Selenium Reagents as Catalysts

Fateh V. Singh,* Thomas Wirth* b

Organoselenium chemistry is now become an important tool in synthetic and medicinal chemistry. Organoselenium reagents are more commonly known as electrophiles but there are few organic transformations where they act as nucleophiles. These reagents have been successfully employed to achieve number of synthetically important transformations such as oxyselenenylation, selenocyclisation and selenoxide eliminations etc. In past two decades, another episode of their success is introduced as they have developed as potential catalysts in organic synthesis. Various selenium-catalysed approaches such as oxidation, reduction, cyclisation, rearrangement and stereoselective reactions have been successfully investigated. During these reactions, a number of organic and inorganic oxidants have been employed to regenerate different active catalytic species in situ. In this review article, recently developed selenium-catalysed reactions are covered including stereoselective reactions.

Introduction

Although first organoselenium compound was synthesized in 1847 by F. Wohler, C. Siemens1 but the progress of organoselenium chemistry was quite slow until the discovery of selenoxide eliminations in 1970s.2 Organoselenium reagents are known to exhibit some toxicity and first time it was disclosed in 1930s.3a Eventually, the selenium was found as an essential dietary trace element.3b Probably, the toxicity of organoselenium species arises due to their exposure for longer period. Notably, the toxicity profile of organoselenium compounds is more safer compare to inorganic selenium compounds.3b,c

Additionally, few mammalian enzymes have been discovered which contain selenocysteine moiety.4 Despite the toxicity issues with them, the chemistry of these reagents is now well established due to their wide applications in organic synthesis5,6 and chemical biology7,8 Organoselenium reagents have been used to achieve various synthetic transformations such as selenenylation, selenocyclisations, selenoxide eliminations and 2,3-sigmatropic rearrangements under mild reaction conditions.9-11 The utility of these reagents in catalysis provide a new dimension to organoselenium chemistry.12 In most of the selenium-catalysed organic transformations, the diselenides are used as catalyst which exhibit moderate toxicity.13 This review highlights the recent progress of organoselenium reagents in catalysis.

Selenium reagents as catalyst

Selenium compounds can exist as both inorganic and organic compounds. More commonly, organic selenium reagents have been used to catalyse organic reactions but there are few reports in the literature where inorganic selenium species are used as catalyst. Inorganic selenium species have been employed to catalyse few organic reactions such as carbonylation of electron-rich and electron-deficient arenes,13 selective reduction of double bonds in α,β-unsaturated compounds,14 dihydroxylation of alkenes,15 oxidation of aromatic amines16 and synthesis of N-containing heterocycles.17 In past decade, the organoselenium catalysts have been identified as an asset in organoselenium chemistry and various organic transformations have been developed using these catalysts.

Selenium-catalysed oxidation reactions

Since long time, organoselenium reagents are known for their powerful oxidizing behaviours.18 Various oxidation reactions have been developed by using the combination of organoselenium catalyst with some selective terminal oxidants such as hydrogen peroxide,19 tert-butyl hydroperoxide (TBHP)20 and iodoxybenzene (PhIO)21 and ammonium persulfate.22

Selenium-catalysed oxidation of alcohols

The oxidations of alcohols can be used to achieve various synthetically important carbonyl compounds and carboxylic acids which make this reaction more suitable in organic chemistry.23 In the beginning, the oxidation of alcohols was achieved by using stoichiometric amounts of selenium-based oxidants18 while the first catalytic use of selenium reagents was reported in the oxidation of alcohols in 1996 by Onami and his coworkers.24 Furthermore, the same research group achieved the oxidation of alcohols 1 to carbonyl compounds 5 using catalytic amount of bis[2-(2-pyridyl)phenyl] diselenide 3 in the presence of N-chloro-4-chlorobenzenesulfonamide sodium salt 2 as oxidant (Scheme 1).25
The mechanism for the selenium-catalysed oxidation of alcohols is initiated via formation of an intermediate 4 by the reaction of alcohol 1 with bis[2-(2-pyridyl)phenyl] diselenide 3 and N-chloro-4-chlorobenzenesulfonamide sodium salt 2 as oxidant. Furthermore, the intermediate 4 undergoes oxidative cleavage and forms carbonyl compound 5 while generating another selenium intermediate 6. Furthermore, the intermediate 6 reacts with N-chloro-4-chlorobenzenesulfonamide sodium salt 2 to form intermediate 7 which subsequently reacts with alcohol 1 to continue the catalytic cycle.

In 2009, the oxidation of benzyl alcohol 8 was achieved by replacing terminal oxidant N-chloro-4-chlorobenzenesulfonamide sodium salt 2 with tert-butyl hydroperoxide (TBHP) using diphenyl diselenide 9 as catalyst (Scheme 2). The oxidation was investigated in different polar and non-polar solvents and benzaldehyde 10 was obtained in highest yields using toluene as solvent (Scheme 2). Additionally, the over oxidized product benzoic acid 11 was also observed but only as a minor product. Probably, benzene selenenic acid anhydride (BAA) 12 is operating as active catalytic species which was generated by the oxidation of pre-catalyst diphenyl diselenide 9 with oxidant TBHP.

