nicotinates 4 in moderate to excellent yields (44–98%) (Scheme 5). Both electron-donating and electron-withdrawing groups were well-tolerated, demonstrating the versatility of this mild protocol.

![Scheme 5. Synthesis of 5-organochalcogenated nicotinate derivatives 4.](image)

The proposed reaction mechanism is based on the activation of diorganyldichalcogen by the copper salt (Scheme 6). Polarization of the chalcogen–chalcogen bond to a Cu(II) complex promotes electrophilic regioselective addition to the alkyne moiety followed by intramolecular nucleophilic azide attack I (Scheme 6). Subsequent deprotonation of intermediate II leads to the desired nicotinate product 4 and seleno- or thiophenol, which promptly oxidizes to its corresponding diselenide/disulfide, completing the catalytic cycle.
A series of selenium-containing fluorinated γ-lactams 5 were synthesized by Sun, Zhang, and co-workers through Cu(I)-catalyzed radical cascade selenodifluoromethylation of N-allylphenylacetamides [42]. Using CuI/phenantroline as the catalytic system and diaryl, dialkyl, or diheteroaryl diselenides as the organochalcogen source, nineteen selenium-containing α,α-difluoro-γ-lactams 5 were prepared in moderate to excellent yields (46–91%) (Scheme 7).

Based on control experiments, a possible radical cascade cyclization mechanism was proposed. First, Cu(I) and N-allylphenylacetamide react via an SET (single-electron transfer) process producing Cu(II) species and the difluoroalkyl radical intermediate III (Scheme 8). Then, the cycle proceeds toward a 5-exo-trig cyclization, leading to the radical intermediate IV, which is captured by the diorganyl diselenide to yield the desired product 5 and a selanyl radical. The latter is eventually reduced to selanyl bromide (RSeBr) and Cu(II) to Cu(I) to re-enter into the catalytic cycle.
Scheme 8. Proposed radical cascade mechanism for the synthesis of 5.

A series of polysubstituted 3-chalcogenated indoles 6 were synthesized by Liu and co-workers (2019) via a Cu-catalyzed multicomponent one-pot reaction involving Sonogashira coupling reaction, N-cyclization, and electrophilic sulfenyl/selanyl substitution [43]. Using N-(2-bromophenyl)trifluoroacetamides, an aryl or alkyl alkyne, diorganyl diselenide/disulfide, and CuI/proline as the catalyst system, the indole target products 6 were obtained in 65–96% yield (Scheme 9).


Two possible catalytic routes were proposed for this reaction (Scheme 10). First, the Cu-acetylide intermediate V is formed by the reaction of terminal alkyne with copper complex. Then, the in situ generated copper-acetylide reacts with aryl bromide to form the transition state VI leading to the key coupling intermediate VII, while the dichalcogen is oxidized to the corresponding cationic species. For pathway A, trifluoroacetyl-promoted annulation leads to the target 3-chalcogenated indole product 6. For pathway B, the coupling intermediate VII undergoes intramolecular cyclization to afford an indole anion that traps the cationic chalcogen species, leading to the N-heterocycle product 6.


In 2020, Sarkar and co-workers developed an interesting two-component Cu(I)-catalyzed regioselective cyclization cascade strategy for the synthesis of diorgano-chalcogenyl-substituted indolizinones 7 from a wide variety of substituted pyridine homologated ynones [44]. All reactions were carried out at room temperature and open-air atmosphere using CuI (10 mol %) as the catalyst and diorganyl dichalcogenides as the chalcogen source. Under these conditions, the desired chalcogen-decorated indolizinones 7 were obtained in high to excellent yields (80 to 96%) (Scheme 11).
The proposed reaction mechanism starts with formation of the dinuclear diorganochalcogen-Cu(III) complex, which is the species involved in the activation of starting ynone. The intramolecular 5-exo-dig ring annulation followed by the reductive elimination of VIII furnishes the mono-organochalcogen-indolizinone intermediate IX, which had the acidic hydrogen exchanged by iodine with the aid of base, affording X. Finally, subsequent oxidative addition of the Cu(III)–organochalcogen species followed by reductive elimination leads to the target product 7 (Scheme 12).
of cyanoalkylsulfonylated pyrrolidines 8 in moderate to good yields (34–92%) (Scheme 13) [45]. This mild protocol provided direct access to twenty-eight organoselenated pyrrolidines 8 employing CuOAc (10 mol%) as Cu(I) source and DCE as the solvent at 80 °C, demonstrating high functional group compatibility.

\[
\begin{align*}
\text{R}^1 &= \text{H, aryl; } \text{R}^2, \text{R}^3, \text{R}^4 = \text{aryl; R}^5 = \text{H, OBn, aryl, alkyl} \\
\end{align*}
\]

Selected examples

![Selected examples](image)


The suggested mechanism for this selenosulfonylation reaction starts with a single-electron transfer from Cu(I) to cycloketone oxime ester to form an iminyl radical XI (Scheme 14). In the sequence, C–C bond cleavage results in the formation of a carbon radical intermediary, which is promptly captured by DABCO·(SO₃)₂ to produce the sulfonyl radical XII. Addition of XII to 1,6-enzyme forms an alkyl radical intermediate that undergoes 5-exo-dig cyclization to provide vinyl radical XIII. Finally, the reaction between radical species XIII and diphenyl diselenide affords the target pyrrolidine 8.

\[
\begin{align*}
\text{R}^1 &= \text{H, aryl; R}^2, \text{R}^3, \text{R}^4 = \text{aryl; R}^5 = \text{H, OBn, aryl, alkyl} \\
\end{align*}
\]

Scheme 14. Proposed mechanism for the Cu-catalyzed selenosulfonylation of 1,6-enynes.

