Recent advances in tandem selenocyclization and tellurocyclization with alkenes and alkynes

Kai Sun,*a,b Xin Wang,a Chao Li,b He Wangb and Lei Li*b

Seleno-containing heterocycles exist widely in pharmaceutical molecules and the skeletons of natural products. The addition of organoselenium to alkenes and alkynes via intramolecular tandem selenocyclization is an efficient method for preparing selenofunctionalized heterocycles. In this protocol, multiple bonds are formed in a single reaction without the need to isolate intermediates. This review highlights recent progress in this rapidly growing area with an emphasis on the scopes, limitations and the mechanisms of these different reactions. Besides, tandem tellurocyclization with alkenes and alkynes is also briefly discussed.

1. Introduction

Organoselenium compounds are considered an important class of molecules in organic synthesis. These compounds are widely applied in materials and catalysis and as intermediates in organic synthesis. In addition, organoselenium compounds have been shown to have pharmacological activities such as anticonvulsant, antioxidant, antidepressant, anticancer, antitumor, anti-inflammatory and antiviral properties. The introduction of a selenium atom into a potentially biactive molecule can dramatically increase the native biological activity of the substrate. Meanwhile, heterocycles, which exist in natural products and biologically active molecules, play significant roles in the pharmaceutical and agrochemical industries. For all these reasons, continuous research effort has been devoted to the development of useful methods for synthesizing selenofunctionalized heterocycles. Currently, one way to access these compounds is the direct functionalization of the heterocycle precursor with a selenium source via transition metal catalysis. However, this method is limited by its poor regioselectivity and direct use of preformed or commercially available heteroaromatic counterparts. Alternatively, the addition of organoselenium to alkenes and alkynes via intramolecular tandem selenocyclization is an efficient protocol for preparing selenofunctionalized heterocycles. In this protocol, multiple bonds are formed in a single reaction without the need to isolate intermediates.

Over the past decade years, the selenocyclization of the selenium electrophiles (e.g., ArSeCl, ArPhBr, and ArthSe) with alkenes or alkynes have been deeply developed. However, the sensitivity to moisture and a short shelf life limited the appli-

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Kai Sun was born in Shan'xi, China in 1983. He received his Ph.D. degree in organic chemistry from Northeast Normal University in 2013 under the supervision of Prof. Qian Zhang. In July 2013, he joined the College of Chemistry and Chemical Engineering, Anyang Normal University, where he is an associate professor. His current research is focused on radical C–H functionalization and green synthetic chemistry.

Xin Wang was born in Heilongjiang, China and received her MS degree from Northeast Normal University in 2012. In July 2013, she joined the College of Chemistry and Chemical Engineering, Anyang Normal University. In 2019, she pursued her Ph.D. degree in Zhengzhou University. Her research program is drug design, structural identification and structural modification of natural products.
cation. In contrast, diselenides are easily accessible and operable selenium reagents in organic synthesis, making them a good choice for selenocyclization. Although some approaches have been reported for the intramolecular tandem selenocyclization reactions of diorganyl diselenides with alkenes and alkynes, few efforts have systematically reviewed tandem selenocyclization with alkenes and alkynes. In consideration of recent research progress and to better understand selenium-based intramolecular tandem selenocyclization, this review article firstly introduce the traditional selenocyclization with some selenium electrophiles, and then summarize the latest contributions to selenocyclization reactions of diorganyl diselenides with alkenes and alkynes between 2010 and 2020 and highlights the insights gained from previous methodological and mechanistic studies. The content is categorized by the type of catalysis, including metal catalysis, visible-light catalysis, electrochemical catalysis, organocatalysis, and other catalysis types involving hypervalent iodine- and peroxide-promoted reactions.

2. Traditional selenocyclization

Since the discovery in the late 1960s that species of type RSeX added stereospecifically to simple alkenes to the formation of a selenolactone, these reactions were extensively developed to construct the selenofunctionalized heterocycles. Mechanistically, seleniranium ion was formed by the addition of RSeX to unsaturation bond, which then was captured by a pendant nucleophilic group to generate a cyclic product with chemo-, regio-, stereo-specificity (Scheme 1). For example, in 2013, the group of Shaw reported tandem monocyclization and bicyclization reactions between alkenes and PhSeCl in the presence of catalytic quantities of Sc(OTf)3 to access polysubstituted tetrahydroquinoline and octahydrophenanthridine in moderate to high yields (Scheme 2). In this process, two rings, three bonds, and three stereogenic centers were formed with excellent stereo- and regio-control in one step.

Moreover, N-(2-nitrophenylselenenyl)succinimide (NPS) was also used as the electrophilic selenium source. In 2015, Yeung and co-workers described an enantioselective selenolactonization of olefinic acids and NPS, using hydroquinidine and DHQD PHAL as the catalyst (Scheme 3). A series of functional groups were tolerant with this catalytic system, giving the corresponding selenolactones with good yields and ee values. Additionally, heteroaromatic substrate was also reacted well in this catalytic system.

Chao Li received his BE degree from Zhoukou Normal University in 2019. He is now pursuing his MSc degree under the guidance of Prof. Lei Li at Liaoning Shihua University.

He Wang was born in 1986 in Jilin, China. He received his Ph.D. in 2014 at Northeast Normal University under the supervision of Prof. Yu-Long Zhao. After a postdoctoral training with Prof. Xingwei Li at Dalian Institute of Chemical Physics Chinese Academy of Science, he started his independent academic career at Liaoning Shihua University in 2016. His research interest includes radical transformations and the development of new synthetic methods in the organic synthesis.
Although cyclohexyl substrate was accommodated in 89% yield, the ee was only 16% under this catalytic protocol. The mechanism study shows that the large catalyst pocket was required for this transformation to avoid racemization of the chiral episeleniranium ion, introducing high enantioselectivity.