In 2012, the oxidation of secondary alcohols 1 to ketones 5 was developed by using the combination of isoselenazolone catalyst 13 and bromine as an oxidant (Scheme 3). Various acyclic and cyclic aliphatic substrates were successfully oxidized to corresponding ketones in high yields during these investigations. The mechanistic studies suggest that the isoselenazolone catalyst 13 oxidized by bromine to form isoselenazolone(IV) dibromide 14, which is the key intermediate for the oxidation of aliphatic substrates 1.

Selenium-catalysts are not only limited to oxidation of alcohols but successfully applied for the oxidation of thiols. In 2012, Santi and co-workers introduced the selenium-catalysed oxidation of thiols 12 to disulfides 17 using PhSeZnCl 16 as catalyst in the presence of hydrogen peroxide (Scheme 4). The course of oxidation reaction depends on the nature of substrates used and no reaction was observed when cysteine and homocysteine were used as substrates. Notably, the oxidation of aliphatic thiols proceeded in higher yields compared to aromatic thiols. This is one of the rare cases of selenium catalysis where nucleophilic organoselenium species were employed as catalysts.

**Scheme 1.** Selenium-catalysed oxidation of alcohols 1 to carbonyl compounds 5 using bis[2-(2-pyridyl)phenyl] diselenide 3 as catalyst and N-chloro-4-chlorobenzenesulfonamide sodium salt 2 as oxidant.

**Scheme 2.** Selenium-catalysed oxidation of benzyl alcohol 8 to benzaldehyde 10 using diphenyl diselenide 9 as catalyst in the presence oxidant TBHP.

**Scheme 3.** Selenium-catalysed oxidation of secondary alcohols 1 to ketones 5 using isoselenazolone 13 as catalyst bromine as an oxidant.

**Scheme 4.** Selenium-catalysed oxidation of thiols 12 to disulfides 17 using PhSeZnCl 16 as catalyst in the presence of H$_2$O$_2$.
Selenium-catalysed epoxidation of alkenes

The progress of organoselenium reagents in catalysis began with the epoxidation of alkenes by Hori and Sharpless in 1978. In this report, various arylselenenic acids were investigated as catalysts for the epoxidation of olefins in the presence of hydrogen peroxide. Another report on selenium-catalysed epoxidation of alkenes was published in 1999 where 2,4-bis(perfluorooctyl)phenyl butylselenide was used to catalyse the epoxidation of both cyclic and acyclic olefins using 60% H₂O₂ as an oxidant in fluorous biphasic system. The epoxidation products were isolated in moderate to excellent yields (Scheme 5). Interestingly, the catalytic species was recovered successfully by phase separation and reused up to ten times without reducing product yields and increasing reaction times. Furthermore, the selenoxides were found as effective catalysts for the epoxidation of unsaturated substrates using same terminal oxidant. In 2009, Arends and co-workers employed glycerol-based solvents as green reaction media to develop the selenium-catalysed approach for the epoxidation of olefins using the combination of the catalyst bis[3,5-bis(trifluoromethyl)-diphenyl]diselenide and hydrogen peroxide as oxidant. Additionally, the toxicity profile of solvents and catalysts used in this reaction was also studied. Both solvents and catalysts were found safe to perform these oxidation reactions.

Selenium-catalysed hydroxylation of alkenes

The chemistry of selenium-catalysed hydroxylation of alkenes was reported by Knochel and coworkers. Trans-hydroxylation of olefins were achieved in useful yields using a fluorous biphasic system. Later on, the combination of SeO₂ catalyst with H₂O₂ was demonstrated as an effective catalytic system for trans-dihydroxylations of olefins. Olefinic substrates installed with aliphatic and aromatic functionalities were successfully oxidized to trans-diols in good yields under mild reaction conditions (Scheme 6). Additionally, the mechanistic studies revealed that the oxidation reactions were working via formation of perselenic acid as an active catalytic species, which was generated in situ by the reaction of SeO₂ with water followed by H₂O₂.

![Scheme 5. Selenium-catalysed epoxidation of alkenes using fluorous selenide as catalyst in the presence of hydrogen peroxide.](image)

![Scheme 6. Selenium-catalysed trans-dihydroxylation of olefins using SeO₂ as catalyst in the presence of H₂O₂.](image)

![Figure 1. Structures of organoselenium catalysts 9, 24 and 25.](image)

![Scheme 7. Selenium-catalysed trans-hydroxylation of cyclohexane using different catalysts 9, 24 and 25.](image)

The catalyst showed high catalytic activity at 1.0 mol% catalytic loading (see Scheme 7 and Table 1, entry 1). The reaction time was reduced significantly when diaryl diselenide equipped with CF₃ groups was used as catalytic selenium species (Table 1, entry 2). Moreover, the same hydroxylation reaction was performed at 100 mmol scale and oxidation product was obtained in 82% yield. Further the recyclable nature of catalyst makes this approach more suitable for industrial applications. In 2016, Zhu and others introduced polymer-supported organoselenium catalyst, which exhibited good catalytic activity with cyclohexene in water. Moreover, the catalytic reactions were performed at different catalytic loadings and it was observed that the catalytic loading directly influences the rate of reaction (Table 1, entries 3-5). Notably, the catalytic species was recovered and reused without losing its catalytic potential.