2.1.2. O-Based Heterocycles

In 2013, Wang and co-workers reported the synthesis of 2-chalcogenyl-benzofurans 9 by reacting 2-(gem-dibromovinyl)phenols with diorganyl dichalcogenides and using copper(I) iodide (10 mol%) as a catalyst (Scheme 15) [46]. The optimal conditions still consist of using tBuOLi as a base and metallic Mg as an additive in DMSO as solvent at 110 °C. The most striking feature of this protocol was the tolerance of both electron-donating and electron-withdrawing groups directly attached to the phenol moiety without apparent sensitivity to the electronic features of the substituents. Diorganyl disulfides and diorganyl diselenides were found to be efficient reagents to this reaction, affording the products 9 in good yields.
Based on detailed control experiments and the related literature, the authors proposed the following mechanism (Scheme 16). Initial Ullmann-type reaction catalyzed by copper furnishes 2-bromobenzofuran XIV. In parallel, reaction of diorganyl dichalcogenide with Cu(0), generated in situ from the reduction in Cu(I) with Mg(0), provides copper(II) and copper(I) intermediates, which reacts with XIV via oxidative addition, giving XV. Finally, the reductive elimination step regenerates the transition-metal and furnishes product 9.

In 2015, Buchwald and Zhu depicted the enantioselective radical cyclization of 4-arylpent-4-enoic acids to synthesize functionalized chiral lactones 10 via copper-catalyzed reaction (Scheme 17) [47]. Reactions were conducted using sulfonyl chlorides as sulfur sources in a catalytic system based on Cu(MeCN)4PF6 (10 mol %), (S, S)-BuBox (10 mol%) as ligand, and Ag2CO3 as base and chloride scavenger in ethyl acetate as solvent at room temperature. Under optimal conditions, enantiomerically-enriched sulfonyl-substituted lactones were obtained in high yields and good enantioselectivity. Finally, this key enantioselective lactonization still covered oxyazidation, oxyarylation, diacyloxylation, and oxyalkylation reactions.
A series of sulfonated cyclic ethers 11 were depicted via heterocyclization of enols with sodium sulfinates as an organic sulfur source that is readily accessible and stable (Scheme 18) [48]. The best reaction conditions involved the use of copper(II) bromide (10 mol%) in DMF as solvent at 120 °C under air for 24 h. The reactions were conducted using terminal and internal enols, which enabled the preparation of a series of four to seven membered cyclic ethers, including dihydrobenzofuran, lactone, and a norbornene derivative. Furthermore, the reaction conditions were compatible with several aryl and alkyl sulfinates bearing both bulky, electron-donating and electron-withdrawing groups at ortho, meta, and para positions, which furnished the desired products 11 in good yields.

After screening several experiments, a radical mechanism was proposed. Initially, sodium sulinate is reduced by Cu(I) resulting in Cu(II) species and reactive sulfur radical species via disulfide intermediate. Thereafter, addition of sulfur radical species to the enol double bond provides the alkyl radical species XVI which undergoes oxidation, resulting in a carbocation-type intermediate XVII. Subsequently, species XVII suffers an intramolecular nucleophilic attack of the neighboring oxygen atom, furnishing 11 and regenerating Cu(I) to the next catalytic cycle (Scheme 19).
The same research group developed a mild protocol for the regioselective synthesis of selanlated cromanol 12 and aurone 13 derivatives from homo-propargyl and propargyl alcohols, respectively [49]. The optimal reaction conditions involved the use of CuI (10 mol%) as catalyst, Na₂CO₃ as the base, and DMF as the solvent resulting in the selanyl methylene 4-chromanol 12 and selanyl aurone 13 products with an up to 96% yield (Scheme 20). The attempts to employ diorganyl ditellurides and disulfides as the chalcogen sources were unsuccessful.


The proposed reaction mechanism proceeds through a similar pathway shown previously in Scheme 12, with the initial copper-organochalcogen complex formation. This dinuclear species is responsible for activating the starting ynol, which suffers a 6-exo-dig (Scheme 21A) or a 5-exo-dig (Scheme 21B) ring annulation, followed by a reductive elimination leading to the desired selanyl-substituted chromanols 12 and aurones 13, respectively.

Scheme 21. Proposed mechanism for the synthesis of (A) chromanols 12 and (B) aurones 13.

2.1.3. Chalcogen-Based Heterocycles
An efficient synthetic approach to the synthesis of highly functionalized selenophenes 14, 15, and 16 via Cu(II)-catalyzed reaction between several \((E,E)-1,3\)-dienyl bromides and KSeCN as selenium source has been reported by Ranu and co-workers (Scheme 22) [50]. The standard condition uses 20 mol% of CuO Nps as catalyst and DMF as solvent, at 110 °C for 3 h to 12 h. Initially, a diversity of substituted 1,3-dienyl bromide derivatives underwent selanylation/cyclization reaction, producing the corresponding selenophenes 14 in 75% to 95% yields. Moreover, when 1,3-di-\(\text{gen}\)-dibromides were employed under optimal conditions in the presence of 3 equiv. of KSeCN, 2-selanyl bisselenophenes 15 were obtained as product. In addition, under the same conditions, the selanylation followed by cyclization reaction was extended to a 3-bromo-1,3-dienyl bromide which gave the 3-selanyl bisselenophene 16 in 85% yield. To complete the investigation, the synthesis of five differently substituted thiophenes 17 was explored in the presence of thiourea as a sulfur source under similar optimized reaction conditions obtaining the expected products in 80% to 90% yields. Particularly, KSCN was inefficient in providing the desired products.