Allenes owing to two cumulative carbon–carbon double bonds have some unique chemical properties. For example, in 2004, the Ma’s group demonstrated a electrophilic cyclization of 2,3-allenoic acids with PhSeCl for the synthesis of β-organoselenium butenolides (Scheme 4). The reaction showed a broad substrate scope, and 4-mono-substituted, 2,4-disubstituted, and 2,4,4-trisubstituted 2,3-allenoic acids can all be applied to afford the corresponding products in 77–98% yields. Moreover, this protocol can also be compatible to the corresponding electrophilic cyclization of PhSCI.

In 2012, Alcaide and co-workers disclosed an electrophilic selenocyclization of 2-indolinone-tethered allenols with various selenenylating reagents, affording different heterocycles, which was shown good chemoselectivity (Scheme 5). PhSeBr, N-phenylselenosuccinimide (NPSS), or diphenyl diselenide as donors of PhSe⁺ in reactions with 2-indolinone-tethered allenol XX delivered spirocyclic selenolactams, and PhSeBr was the optimal selenenylating reagents, giving the target product with 71% yield in 1 hour without any additives. Moreover, quinoline-2,3-diones were obtained by using NPSP and catalytic amounts of p-toluenesulfonic acid (PTSA) in dichloromethane at room temperature. The mechanism of NPSP-promoted ring expansions was proposed in Scheme 5. First, the addition of PhSe⁺ cation to the proximal allenic double bond produces the intermediate. The intermediate has two regioisomer: and which occur a ring expansion to give the corresponding products and . The migration of the phenyl group is preferred to the migration of the carbonyl one, and is the major product.

In subsequent work, Alcaide and coworkers reported a metal-free oxidative selenofunctionalized reaction between allenes and diphenyl diselenide (Scheme 6). This reaction

Lei Li was born in 1989 in Jilin, China. She received her Ph.D. in 2016 at Northeast Normal University under the supervision of Prof. Yu-Long Zhao. She started her independent academic career at Liaoning Shihua University in 2016. Her current research interest mainly focuses on the photoinduced reactions and innovation of synthetic methods in the organic synthesis.

Scheme 3 NPSP promoted synthesis of enantioselective selenolactonization.

Scheme 4 PhSeCl promoted synthesis of β-organoselenium butenolides.

Scheme 5 The selenocyclization of 2-indolinone-tethered allenols for the synthesis of spirocyclic selenolactams and quinoline-2,3-diones.

Scheme 6 The synthesis of α-seleno-α,β-unsaturated carbonyls and selenated furan.
employed 1-fluoropyridinium compounds as oxidative functionalization reagents to access two types of α-seleno-α,β-unsaturated carbonyls (α-selenoenals 19 and α-selenoenones 20) by changing the substituents at the allenic end. In the case of allenone as a substrate, the α-selenoenone was failed to obtained, and the cyclized selenated furan 22 was afforded in 63% yield. The protocol disclosed the oxidation of (PhSe)$_2$ promoted by 1-fluoropyridinium triflate to generate the electrophilic species PhSe(OTf).

3. Diorganyl diselenides promoted selenocyclization

3.1 Transition metal-catalyzed selenocyclization

3.1.1 Iron(III)-promoted selenocyclization. Over the past decade, iron salts have appeared as alternative and promising catalysts for a wide range of organic transformations due to their low cost, good stability, abundance, ease of handling, and excellent tolerance toward various functional groups. The use of catalytic and stoichiometric quantities of iron(III) salts is a particularly efficient strategy to promote the selenocyclization of diselenides with alkenes or alkynes. Fundamentally, iron(III) salts act as Lewis acids and coordinate with selenium, which enhances the polarization of the diselenide bonds and facilitates electrophilic alkene selenocyclization with nucleophiles.

The group of Zeni reported a series of iron(III)-promoted cyclization of alkynes and diselenides. This strategy provides a new approach to obtain various selenofunctionalized heterocycles such as benzof/furs chromenones, indoles, isoxazoles, benzoxazines, dihydrofurans, isochromenimines, naphthalenes from readily accessible starting materials under mild conditions with efficiency and operability (Scheme 7). The authors proposed the mechanism that the key of these selenocyclizations are the iron-seleno complex generated from the reaction of FeCl$_3$ and diorganyl diselenide (RSe)$_2$. The electrophilic portion of the selenium species coordinates to the triple carbon–carbon bond to generate the seleniranium ion 26. The cyclized cationic intermediate 27 is then generated via intramolecular nucleophilic attack. Finally, deprotonation of 27 gives the selenocyclized product 24.

In 2020, the group of Ji established an iron(III) chloride-promoted cyclization between α,β-alkynic tosylhydrazones 28 and diselenides (Scheme 8). The reaction proceeded efficiently in the presence of 1.0 equiv. FeCl$_3$ in 1,2-dichloroethane (DCE) at room temperature, providing a series of 4-(arylselanyl)-1H-pyrazoles 29 with good functional group tolerance. Meanwhile, Koketsu et al. reported seleno-cyclization of alkyne 30 and diselenides, furnishing a series of 6H-isquinolinolino[2,1-a]quinazolin-6-one 31 (Scheme 9). In this reaction, C–N and C–Se were constructed in one step using 1.5 equivalent of FeCl$_3$.6H$_2$O in dichloromethane at room temperature. The plausible mechanisms of these two reactions are similar to above mentioned.