In 2018, Zeni and co-workers described straightforward strategies to synthesize highly substituted selenophene scaffolds by direct incorporation of halogen and chalcogen as substituents (Scheme 23) [51]. Among them, the reaction of butylselanyl propargylic alcohols with diphenyl diselenide catalyzed by copper(I) iodide (20 mol%) was successfully employed to obtain diverse 3-(phenylselanyl)selenophenes 18 in moderate to good yields. Interestingly, simple electrophilic selenium sources, such as PhSeBr or (PhSe)\(_2\)/HCl or (PhSe)\(_2\)/FeCl\(_3\), as promoters were inefficient, furnishing the expected product in satisfactory yields. In contrast, the formation of a copper \(\pi\)-complex favors the intramolecular cyclization, selanylation, and dehydration reaction of the starting propargylic alcohols.
Another notable example comes from a recent report by Wu and coworkers on the chemo- and regio-selective synthesis of selenophenes 19 via Cu(I)-catalyzed [2+2+1] cyclization of terminal alkynes and selenium powder [52]. This strategy applied stable and non-toxic elemental selenium as the chalcogen source, in contrast to the relatively unstable and unpleasant odour of commonly used dialkyl diselenides. Under the optimal reaction conditions, 2,5-disubstituted selenophenes 19 were prepared in 32–89% yields with a diversity of substituents, including aryl, alkyl, and heteroaryl groups (Scheme 24).

The suggested mechanism starts with a DBU-promoted disproportionation of elemental selenium resulting in selenide anion (Se²⁻) and selenite (Se⁴⁺) (Scheme 25). In the sequence, Cu⁰ is oxidized to Cu(I), which is responsible for catalyzing the homocoupling of two molecules of the terminal alkyne, followed by regioselective hydroselenation and subsequent cyclization to furnish the desired products 19.
Scheme 25. Proposed mechanism for the synthesis of 19.

While the strategies discussed above demonstrate intermolecular relationship between chalcogen species and unsaturated substrates, the copper(I)-catalyzed intramolecular cyclization of alkenes bearing a chalcogen (S or Se) group at an appropriate distance from the carbon–carbon double bond is also a versatile way to generate chalcogen-decorated heterocycles. The synthesis of several 2-alkynyl-benzo[b]chalcogenophenes 20 from 2-gem-dibromovinyl aryl chalcogenides has been described (Scheme 26) [53]. The highlights of this synthetic method are the intramolecular cyclization catalyzed by CuBr (20 mol%) providing 2-bromobenzo[b]chalcogenophenes 21 which subsequently undergoes one-pot palladium-catalyzed Sonogashira-type cross-coupling reaction with different terminal alkynyl alcohols.


Mechanistically, vinyl bromide undergoes initial cyclization via copper-catalyzed intramolecular Ullmann-type reaction, forming 2-bromochalcogenophene 21, which was isolated and characterized by NMR spectroscopy. Then, oxidative addition of palladium species to Csp^2-Br bond generates intermediary XVIII, which undergoes transmetallation with alkynyl cuprate, delivering the coupling product 20 after a reductive elimination step. Notably, this methodology is selective for alcohol-containing alkynes, not being compatible with aliphatic or aromatic alkynes (Scheme 27).
2.2. Using Cobalt as Catalyst

The use of cobalt-catalyzing heterocyclization reactions with direct chalcogen incorporation is a field much less explored in organic synthesis. The most recent studies report the carbonylative reaction of terminal and internal alkynes with direct sulfonylation, achieving the synthesis of γ-lactones as product.

Ogawa and co-workers reported a unique method for the thiolative double carbonylation of internal alkynes by using Co2(CO)8 (9 mol%) as catalyst, affording α,β-unsaturated γ-thio γ-lactone derivatives 22 (Scheme 28) [54]. This multicomponent reaction was conducted in acetonitrile as solvent at 140 °C under 4 MPa of carbon monoxide for 17 h. Butenolides bearing both aryl and alkyl sulfides as substituents were synthesized in moderate to good yields. The alkyl thiols reacted poorly in comparison to the aryl thiols having both electron-withdrawing and electron-donating groups at para-position. Interestingly, reactions conducted employing unsymmetrical internal alkynes provided moderate regioselectivity to the γ-lactones obtained, in which the carbonyl group bonded mainly to the less hindered acetylenic carbon. According to the authors, limitations were observed for internal alkynes containing carbonyl substituents which did not provide the desired products.

Scheme 27. Proposed mechanism for the synthesis of 20.

a sulfur–cobalt bond. After that, two subsequent CO insertions furnish the carbonyl intermediate XX. Finally, intramolecular cobalt–oxygen bond formation followed by reaction with internal alkyne provides lactone 22 and regenerates complex XIX to the next cycle (Scheme 29).

Scheme 29. Proposed mechanism for the synthesis of 22.

Later, the same group reported the use of Co(CO)₈ as a catalyst for thiolative lactonization reactions of internal alkynes bearing a hydroxyl group with diorganyl disulfides under carbon monoxide (2 MPa) atmosphere (Scheme 30) [55]. The reaction was conducted in toluene as solvent at 140 °C for 20 h. Under these reaction conditions, nine γ- and δ-lactone derivatives 23 bearing an exo-methylene unit functionalized with sulfur were isolated in 19% to 76% yields. It is important to emphasize that for all synthesized products, the CO entered regioselectively into the alkyne, and the sulfide remained preferentially located at the cis position in relation to the carbonyl group. Alternatively, the authors demonstrated the thiolative lactonization reaction of acetylenic alcohols catalyzed by Pd(PPh₃)₄ (5 mol%). This new protocol tolerated strong electron-donating and electron-withdrawing groups attached to both diaryl disulfides and aryl alkynes.


2.3. Using Iron as Catalyst

Iron salts promoting cyclization processes have been widely recognized in terms of their tolerance toward several functional groups. Moreover, reactions conducted in the presence of iron have reported advantages in terms of relative stability, abundance, low-cost, and low toxicity, when compared to other transition metals. The subsequent papers report on iron-catalyzed cyclization reactions leading to heterocyclic systems such as
oxazole, isothiazolone, dihydrofuran, lactone, benzo[c]heteroaromatics, and several benzo-fused 6- to 8-membered rings.

2.3.1. N-Based Heterocycles

Deng and coworkers have reported an elegant strategy to prepare methylsulfenyl oxazoles 24 by the tandem annulation of N-propargylamides in the presence of diorganyl disulfides [56]. The standard reaction condition was set under thermal conditions for 12 h, in the presence FeBr₃ (10 mol%), I₂ (4 equiv.), and anhydrous MeCN (2 mL), allowing the preparation of twenty-one methylsulfenyl oxazole derivatives 24 in poor to very good yields. Despite the good substrate tolerance, limitations were faced when alkyl substrates were submitted to the protocol, as well as when disulfides were replaced by diorganyl diselenides derivatives (Scheme 31).

![Scheme 31. FeBr₃-catalyzed annulation reaction of N-propargylamides for the synthesis of oxazole 24 derivatives.](image)

In 2021, Yan and coworkers reported an ingenious synthetic approach to prepare isothiazolone derivatives 25 through an Fe-catalyzed multicomponent annulation of cyclopropenones, anilines, and elemental sulfur [57]. Thus, authors have set the best reaction condition by reacting the substrates in the presence of Fe(OTf)₃ (5 mol%), Tf₂O (25 mol%), and DMSO, with the resulting mixture stirred for 4 h at 140 °C. Therefore, the protocol allowed the synthesis of twenty-three isothiazolone derivatives 25 in moderate to good yields (28–73%), presenting an acceptable electronic and steric group tolerance. A huge limitation faced by the method is the simultaneous formation of the 4,5-diphenyl-3H-1,2-dithiol-3-ones 26 as a minor product, which were significantly yielded (12–37%) in all experiments. It is worth mentioning that the protocol was satisfactorily scaled-up from 0.2 mmol to 3 mmol, yielding the desired product 25a in 60%. Additionally, the authors expanded the protocol for the synthesis of iso-1,2-selenazolones 27 by employing elemental selenium as reagent, in the presence of FeCl₂ (10 mol%) as a catalyst and DMSO as solvent. After being stirred for 3 h at 140 °C, six iso-1,2-selenazolones 27 were accessed in moderate yields (51–57%) (Scheme 32).
Based on control experiments, authors have proposed a plausible reaction mechanism which initially involves the Fe-catalyzed ring opening of the cyclopropenone, driven by the nucleophilic attack of the nitrogen lone electron pair. This step furnishes the \(\alpha,\beta\)-unsaturated amide intermediate, which promotes the cyclooctasulfur activation by another ring opening event, generating the intermediate XXI. Thus, an intramolecular cyclization process releasing elemental sulfur to the reaction medium provides the cyclic ionic intermediate XXII, which is finally oxidized towards the desired product 25a (Scheme 33).

2.3.2. O-Based Heterocycles

In 2015, Zeni and coworkers reported a fashioned synthetic approach to construct 3,4-bis(organoselanyl)-2,5-dihydrofurans 28 by reacting 1,4-butyne-diols and diorganyl diselenides [58]. The optimized reaction condition was established by employing catalytic amounts of FeCl₃·6H₂O (20 mol%) and DCE as solvent, and the transformations were conducted from 0.5 h to 24 h to deliver a library of thirty-seven chalcogen-functionalized 2,5-dihydrofurans 28. The protocol demonstrated excellent substrate tolerance once many 1,4-butyne-diol derivatives could be smoothly employed as substrates. Besides, electron-rich and electron-deficient diorganyl diselenides reacted efficiently to give the respective
product 28 derivatives, as well as diphenyl disulfides, which were employed to prepare three sulfur-decorated 2,5-dihydrofuran 28 analogues (Scheme 34). In addition to these important results, authors also have expanded the reaction scope by employing pentyn-1,5-diol and 4-amino-butynol as substrate to prepare 4,5-bis(organoselanyl)-3,6-dihydro-2H-pyran 29 and 3,4-bis(organoselanyl)-2,5-dihydro-1H-pyrrole 30 derivatives, respectively. A total of four selenium-decorated 3,6-dihydro-2H-pyrans 29 were prepared in poor to moderate yields (48–74%), while five selenium- and sulfur-decorated dihydro-1H-pyrroles 30 were accessed in poor to very good yields (35–85%). It is worth mentioning that authors also have employed the 3,6-dihydropyran 29a as a substrate to perform a Kumada-type coupling reaction using Pd(PPh₃)₄ (10 mol%) as catalyst, with the coupling product obtained in a yield of 57%.