3.1.2 Copper catalyzed selenocyclization. Copper salts can act as catalytic cross-coupling agents, Lewis acids, and oxidizing agents in organic synthesis with the relatively low cost of copper and the realization of catalysis in many instances. Among them, copper-facilitated selenocyclization reactions between the diselenides and alkenes or alkynes have been widely applied as one of the most powerful tools for the synthesizing of seleno-heterocycle. For example, in 2017, Zeni and coworkers accomplished copper catalyzed cyclization of propargyl pyridines 32 with diorganyl diselenides (Scheme 10). The reaction was catalyzed by 20 mol% of CuI with 2 equiv. Na$_2$CO$_3$ as a base in DMF at 60 °C. A variety of propargyl pyridines and diorganyl diselenides were screened, and a wide range of 2-(organoselenyl)-indolizine 33 were obtained in generally good yields. Notably, when propargyl pyridines was equipped with a terminal alkyne, the indolizine with two phenyl selenium groups in the structure (34) was obtained in 30% yield. However, employing dibutyl diselenide as organoselenium source, the desired product was not obtained in 30% yield. However, employing dibutyl diselenide as organoselenium source, the desired product was not obtained in 30% yield. However, employing dibutyl diselenide as organoselenium source, the desired product was not obtained in 30% yield.
detected, and the corresponding 2-hydrogenated indolizine 35 was obtained via beta-selenoxide elimination.

To get insight the mechanism aspect of this cyclization, some control experiments were performed. These experiments revealed that the copper-selenolate species 36 generated by mutual action between copper(i) iodide and diorganyl diselenide was essential for the reaction. In the mechanism (Scheme 11), an intermediate 37, as an electrophile through the activation by coordination of the Cu(i) ion to the alkyne, is formed. Intermediate 37 is then converted into 38 via intramolecular nucleophilic attack of N atom. Deprotonation then produces the 2-copper-indolizine 39. The subsequent reductive elimination of copper leads to the formation of the final product 33.

A similar transformation was achieved by Godoi.22 The selenocyclization between 2-alkynylphenols and diorganyl diselenides enabled selenocyclization provided 3-organoselanylbenzo[b]furan derivatives in moderate to good yields (Scheme 12). In contrast to the Zeni’s work,21 this reaction did not need any base and worked smoothly in DMSO at room temperature by promotion of 1.5 equiv. CuI. The protocol performed excellent functionality tolerance. 2-Alkynylphenol, containing electron-donating groups, electron-withdrawing groups and halogen groups were all tolerated. Moreover, naphthyl-substituted alkyne also reacted well in this catalytic system. In particular, low reactive aliphatic alkyne was accommodated with moderate yields. Moreover, the dialkyl diselenides was proven to be applicable in this reaction.

Notably, 3-organoselanylbenzo[b]furan could be used to prepare for different functionalized benzo[b]furans, demonstrating the synthetic applicability of this protocol.

In 2018, Zhong and co-workers developed a copper-catalyzed tandem selenoamination reaction of alkenes, successfully affording a series of seleno-N-heterocycles (e.g., indoline, tetrahydroquinoline, pyrroline, and piperidine derivatives) with 73–93% yields (Scheme 13).23 In this approach, 10 mol% of CuBr2 was utilized in DMSO at 120 °C in air. During the mechanistic investigation, oxygen and DMSO as co-oxidants were necessary for this transformation. Moreover, radical quenching experiments suggested a radical mechanism is not likely the case in the present catalytic system. As shown in Scheme 13, the Se–Se of diselenide could be polarized by CuBr2 to access the coordination 44, which undergoes an electrophilic addition to the olefin moiety of 42. The intramolecular nucleophilic attack by nitrogen and deprotonation then furnish the desired product 43 and selenophenol.
Selenophenol is oxidized to diselenide by O$_2$ and DMSO, and re-enter to the catalytic cycle.

Soon after, Reddy’s group reported a CuCl$_2$-catalyzed synthesis of selenyl nicotinates from enynyl azide 45 with diorganyl diselenides (Scheme 14).$^{24}$ The enynyl azide bearing aryl groups with different electron-donating or electron-withdrawing groups and 2-thienyl all underwent this transformation smoothly, leading to desired 5-selenyl nicotinates 46 with yields ranging from 78–98%. It is worth noting that aryl-substituted, heterocyclic, and alkyl-substituted diselenides are also compatible to this reaction. The mechanism for this intramolecular selenoamination is similar to that described in Zhong’s work.$^{23}$

In 2018, Xu and co-workers demonstrated a selenocyclization of 2,3-allenoic acids 47 with diselenides in the combination of CuCl and (NH$_4$)$_2$S$_2$O$_8$ as catalytic oxidation system (Scheme 15).$^{25}$ The reaction enabled sulfenylation/cyclization and subsequent oxidation to provide selenylated butenolides 48 in 63–82% yields. [NH$_4$]$_2$S$_2$O$_8$ played dual roles as a radical initiator as well as oxidant. Moreover, selenylated butenolides could be applied for synthesis of the corresponding furan derivatives.

The proposed mechanism by the authors was depicted in Scheme 16. First, a selenyl radical is formed via the homolysis of RSeSeR in the presence of [NH$_4$]$_2$S$_2$O$_8$. The addition of selenyl radical to 2,3-allenoic acids gives the radical intermediate 49. The further oxidation of intermediate 49 by Cu(n) affords the intermediate 50. Finally, the intramolecular attack of intermediate 50 leads to the cyclized products 51. Another pathway is also proposed. Cu(ii) coordinated to 2,3-allenoic acids, generating the complex 51. Then, the addition of selenyl radical to 51 gives Cu(iii) intermediate 52. Finally, reductive elimination is occurred to release the desired product 48.