The authors proposed that the transformation is mainly triggered by the in situ formation of a reactive complex by the reaction between the Fe(III) species and diorganyl diselenides [57]. This species can coordinate with the benzyl hydroxyl unit, allowing the formation of a highly stabilized benzyl carbocation XXIII, which is quickly converted into the allene intermediate XXIV. Then, the product 28a is reached by sequential events, e.g., a nucleophilic addition followed by an electrophilic annulation (Scheme 35).
Recently, Tang, Zhang, and coworkers published a process of lactonization of enoic acids catalyzed by FeCl₃ in the presence of diorganyl dichalcogenides to access chalcogen-decorated γ-lactones and δ-lactones 31 through a simple, atom-economic, and environmentally friendly protocol [59]. By the reaction optimization study, the authors set the best reaction condition by mixing the starting materials in the presence of FeCl₃ (10 mol%), KI (0.5 equiv.), and MeCN, stirring the resulting mixture for 24 h at 80 °C under open-air conditions. The developed protocol presented good substrate tolerance once a variety of electron-rich and electron-deficient enoic acids and diorganyl dichalcogenides could be suitably employed as substrates. On the other hand, limitations were faced when a dialkyl disulfide derivative (R² = tBu) was employed as substrate, in which the desired product was obtained in trace amounts. It is worth mentioning that the protocol was satisfactorily scaled up to a gram-scale, without significant lack of efficiency (Scheme 36).

Several control experiments were carried out, indicating that the process mainly follows radical chain events. Thus, authors have proposed a reaction mechanism which is triggered by an Fe(III)-mediated initial iodine anion (I⁻) oxidation to the iodo-centered radical through an SET process. Then, the iodine radical species reacts with the S-S bond to afford a thyl radical species which adds in the C-C double bond, yielding the benzyl radical intermediate XXV. Thereafter, this radical species undergoes an SET oxidation, being converted to the benzyl carbocation, which finally is converted into the desired lactone 31 by an intramolecular annulative process (Scheme 37).

2.3.3. Chalcogen-Based Heterocycles

In 2017, Zhang and coworkers reported an elegant method to perform a thiocyclization of trifluoromethylated propynlys, in the presence of diorganyl disulfides, to construct the 2-trifluoroacetyl benzothiophene derivatives 32 by the sequential formation of C-S and C-C bonds [60]. The reactions were carried out in the presence of FeCl₃ (20 mol%) as catalyst, benzoyl oxide (10 mol%) and I₂ (2 equiv.) as an oxidative system, and MeNO₂ as
solvent, after which the resulting mixture was stirred for up to 12 h at 120 °C. Under these conditions, a library of 2-trifluoroacetyl benzothiophenes 32 were satisfactorily prepared in moderate to very good yields. The methodology presented good substrate tolerance to electron withdrawing and donating groups, as well as to bulky and ortho-substituted substrates. In addition, the authors demonstrated the feasibility of the protocol to employ diphenyl diselenide as substrate, resulting in 32g of a product in a yield of 62% (Scheme 38).

Selected examples

![Scheme 38. FeCl3-catalyzed cyclization of propynyls with disulphides and diselenides.](image)

Based on control reaction experiments and on the literature, authors have proposed a plausible reaction mechanism which initially involves an FeCl3-catalyzed Meyer-Schuster rearrangement to produce the active allenol intermediate XXVI. In parallel, the homolytic cleavage of the S-S bond, mediated by BPO and I2, delivers the thiyl radical (PhS·) in the reaction medium, which promotes a selective addition to the allenol XXVI, reaching the allyl radical intermediate XXVII. Subsequently, a keto-enol tautomerism and an intramolecular radical electrophilic annulation affords the cyclohexadienyl radical intermediate XXVIII. Finally, a successive oxidation drives the reaction toward the formation of the desired aromatic product 32a through an SET and deprotonation process (Scheme 39).

![Scheme 39. Proposed mechanism for the synthesis of 32.](image)

2.3.4. Miscellaneous

Lv, Li, and coworkers reported a regio-divergent carbochalcogenylation of inactivated alkenes through an FeCl3-catalyzed annulation process in the presence of electrophilic N-chalcogenophatalimides as sulfur or selenium source reagents [61]. The protocol involves the application of simple reaction conditions by mixing the starting materials and FeCl3 (10 mol%) in DCE and heating the resulting mixture for 12 h at 100 °C under N2 atmosphere. The developed protocol provided the synthesis of a library of thirty-five medium-sized sulfur-decorated rings (6-, 7- and 8-membered rings) 33 and 34, in addition to nine selenium-based derivatives 33 in poor to excellent yields. The methodology presented good scalability when scale up experiments were carried out. In general, the
protocol presented good substrate tolerance to electron-rich alkenes and heteroaromatic derivatives. However, limitations were found when electron deficient substrates ($R^1 = 4$-NO$_2$) and heteroaromatic systems (quinoline) were employed, suppressing the formation of the desired products (Scheme 40).

![Scheme 40. Fe(III)-catalyzed carbosulfenylation of inactivated alkenes.](image)

The authors performed several control experiments, including kinetic isotopic effect and radical scavenger experiments, aiming to gain insights toward the role of iron in the reaction. Thus, a plausible reaction mechanism was initially proposed involving the activation of the $N$-sulfenylphthalimides by the FeCl$_3$ catalyst. Therefore, the alkene undergoes a sulfenyl addition to afford the thiiranium intermediate $\text{XXIX}$, as well as the Fe(III)-based anion. This event is followed by the intramolecular ring opening reaction by the attack of the aryl group, yielding the dearomatic intermediate $\text{XXX}$. It is worth mentioning that authors drew attention to the fact that the endo/exo selectivity in the ring opening event depends on the length of the carbon chain between the C-C double bond and the aryl ring. Finally, the Fe(III)-based anion performs a deprotonation of the intermediate $\text{XXX}$, affording the expected aromatic products $33$ or $34$ and releasing the FeCl$_3$ to restart the catalytic cycle (Scheme 41).

![Scheme 41. Proposed reaction mechanism for the carbosulfenylation of alkenes.](image)
2.4. Using Palladium as Catalyst

Palladium catalysis in organic synthesis is a powerful methodology to promote several transformations, including the C-C and carbon–heteroatom (C–N, C–O, C–S, and C–Se) bond formation. In addition, reactions involving palladium are used to provide high efficiency and excellent chemoselectivity. A special group of transformations is represented by palladium π-alkyne chemistry with the direct introduction of an organochalcogen unit into a newly formed N-heterocyclic system.

The synthesis of highly functionalized 1,2-dihydrobenzo[cd]indoles 35 was proposed by Zhang, Zhou, and co-workers under palladium(II) chloride-catalyzed thiolation/cyclization reaction of 8-alkynylnaphthalen-1-imines (Scheme 42) [62]. The main features of this work raise the fact that the reaction is regioselective, enabling the intramolecular 5-exo-dig cyclization and stereoselective, giving the 2-(arylthio)alkylene-containing N-heterocycle in (E)-configuration. The procedure was compatible with differently substituted sulfonyl, acyl, and alkyl groups directly bonded to the nitrogen atom. Moreover, the use of dialkyl disulfides, diaryl disulfides, and diphenyl diselenide was also evaluated, giving the corresponding products in moderate to good yields under optimal conditions.

![Scheme 42. Synthesis of (E)-2-(arylchalcogenyl)alkylene-1,2-dihydrobenzo[cd]indoles 35.](image)

A plausible pathway for this cyclization involves the formation of a sulfenylpalladium species, which subsequently coordinates with the Csp-Csp bond of the naphthalen-1-amine, becoming the triple bond available to intramolecular aza-cyclization. After cyclization, intermediate XXXI is formed, which allows the reductive elimination of palladium species, giving product 35 and regenerating the catalyst to the next cycle (Scheme 43).
In 2019, Li, Jiang, and co-workers reported an NHC-Pd(II) complex (0.25 mol%) catalyzing a three-component reaction using acetylenic oximes, aryl iodide, and Na₂S₂O₃ as an inorganic, odorless, and stable sulfur source to prepare a wide array of 4-(organylthio)isoxazoles 36 (Scheme 44) [63]. The ionic liquid [Cpmim]Cl was elected as the best solvent at 80 °C under aerobic conditions. A range of 4-(organylthio)isoxazoles 36 bearing both electron-rich and electron-poor groups were obtained in moderate to good yields. Notably, aliphatic substituents in both terminal acetylenic position or directly bonded to the Csp² of the oxime were well tolerated. Moreover, the employment of O-alkyl oximes showed themselves to be promising as reaction partners, delivering the cyclic products in moderate yields. Despite the broad scope and group compatibility, limitations on product formation were observed for strong electron-withdrawing groups bonded to acetylenic oximes that hampered the sulfur-transfer to the isoxazole. Still, the use of alkyl iodides instead of aryl iodides were not compatible with the present protocol.

Mechanistically, the authors proposed the trans-oxypalladation of oximes furnishing the isoxazole palladium(II) complex XXXII. Subsequently, the reaction of XXXII with sodium S-arylthiosulfate gives rise to a palladium thiosulfate intermediate XXXIII, which, via reductive elimination, delivers product 36, releases SO₃, and regenerates palladium species to the next catalytic cycle (Scheme 45).
2.5. Using Silver as Catalyst

Silver-catalyzed radical intramolecular cyclization reactions of unsaturated systems in the presence of elemental selenium or sodium sulfinites have been demonstrated. This synthetic tool has proven to be useful for the preparation of different chalcogen-containing heterocycles including isoxazoles, spiro-cyclohexadienones, lactones, isochromenones, and benzochalcogenophenes.

2.5.1. N-Based Heterocycles

Zhou, Liu, and co-workers reported an efficient and versatile protocol for the synthesis of a wide variety of selenyl-decorated isoxazoles 37 catalyzed by AgNO₃ from o-methyloximes, selenium powder, and organoboronic acids as reagents (Scheme 46) [64]. The reaction conditions involved the use of DMSO as solvent at 120 °C and the O₂ atmosphere proved to have a key role in this reaction. Using this protocol, a series of twenty-nine 4-organoselenylisoxazoles 37 were prepared in 40% to 93% yields.

![Scheme 46. Synthesis of selenated isoxazoles 37.](image)

The proposed mechanism is presented in Scheme 47. It involves the Ag-catalyzed formation of an aryl radical which is captured by Se⁰, leading to the formation of an organylselenium radical intermediate. Then, this radical is oxidized to cationic selenium species, which reacts with the o-methyloxime, forming cationic species XXXIV and, after hydrolysis, yields the desired Se-containing cyclic product 37 and methanol as a by-product.
In 2022, Reddy and coworkers reported an elegant protocol to perform the simultaneous C-Se and C-C bond formation through Ag-catalyzed oxidative dearomatization multicomponent process by reacting carbonylated-alkynes with boronic acids and selenium powder [65]. The best reaction condition still employs AgNO$_2$ (10 mol%) as catalyst, K$_2$S$_2$O$_8$ (2.5 equiv.) as oxidant, and 1,4-dioxane as solvent, with the resulting mixture stirred at 120 °C, from 10 to 16 h. The developed protocol allowed the synthesis of forty-two spirocyclic products $38$ in an up to 90% yield. This protocol presented a good substrate tolerance, since a wide diversity of electronic activated and deactivated boronic acids (aryl, heteroaryl, and alkyl) were suitably employed, as well as Csp-substituted groups (Scheme 48).