Organofluorine compounds constitute an attractive class of compounds that have attracted significant attention from researchers in a variety of disciplines. In 2019, the group of Sun successfully synthesized a series of 4-seleno-substituted $\alpha,\alpha$-difluoro-$\gamma$-lactams 54 using N-allyl-2-bromo-2,2-difluoroacetamides 53 and diorganyl diselenides catalyzed by 10 mol% CuI in DCE at 120 °C under external-oxidant-free conditions (Scheme 17).$^{26}$ Various N-aryl-substituents of bromodifluoroacetamides with different electron-donating or electron-withdrawing groups undergo this transformation smoothly, leading to desired products with yields ranging from 63–82%. Notably, N-alkyl-substituted bromodifluoroacetamide could proceed well in this reaction. Furthermore, diphenyl diselenides, 1,2-di(thiophen-2-yl)diselane and dimethyl diselenide were also compatible to this reaction.

Regarding the mechanism, control experiments and radical quenching experiments demonstrated this process proceeded through a radical pathway. The authors proposed the following possible reaction mechanism (Scheme 18).
A single-electron transfer (SET) between Cu(I) and 53 occurs to afford a Cu(II) species and radical intermediate 55. Next, the addition of the fluoroalkyl radical to the unsaturated double bond affords alkyl radical intermediate 56 via a 5-exo-trig cyclization. The alkyl radical intermediate 56 reacts with diphenyl diselenide to form the desired product 54 and selenyl radical, which further reduces Cu(II) to Cu(I) and selenyl anion (PhSeX) to complete the catalytic system.

3.2 Visible light-promoted selene cyclization

Recently, photoredox catalysis has emerged as a useful tool for radical reactions via visible light-induced processes. Compared with previous methods, photoredox catalysis is inexpensive and has the advantages of environmentally-benign (it does not require excess amounts of transition metals or oxidants), high efficiency and easy to use. Notably, diselenide bonds possess a lower bond energy (172 kJ mol$^{-1}$), which could facilitate the generation of selenium radical species via the homolytic cleavage of the Se-Se single bond under visible-light irradiation without any photocatalyst. Therefore, the construction C-Se to synthesize selenofunctionalized heterocycles under visible-light irradiation has become more appealing.

In 2013, Ragains and co-workers reported a visible light-promoted selene cyclization of alkenes at room temperature (Scheme 19). In this reaction, bench-stable PhSeSePh is combined with CBr$_4$ under the irradiation of a 5 W blue light-emitting diode (LED), resulting in the in situ generation of reactive PhSeBr. This reaction showed a broad substrate scope, generating O-heterocycles in high yields along with N-heterocycles in moderate to high yields. Notably, diphenyl ditelluride was successfully suitable for this strategy to afford the tellurofunctionalization products in 53–75% yields in dichloromethane as solvent. To further demonstrate the application of this method, the Amaryllidaceae alkaloid γ-lycorane was synthesized. Mechanistic studies and DFT calculation suggested visible light irradiation promoted the phenylselenyl radical abstraction of bromine from CBr$_4$ to generate phenylselenyl bromide in situ. The detailed mechanism of these reactions is still under investigation.

Later, the group of Liu developed a visible light-driven selenocyclization of N-allylamides in MeCN in the presence of 2 mol% 4CzIPN under visible-light and in air (Scheme 20). While dihydroisoxazole was produced in 73% yield without any photocatalyst under these optimized reaction conditions, the use of 4CzIPN as a photocatalyst promoted the reaction process. In contrast to other selenocyclization reactions, this protocol only needed 60 mol% diselenides. In addition, many substituted the allylic amides and various diselenides were well tolerated in this transformation and gave the corresponding products 60 in good to excellent yields. Inspired by this result, a series of heterocycles were prepared by investigating the scope of the nucleophilic reagent, generating the corresponding products 62 in 51–98% yields. A possible reaction mechanism (Scheme 20) was proposed based on fluorescence quenching experiments. In this mechanism, the ground state 4CzIPN is excited to *4CzIPN under visible light irradiation. The excited state then undergoes a SET reaction...
with diphenyl diselenide to generate \((\text{PhSe})_2^+\) radical cation and \(4\text{CzIPN}^-\) radical anion. Then, the molecular oxygen oxidized \(4\text{CzIPN}^-\) to the ground state completes the photoredox cycle. Meanwhile, the addition of diselenide radical cation \((\text{PhSe})_2^+\) to \(N\)-alkenylamide 59 produces seleniranium cation 63, which undergoes intramolecular nucleophilic cyclization to obtain the desired product 60.

In 2017, an efficient approach for the preparation of selenium substituted spiro[4,5]trienones based on visible light-induced selenium radical-cyclization of \(N\)-aryl alkynamides 64 under oxygen atmosphere at room temperature without external photocatalyst was described for Baidya and coworkers (Scheme 21).30 This reaction showed a wide range of functional groups tolerances. Diverse \(N\)-aryl alkynamide and diaryl diselenides bearing electron-donating as well as electron-withdrawing groups in aryl ring can achieve the products 65 in moderate to excellent yields. In addition, good yields were achieved in gram-scale reactions. A spiro-ring-opening strategy was realized to give fully substituted acryl amides 66. Based on several control experiments, a possible radical pathway mechanism was proposed. First, under visible light irradiation, the addition of selenyl radical produced via homolytic cleavage of the Se–Se single bond to the triple bond produces a vinyl radical 67. Subsequently, intramolecular radical ipso-cyclization affords 68. Oxidative dearomatization would then occur under oxygen atmosphere and in the presence of diyl diselenide to afford the desired product.

In 2017, the group of Wang developed a facile route to prepare 3-selenylindoles from \(N\)\((2\)-(ethyl)aryl)benzenesulfonylamide 70 and diaryl diselenides under 3 W blue LED irradiation (Scheme 22).31 The authors optimized reaction conditions and found that \(H_2O_2\) (30% aqueous solution) as oxidant was necessary for this transformation. Moreover, this methodology exhibited good functional group tolerance, giving rise to the 3-selenylindoles 71 in moderate to excellent yields. With the result of radical-trapping experiment, a radical free mechanism was proposed. Initially, hydroxyl radical generates from the homolytic cleavage of \(H_2O_2\) under blue LED irradiation. Then a single electron transfer between 70 and hydroxyl radical gives the intermediate 72. After the intramolecular cyclization and deprotonation, radical intermediate 74 is formed. Finally, the reaction between diphenyl diselenide and 74 leads the desired product 71 and phenylselenyl free radical. The phenylselenyl free radical further reacts with 74, delivering the final product.

In 2019, Xu and coworkers reported a Se radical-triggered multi-component tandem cyclization of alkyne-tethered cyclohexadienones 75 and diaryl diselenides under the irradiation of 25 W white LEDs at 40 °C temperature (Scheme 23).32 This reaction gave 5-hydroxy-3-selenyl-4a,8a-dihydro-2\(H\)-chromen-6\(H\)-ones 76 in 40–88% yields in the presence of 2 equiv. \(H_2O_2\) and CsOAc in chlorobenzene at 40 °C. Moreover, the reaction could be performed in the absence of a base in dry toluene at 60 °C, producing 3,5-diselenyl-4a,8a-dihydro-2\(H\)-chromen-6\(H\)-ones 77 in 62–81% yields. These results demonstrate water is crucial for this transformation. To gain more insight into the effect of water, some control experiments were performed. First, decreasing the amount of \(H_2O_2\) to 1 equiv. provided 76 in 40% yield and 77 in 30% yield. Next, 77 was converted to the desired product 76 under the standard conditions indicating that 77 is a possible intermediate. \(^{18}\)O-Labelling experiments showed that the oxygen atom of the hydroxyl group originated from water. Moreover, a radical-trapping experiment using 2,2,6,6-tetramethylpiperidine-1-oxyl


Scheme 22 Visible light-promoted synthesis of 3-selenylindoles.

Scheme 23 Visible light-promoted synthesis of selenyl chromenones.
(TEMPO) was performed to probe the possibility of a radical mechanism in this transformation.

Through a series of experimental observations and surveys of previous literature, they proposed the following possible reaction mechanism (Scheme 24). First, under visible-light irradiation, phenylselenyl free radical generated from diphenyl diselenide undergoes a radical addition to substrate 75 to produce alkyl radical 78. Subsequently, intramolecular radical cyclization gives intermediate 79, which is trapped by another phenylselenyl free radical to deliver the product 77. In the presence of CsOAc, nucleophilic substitution occurs with water and 77, leading to the desired product 76. Interestingly, some products showed potent inhibition activities against cancer cell growth in vitro.

In 2020, Xu and coworkers further developed visible light-induced selenocyclization reaction of indolyl-ynones 80 with diselenides at room temperature under air atmosphere (Scheme 25).13 Diverse 3-selenospiroindolenines bearing various functional groups were obtained in moderate to good yields. Similarly, phenylselenyl free radical is generated from diphenyl diselenide under visible-light irradiation. The desired product is then obtained through the radical addition/oxidation/deprotonation pathway. Compounds 81a and 81b were tested for in vitro anticancer activity by MTT assay and showed potent inhibitory activity against cancer cell growth.

Very recently, the group of Wang disclosed a regio- and chemo-selective radical cascade cyclization of 1,6-ynones 82 and areneselenosulfonates 83a under 34 W blue LED irradiation in the air without any photocatalysts (Scheme 26).34 Numerous substrates (82) were examined, and the corresponding cyclized products (84) were obtained in good to excellent yields. This reaction also proceeded smoothly using diaryl diselenides 83b with 1,6-ynones, and observed desired products with moderated to goods yields. However, this method was not applicable when the chain length was increased from one to two or three. The internal alkene and free amine in enyne were also not tolerant for this transformation. This protocol offers an efficient approach to build selenium substituted pyrrolidine derivatives via multiple chemical bond constructions in 5-exo-dig fashion, including one C–S bond, one C–Se bond, and one C–C bond.

Notably, some control experiments indicated the reaction proceeded in a radical way, and the visible-light irradiation was necessary. The reactivity of the chalcogen group in the reaction was tested by the combination of 82a with 83a and 83b. The result suggested that tosyl radical was more reactivity than phenylselenyl, demonstrating the regio- and chemoselectivity. The proposed mechanism is described in Scheme 27. The tosyl (85) and phenylselenyl free radical (86) are generated by visible light irradiation. Tosyl radical 85 is added to 1,6-ynones 82a to generate alkyl radical intermediate radical 87. Then intramolecular 5-exo-dig cyclization gives rise to the corresponding vinyl radical 88, which is further trapped by phenylselenyl free radical (86) to generate desired product 84a. The reverse transformation products were not observed, probably due to the higher stability of the tertiary alkyl radical intermediate 87 compared to the vinyl generated by the tosyl...
was substituted on the aryl group. However, terminal alkyne was ineffective for this transformation. Moreover, the reaction can be conducted on a gram scale with excellent efficiency, demonstrating the practical application in future industry. Comparing to the previous report on the related selenocyclization reaction of alkynoates and alkynamides by Zeni’s and Liu's work, this strategy requires no transition metals or chemical oxidants. Cyclic voltammetric (CV) experiments show that diphenyl diselenide had a lower oxidative potential than the substrate, indicating that diphenyl diselenide is more easily electrochemically oxidized to generate phenylselenium radical than the alkyne moiety.