Based on control experiments and on the literature data, the authors have proposed a plausible reaction mechanism to describe the transformation events. Initially, persulfate ion (S$_2$O$_8$)$^2-$ promotes the oxidation of Ag(I) to Ag(II), which triggers the homolytic cleavage of the C-B bond, yielding the aryl radical intermediate, which is trapped by Se$_0$ to produce the selenium-centered radical intermediate. Then, a radical addition to the C-C triple bond affords the key intermediate XXXV, which undergoes an intramolecular annulation to be converted into the radical intermediate XXXVI. Finally, oxidation promoted by the persulfate ion drives the reaction to the formation of the desired products $38$ (Scheme 49).
2.5.2. O-Based Heterocycles

Sulfonated α-methylene γ-lactones 39 were efficiently synthesized through silver-catalyzed radical addition followed by intramolecular cyclization reaction of 1,6-enynes with sodium sulfonates (Scheme 50) [66]. The protocol reports the use of AgNO₃ (10 mol%) as catalyst, K₂S₂O₈ as oxidant, and HNO₃ as additive, which is believed to accelerate the reaction, in acetonitrile at 90 °C for 12 h. Under these conditions, sodium alkyl- and aryl-sulfonates bearing both electron-donating and electron-withdrawing groups were compatible, resulting in the expected sulfonated butyrolactones in moderate to good yields and E/Z ratios higher than 20:1 in most cases. Additionally, different alkyl and aryl substituents attached to 1,6-enynes were tolerated under optimal conditions. The reaction scope demonstrated a good functional group tolerance and could be carried out even on a gram scale. Notably, heterocyclic-substituted sodium sulfinate, as well as terminal alkyne, did not undergo the reaction.

Scheme 50. Synthesis of sulfonated α-methylene γ-lactones 39.

A reaction mechanism was proposed based on control experiments, electron spin resonance (ESR) experiments, and mass spectrometry (ESI-MS) analysis, as demonstrated in Scheme 51. First, the key intermediate sulfonyl-silver complex is formed by the reaction of sodium sulfinate with AgNO₃. Then, the reaction of 1,6-enyne by both sulfonyl radical (path A) or silver(I) species (path B) generates alkyl radical species XXXVII. Subsequently, an intramolecular radical addition/cyclization reaction provides the lactone-containing vinyl radical, which is reduced via Ag(II)-promoted SET process, producing XXXVIII. Finally, protonation of XXXVIII affords the desired lactone 39.
Soon after, the same group reported the efficient synthesis of sulfonated 3-carbon-ylbenzofurans 40 starting from alkynyl vinyloxy benzenes and sodium sulfinites (Scheme 52) [67]. The starting materials, AgNO₃ (20 mol%) as catalyst and K₅S₅O₈ as oxidant, were placed to react in acetonitrile at 85 °C for 6 h. The most striking features of this protocol are the wide tolerance for alkyl, electron-deficient, and electron-rich substituents attached to both 1,6-enynes and sulfinites, for the preparation of highly functionalized-benzofurans under mild conditions and in a step-economic process.

A concise methodology for the synthesis of Se-containing benzofurans and benzothiophenes 41 by Ag-catalyzed radical cyclization of 2-alkynyl(thio)anisoles, Se powder, and arylboronic acids was developed by Zhou, Liu, and co-workers in 2019 (Scheme 53) [68]. Under the optimal reaction conditions, which included AgNO₃ (20 mol %) as catalyst and DMSO as solvent under O₂ atmosphere at 100 °C, a series of selanylated heterocycles 41 were prepared in yields ranging from 30% to 97%.
Scheme 53. Synthesis of selanylated benzofurans and benzothiophenes 41.

This methodology was also applied to intramolecular silver-catalyzed radical cyclization, which afforded polycyclic selenium-containing heteroaromatics 42a and 42b in 22% and 25% isolated yields, respectively (Scheme 54).

Scheme 54. Ag-catalyzed intramolecular cyclization for the synthesis of Se-containing heterocycles 42.

According to the proposed mechanism (Scheme 55), initial conversion of arylboronic acid to the corresponding aryl radical species mediated by the catalytic system of AgNO\(_2\)/O\(_2\) occurs. Then, in situ radical trapping by elemental selenium leads to the selenium-centered radical intermediate, which reacts with 2-alkynyl(thio)anisole, forming the alkenyl radical species XXXIX. Finally, intramolecular radical cyclization forms the desired Se-containing heterocycles 41, while the remaining methyl radical is converted to formaldehyde or methane.

Scheme 55. Proposed radical reaction mechanism for the synthesis of 41.
One year later, the same research group described the first synthesis of Se-containing isochromenones 43 by AgNO$_2$-catalyzed cyclization reaction (Scheme 56) [69]. This three-component protocol showed good efficiency for a series of alkylnylarylesters and arylboronic acids bearing different substituents on the aromatic ring, using elemental selenium as chalcogen source. As the catalyst, AgNO$_2$ proved to give the best yield, although other silver salts such as AgSbF$_6$ and Ag$_2$SO$_4$ also catalyzed the cyclization reaction, albeit with lower yields. The optimum reaction conditions were dioxane as solvent at 120 °C under open-air atmosphere, resulting in a series of twenty-one selenated isochromenones 43 in 36–92% yield. The proposed mechanism for this reaction is similar to that described in Scheme 55, with the formation of selenium-centered radical as the key step.

![Scheme 56. Synthesis of Se-containing isochromenones 43 by AgNO$_2$-catalyzed cyclization reaction.](image)

2.6. Using Indium as Catalyst

Indium salts have been widely recognized due to their high tolerance with oxygen- and nitrogen-containing functional groups. Furthermore, indium(III) exhibits catalytic activity as a soft Lewis acid, activating both C-heteroatom and C-C unsaturated systems, and finding application in the synthesis of organic cyclic compounds.

In 2020, Hu, Li, and coworkers reported a fashioned unprecedented protocol for the 1,3,4-trifunctionalization cascade of 1,3-enynes, allowing the simultaneous formation of C-S, C-N, and C-O bonds by a sequence of sulfonating, isomerization, nitration, and annulation events [70]. The authors have set the best reaction condition by reacting 1,3-enynes in the presence of sodium sulfonate, t-butyl nitrite (TBN), and InBr$_3$ (10 mol%), employing MeCN as solvent, with the resulting mixture stirred for 8 h at 60 °C under argon atmosphere. Through this reported method, thirty-three 5-sulfonylisoxazoles 44 derivatives were prepared in poor to very good yields, presenting an excellent substrate tolerance. Among the synthetized derivatives, an Ibuprofen analogue 44d is a remarkable example which shows the potential of this protocol in a late-stage functionalization of natural products (Scheme 57).
Scheme 57. In(III)-promoted radical-mediated 1,3,4-trifunctionalization of 1,3-enynes.

After performing reactions in the presence of radical inhibitors, the authors proposed a plausible radical reaction mechanism. Thus, initially, sodium sulfinate reacts with butyl nitrite, yielding a sulfonyl radical species and a NO radical species. After that, a selective radical addition across the C-C double bond of 1,3-enyne gives the intermediate XXXX, which is in resonance with radical allenyl species XXXXI. Then, a coupling with NO radical species produces the allenyl species XXXXII, which undergoes intramolecular nucleophilic cyclization, delivering the desired isoxazole 44. According to the authors, the role of InBr₃ might be both as a Lewis acid to activate the sulfonyl radical intermediate and as facilitator to the cyclization step (Scheme 58).

Scheme 58. Proposed mechanism for radical-mediated 1,3,4-trifunctionalization of 1,3-enynes.

2.7. Using Nickel as Catalyst

Nickel is an earth-abundant and low-cost transition metal, suitable to achieve several chemical transformations in organic synthesis. Although less used in organochalcogen chemistry when compared to copper and palladium, the synthetic utility of a nickel complex in a chalcogenative heterocyclization reaction has also been demonstrated.

Selander, Zhou, and coworkers have reported a strategy to perform a radical cyclization and ring opening of oxime esters in the presence of diorganyl diselenides, with the process catalyzed by Ni(0) or Fe(II) species [71]. In this sense, the authors developed two methods to perform the synthetic transformations efficiently. The method A involves mixing the oxime ester, diorganyl diselenides, and Ni(COD)₂ (20 mol%) as catalysts and 1,10-phenanthroline (20 mol%) as ligand in the presence of 1,4-dioxane as solvent and Et₃N as base, with the resulting mixture stirred for 12 h at 90 °C. On the other hand, the method B was set just by using FeCl₂ (20 mol%) instead of Ni(COD)₂ as catalyst, and extending the reaction time from 12 to 24 h. Under these conditions, the authors conducted the synthesis of organoselenium-decorated pyrrolines 45 and alkyl nitriles 46 by employing γ,δ-unsaturated oximes or cycloketone oximes, respectively. The protocol presented remarkable
substrate tolerance, since a wide variety of electron-poor and electron-rich substituents were satisfactorily employed, despite being satisfactorily scaled-up from 0.2 mmol to 0.8 mmol (Scheme 59).

\[
\text{Ni(0) or Fe(II)-catalyzed radical cyclization reactions of oxime esters with diselenides.}
\]

According to control experiments and the literature data, the authors proposed a similar reaction mechanism for both metal species (Ni and Fe). The transformation starts with the metal-promoted homolytic cleavage of the N-O bond via an SET process, giving the iminyl radical species XXXIII, which quickly undergoes an intramolecular radical annihilation, being converted into the cyclic intermediate XXXIV. Finally, the carbon-centered radical intermediate XXXIV reacts with diorganyl diselenide, yielding the desired product 45 and releasing selenium-centered radical species to the reaction medium, which are instantly oxidized to the respective diselenide (Scheme 60).

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\text{3. Conclusions and Perspectives}
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The structural diversity achieved in the transition metal-catalyzed synthesis of organo-achalcogen-containing heterocycles provides the direction to design and synthesize advanced molecules for biological and new material applications. The results summarized in this review demonstrate the importance and versatility of both alkenes and alkynes as starting materials to prepare differently functionalized heterocyclic compounds. The most
recent approaches addressed the reactions of several organic and inorganic chalcogen species as precursors that enable the incorporation of a sulfur, a selenium, or a tellurium atom into five-, six- and seven-membered cycles. From this point of view, the chalcogenative annihilation of acyclic unsaturated compounds catalyzed by transition metals represent a current opportunity to construct libraries of new molecules for fine applications. Transition metals are an indispensable toolbox for organic synthesis, but some drawbacks associated with their use can be evidenced: the low abundance and high cost of some noble metals, lack of mechanistic understanding of catalytic processes, toxicity, and environmental concerns. Although these are difficulties, they provide opportunities for researchers to achieve new chemical bonds and organic structures in high yields and selectivities not reached by other methods. In this sense, novel advancements arising from photo-redox chemistry, electrochemistry, flow chemistry, and the use of sustainable solvents are under intense development. From this point of view, future perspectives on chalcogenative heterocyclization reactions support applications of classical transition-metal catalysis in conjunction with environmentally friendly platforms. The current diversity of metals used for the synthesis of organocalcogen-decorated heterocycles also demonstrates the direction of using earth-abundant and low-cost metals. The big challenges are the development of stable, selective, and reusable catalysts applicable to rational chemo- and stereoselective transformations of interest to the fine chemical and pharmaceutical industry. Finally, the findings described here are very encouraging and we believe that they can help researchers interested in this area to conduct future developments in heterocycle synthesis and organochalcogen chemistry.

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