Based on control experiments and radical quenching experiments, they proposed a possible reaction mechanism (Scheme 29). Diphenyl diselenide initially undergoes anodic oxidation to generate cationic radical intermediate 91, which is decomposed to give phenylselenium radical 92 and phenyl selenium cation 93. Thereafter, the radical addition of 92 to triple bond provides vinyl radical 94 in high regioselectivity. The resulting radical 94 participated in an intramolecular radical reaction to generate intermediate 95, which is further oxidized on anode to afford the cation 96. At last, deprotonation affords the final product 90.

Inspired by this protocol, the group of Guo further developed the electrocatalytic oxidative radical dearomative spirocyclization for the preparation of selenation spiro[4.5]trienones 98 from alkynes 97 with diselenides (Scheme 30). As mentioned above, when the substrates are alkynoates and alkynamides bearing a methoxy group at para substituted of aryl ring, the ipso-cyclization was occurred. Then, they optimized the reaction condition; the reaction worked well in CH3CN/HFIP (v:v = 3:1) at room temperature with nBu4NPF6 as electrolyte. The use of the optimized reaction parameters led to the corresponding 49 examples of selenation spiro[4.5]trien-
ones in moderate to good yields with broad substrate scope and high functional group tolerance. It is noted that diphenyl ditelluride was also compatible for this transformation, giving tellurium-substituted products in good yields. It should be mentioned that terminal alkyne was not suitable for this system.

Notably, scale-up reaction was performed in electrochemical continuous flow system, and nearly the same yield was obtained (73% yield in nearly 15 h on the 10 mmol scale).

The authors also provided the possible mechanism (Scheme 31). Vinyl radical 99 is generated in the similar path and then undergoes intramolecular spirocyclization to provide 100, different from their earlier work. Meanwhile, the anodic oxidation of the intermediate 100 generates oxygenium cation intermediate 102. Finally, the sequential demethylation of cation 102 and the dearomatization of the aromatic ring give access to the desired product.

In 2019, Pan and co-workers reported the electrochemical selenocyclization of olefins and diselenides for the generation of selenomethyl-substituted cyclic ethers, lactones and isobenzofuranones.

Scheme 30  Electrochemically induced synthesis of selenated spiro[4.5]trienones.


Scheme 32  Electrochemically induced synthesis of selenomethyl-substituted cyclic ethers, lactones and isobenzofuranones.

of selenomethyl-substituted cyclic ethers or lactones (Scheme 32). The olefins including unsaturated alcohols and unsaturated carboxylic acids 103, were all suitable for this reaction with NH₄I as electrolyte and electrocatalyst, affording the corresponding products 104 in good yields. Moreover, the difficult-to-synthesize medium-sized ethers (7-, 9-, and 11-membered rings) and 4–6-membered ring lactones could be obtained smoothly. However, the reaction was limited to diphenyl diselenides bearing electron-donating groups (OMe), failing to produce the desired product with 2-vinylbenzoic acid. According to the results of cyclic voltammetry studies and control experiments, the reaction mechanism is depicted in Scheme 32. Iodine ion is first oxidized at anode to produce I⁺, which then reacts with olefinic alcohols to form iodonium cations intermediate 105. Subsequently, intramolecular cyclization and deprotonation lead to intermediate 106. Finally, rapid chemical selenation by diphenyl diselenide gives access to the desired product and a half molar equivalent of I₂. At the cathode, reduction of I₂ and proton to iodine anion and hydrogen completes the reaction cycle.

Dihydrofurans and oxazolines play important roles in numerous biologically active molecules, pharmaceuticals and agronomicals. As a straightforward and highly atom-economic method for synthesizing these derivatives, the selenocyclization of olefinic carbonyls has attracted the attention of chemists. In 2019, the group of Lei realized an electrochemical oxidative cyclization between olefinic carbonyls and diaryl diselenides, providing a practical and economical approach to the preparation of selenium-functionalized dihydrofurans (Scheme 33). This reaction could proceed smoothly in CH₃CN at room temperature with Bu₄NBF₄ as electrolytes, HOAc as additive, graphite as the working anode, and plati-
num as the cathode. This method shows good compatibility for symmetric and unsymmetric olefinic carbonyls with different substituents, giving the corresponding dihydrofurans compounds in moderate to good yields. In addition, this protocol also tolerated unsaturated amides, affording the corresponding seleno oxazolines in moderate to excellent yields.

To gain more insight into this cascade cyclization, they added stoichiometric radical inhibitor TEMPO to reaction systems and perform this reaction under standard conditions. The yield of the desired product decreased obviously, indicating that the process involves a free radical pathway. Based on mechanistic studies, cyclic voltammetry studies, and the literature, the authors proposed two possible reaction pathways (Scheme 34). In path a, the anion radical intermediate is generated by cathode reduction, and then decomposes to give phenylselenium radical and phenyl selenium anion. Then, the radical addition of phenylselenium radical to the alkene results in the formation of C-radical intermediate, which is further oxidized at anode. Finally, an intramolecular cyclization is occurred by nucleophilic attack of the oxygen atom of carbonyl, subsequent deprotonation to render the final product. In path b, the phenylselenium radical is generated by phenyl diselenide anode oxidation and decomposition.

The group of Sarkar reported the similar method for the electrochemical oxidative cyclization of N-allyl amides and diaryl diselenides, providing a practical and flexible approach for the preparation of selenium-functionalized oxazolines (Scheme 35). The reaction could proceed smoothly in CH$_3$CN at room temperature with LiClO$_4$ as electrolytes, and graphite and platinum as the working anode and cathode, respectively. A variety of substituents on both electronic and steric effects can tolerate the oxidative conditions well. Moreover, amides with varying chain length were also compatible in the oxidative cyclization process. Notably, the thiazoline derivative was synthesized from corresponding N-allylthiobenzamide. Comparing to the Lei's work, this method could also be suitable for $\beta,\gamma$-unsaturated oximes and various isoxazolines were achieved under the standard reaction conditions.

A plausible mechanism for this reaction was proposed based on mechanistic studies, cyclic voltammetry studies, and the literature (Scheme 36). In this mechanism, diphenyl diselenide is oxidized to generate cationic radical intermediate,
which is then decomposed to give phenyl selenium cation 93 and phenylselenium radical 92. Further oxidation of phenylselenium radical 92 leads to phenyl selenium cation 93. Subsequently, the addition of phenyl selenium cation 93 to alkenes 112 affords the cyclic seleniranium ion 116, which then is captured by the nucleophile amide oxygen to afford the final product 113. At the cathode, proton is reduced to the hydrogen, completing the reaction cycle.

Very recently, Ackermann and coworkers investigated an electrochemical oxidative cyclization of quinones and diaryl diselenides using a platinum plate anode and cathode under the constant current (10 mA) in an undivided cell (Scheme 37).11 Using lapachol 117, the quinone-hybrid compounds 118 were afforded with moderate to high yield via 6-endo-trig way. When this selenylation method was applied to the C-allyl lawsone 121, 5-exo-dig cyclization occurred to give the corresponding products 122 in good to moderate yields. Unlike a previous report in which a I2/DMSO oxidant system was employed,42 this electrochemical reaction was conducted at room temperature without chemical oxidants. Moreover, some products exhibited considerable antitumor activity, indicating the promising in the application prospects.

**3.4. I2 and hypervalent iodine-catalyzed selenocyclization**

**3.4.1 I2 catalyzed selenocyclization.** In 2013, Braga’s group reported the synthesis of seleno O-heterocycle using molecular iodine as catalyst, DMSO as a stoichiometric oxidant under microwave irradiation without solvent (Scheme 38).42 When using 4-penten-1-ol 123 or 4-pentenoic acid 125 as a substrate, the seleno tetrahydrofuran 124 or seleno-lactone 126 was obtained in excellent yield via the 5-exo-trig pathway. Moreover, lapachol 117 or C-allyl lawsone 121 was also suitable for this transformation, affording the corresponding product in good to high yields. However, nor-lapachol failed in this reaction. A plausible mechanism is proposed in Scheme 30. Initially, RSeI generated through the reaction of diorganyl diselenide with I2 reacts with alkene to form seleniranium ion 127 and HI. Subsequently, intramolecular nucleophilic attack of the oxygen atom from the ester moiety on the carbon centre generates the final products. At the same time, HI is oxidized by DMSO to regenerate I2.

In 2019, Koketsu and co-workers reported an iodine mediated selenocyclization of 2-phenylalkynylquinoline-3-carboxylate 130 with diorganyl diselenides to access seleno pyrano[4,3-b]quinolin-1-one 131 (Scheme 39).43 The reaction featured a wide range of functional group tolerances, including strong/weak electron-withdrawing/donating groups along with alkyl and aryl groups, affording the corresponding products in high yields. The possible mechanism proposed by the authors
is disclosed in Scheme 39. R-Se–I to is generated in situ by the reaction of I2 and [R–Se]2. The electrophilic addition of R–Se–I to compound 130 forms seleniranium ion 132. The intramolecular nucleophilic attack by O atom gives the intermediate 133. Finally, the elimination of Me–I leads to target compounds. In a control experiment, MeI was detected based on NMR spectroscopy.

3.4.2 Iodine(m)-mediated selenocyclization. β,γ-Unsaturated hydrazones and oximes are valuable and versatile building blocks for preparation of pyrazoline and isoxazoline derivatives. In 2017, the group of Cai reported the cascade radical selenocyclization of β,γ-ununsaturated hydrazones 134 via the oxidation of phenyliodine(m) diacetate, giving rise to the corresponding pyrazoline and isoxazoline derivatives 135 in good yields without any metal (Scheme 40). Due to the mild reaction conditions, this method had a wide tolerance for dioxganyl diselenides. When a stoichiometric amount of TEMPO was added under standard conditions, the selenocyclization was completely suppressed, and the adduct was obtained in 84% yield. These results provide clear evidence that the process involves a C-centered radical intermediate formed by intramolecular cyclization. In these transformations, initially, the anionic intermediate is obtained by deprotonation of the β,γ-ununsaturated tosyl hydrazone or oxime in the presence of TBAF. Subsequently, a SET process between intermediate 136 and PhI(OAc)2 occurs to generate radical 137, which subsequently undergoes radical intramolecular cyclization to produce the C-centered radical 138. The diselenide then captures the C-centered radical 138, leading to the final product 135 and the phenylselenyl radical, which could recombine to diphenyl diselenide.

3.5 Peroxide-promoted selenocyclization

As an oxidant, Oxone® has been widely explored in organic synthesis due to its low cost, stability under various conditions, simple handling, and environmental nontoxicity. In 2019, Perin and coworkers described an efficient Oxone®-and dialkyl diselenides-promoted seleno-cyclization of 1,3-diynes 139 for the construction of diverse 5H-selenopheno[3,2-c]isochromen-5-ones 140 (Scheme 41). This protocol enables the formation of four new chemical bonds, including one C–O bond and three C–Se bonds through a double intramolecular cyclization. Aryl- and alkyl-substituted 1,3-diynes were found to be suitable for this transformation. When 2-CH3OC6H4-substituted 1,3-diyne was used as the substrate in the reaction, the yield of the target product was only 40% because of the competing reactions (intramolecular Se-cyclization and O-cyclization). A radical-trapping experiment using TEMPO and hydroquinone suggested this reaction does not involve a radical path. Furthermore, the 77Se NMR experiment indicated that the active electrophilic selenium species are generated by the overoxidation of dibutyl diselenide by Oxone®.

Based on experimental findings, a plausible mechanism is proposed (Scheme 42). Firstly, the reaction of potassium peroxymonsulfate with diselenide affords two electrophilic selenium species C4H9SeOSO3− (141) and C4H9SeOH (142), C4H9SeOH+ (143) is then formed by protonation of 142. Both electrophiles 141 and 143 can react with 1,3-diyne 139 to deliver the cyclic intermediate 146 via the elimination of HSO4− or water. Subsequently, the methyl group leaves under the attack of nucleophile to produce intermediate 149. Finally, the expected product 140 is afforded in the same way as above.

Subsequently, the authors further developed this methodology for the formation of 2,3-bis-organylselenylbenzo[b]chalc-
cogenophenes (Scheme 43)\textsuperscript{46} and 4-organoselanyl-1\textsubscript{H}-pyrazoles (Scheme 44)\textsuperscript{47} by employing chalcogenoalkynes and \(\alpha,\beta\)-alkynyl hydrazones as substrates by promotion of Oxone\textsuperscript{®} and diselenides.

In 2019, the group of Baidya developed an efficient radical selenocyclization of \(N\)-aryl alynamides \textsuperscript{159} using \(K_2S_2O_8\) as an oxidant in DCE at 80 °C (Scheme 45).\textsuperscript{48} This method worked well in a switchable selectivity \textit{ortho/ipso}-cyclization by the change the substituent of \(N\)-aryl alynamides \textsuperscript{159}, resulting in a variety of 3-selenyl quinolin-2-ones \textsuperscript{160} and 3-selenospiro[4,5]triienes \textsuperscript{161} in good to excellent yields. Moreover, diaryl diselenides and dialkyl diselenides were well tolerated in \textit{ortho} cyclization. When propiolamides bearing \textit{para}-fluoro and \textit{para}-methoxy in the \(N\)-aryl ring were reacted with diaryl diselenides, the spiro-cyclic products were isolated in good to high yields. Alkyl-substituted propiolamides were also suitable for the \textit{ortho/ipso}-cyclization. Radical trapping experiments by using TEMPO, butylated hydroxytoluene (BHT) or 1,1-diphenylethylene indicated that the process involves a free radical pathway. The authors carried out the reaction between 4-phenyl-quinolin-2-one and diphenyldiselenide under the standard reaction conditions and found that the selenylation process occurred before the ring-closure step. A tentative radical mechanism was depicted in Scheme 37. Initially, the \(K_2S_2O_8\)-mediated cleavage of the Se–Se bond of diselenide forms an aryl selenium radical, which undergoes a radical addition to \(N\)-aryl alynamide and intramolecular spirocyclization to give radical intermediate \textsuperscript{163}. The intermediate \textsuperscript{163} is oxidized to afford the intermediate \textsuperscript{164}, which is rapidly converted into the desired quinolone product \textsuperscript{160} through 1,2-C-migration and aromatization. When the \(N\)-aryl alynamide bears \textit{para}-F/OMe substituents, the intermediate \textsuperscript{163} further reacts with solvated molecular oxygen to produce intermediate \textsuperscript{166}, which undergoes defluorination/demethoxylation via \(\text{O–O}\) bond cleavage leading to the product \textsuperscript{161}.

In 2019, Liu group reported the \textit{tert}-butyl hydroperoxide (TBHP)-initiated radical cyclization of propargylic aryl ethers \textsuperscript{167} with diaryl diselenides for the synthesis of diverse 3-organoselanyl-2\textsubscript{H}-coumarins \textsuperscript{168} (Scheme 46).\textsuperscript{49} The use of \(N\)-iodosuccinimid (NIS) could be in situ generation ArSeI with diaryl diselenides, increasing the reaction yield. For insight the mechanism, some control experiments were performed. TBHP was essential for this method, not only as radical initiator, but also with \(H_2O\) providing O atom proved via \textsuperscript{18}O-labeling experiment.

According to the proposed mechanism (Scheme 47), aryl selenium radical and propargyl radical are generated in situ in the presence of TBHP as the oxidant and react with each other, leading to the key intermediate \textsuperscript{170}, which was detected by GC. Aryl selenium radical then adds to alkyne triple bond \textsuperscript{170} to produce the highly reactive alkenyl radical \textsuperscript{171}. This radical undergoes intramolecular cyclization onto the phenyl moiety, giving intermediate \textsuperscript{174}, which might be obtained by electrophilic cyclization of PhSeI in another path. Product \textsuperscript{168} is gen-

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**Scheme 43** Oxone\textsuperscript{®} promoted synthesis of 2,3-bis-organyselenylbenzo[b]cogenophenes.

**Scheme 44** Oxone\textsuperscript{®} promoted synthesis of 4-organoselanyl-1\textsubscript{H}-pyrazoles.

**Scheme 45** \(K_2S_2O_8\) initiated synthesis of 3-selenyl quinolin-2-ones and 3-selenospiro[4,5]triienes.

**Scheme 46** TBHP-initiated synthesis of 3-organoselanyl-2\textsubscript{H}-coumarins.
Conflicts of interest

There are no conflicts to declare.

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Notes and references


40 S. Mallick, M. Baidya, K. Mahanty, D. Maiti and S. D. Sarkar, Access to Functionalized 3,5-Disubstituted