![Table 1. Selenium-catalysed trans-hydroxylation of cyclohexane under different reaction conditions.](image)
Selenium-catalysed cleavage of olefinic double bond

Oxidation of olefinic double bond is a useful reaction in synthetic organic chemistry because it provides an easy access for the synthesis of different carbonyl compounds. First time, the involvement of selenium-catalyst for oxidative cleavage of olefinic double bond to carbonyl compounds was introduced by Konwar and co-workers in 2007.\(^{34}\) Recently, Yu and co-workers demonstrated a highly efficient selenium-catalysed approach for the oxidative cleavage of terminal alkenes 27 using 5.0 mol\% of dialkyl diselenide 28 in the presence of hydrogen peroxide using environmentally friendly solvent ethanol.\(^{40}\) The cleavage reactions were found quite slow but carbonyl products were isolated in useful yields (Scheme 8). Various dialkyl diselenides 28 were investigated during these oxidations and dicyclohexyl diselenide 28 (R = c-C\(_6\)H\(_{11}\)) exhibited best catalytic activity. Additionally, this catalytic species 28 (R = c-C\(_6\)H\(_{11}\)) was found to be an efficient catalyst for the cleavage of terminal cyclic alkenes affording cyclic ketones in good yields.

\[
\begin{align*}
29 & \xrightarrow{R^3Se(O)OH} 30 \\
& \xrightarrow{\text{H}_{2}O, \text{EtOH}, 80-120 \ °C, 48-96 \ h} 31 \\
& \xrightarrow{[O]} 32
\end{align*}
\]

Scheme 8. Selenium-catalysed oxidative cleavage of alkenes 27 to ketones 5 using catalytic dialkyl diselenides 28.

On the basis of GC-MS analysis, it was proposed that the cleavage reaction was initiated via the selenium-catalysed epoxidation of alkene 27. Epoxide intermediate 30 undergoes hydrolysis to form diol 31. Diol 31 then forms the further oxidized product 32. On hydrolysis, oxidized product 32 degraded into ketone 5. The active catalytic species 29 generated in situ was probably playing a key role during the synthesis of epoxide intermediate 30 and oxidized product 32.

Selenium-catalysed oxidation of carbonyl compounds

Oxidation of carbonyl compounds is the key reaction in organic synthesis that leads various oxidation products such as carboxylic acids and esters. Organoselenium reagents have been received a particular attention as catalyst for the oxidation of aldehydes and ketones. In the first report on selenium catalysis, the oxidation of carbonyl compounds to carboxylic acids was achieved by using benzeneseleninic acid as catalyst in the presence of H\(_2\)O\(_2\).\(^{41}\) In 2000, selenium(IV) oxide was used as catalyst to develop similar oxidations.\(^{42}\) Ebselen (5-mol\%) was used to catalyse the oxidation of aldehydes to arenecarboxylic acids in the presence of t-butyldihydroperoxide (THBP).\(^{43}\) In 2015, Santi and co-workers developed a green approach for the oxidation of various aliphatic and aromatic aldehydes in water using 2.5 mol\% (PhSe), 9 in the presence of hydrogen peroxide (Scheme 9).\(^{44}\) This oxidative catalytic approach was applicable for substrates having electron-donating and electron-withdrawing functionalities but better yields were obtained with substrates having electron-withdrawing groups. Moreover, the catalytic diselenide species 9 was recovered from the aqueous layer obtained from the extraction of reaction mixture and used in further oxidation reactions. The catalytic cycle is initiated with the formation of benzeneperseleninic acid 34 by the oxidation of diphenyl diselenide 9 that oxidizes aldehydes 33 to corresponding carboxylic acids 36 along with the formation benzeneselenenic acid. Finally, benzeneselenenic acid is reoxidized to benzeneperseleninic acid 35 by H\(_2\)O to continue the catalytic cycle.

In several selenium-catalysed reactions, the oxidation of carbonyl compounds leads the formation of various cyclic and acyclic esters. Different selenium reagents 24, 37 and 38 were newly synthesized and used as catalyst during the investigations of various selenium-catalysed Baeyer–Villiger oxidations (Figure 2).

\[
\begin{align*}
& \xrightarrow{\text{H}_{2}O, \text{Ph}} \nonumber \\
& \xrightarrow{\text{PhSe-OH}} \nonumber \\
& \xrightarrow{\text{H}_{2}O} \nonumber \\
& \xrightarrow{\text{Ph-Se-OH}} \nonumber \\
& \xrightarrow{\text{H}_{2}O} \nonumber \\
& \xrightarrow{\text{Ph-Se-OH}} \nonumber \\
& \xrightarrow{\text{H}_{2}O} \nonumber \\
& \xrightarrow{\text{Ph-Se-OH}} \nonumber \\
& \xrightarrow{\text{H}_{2}O} \nonumber \\
\end{align*}
\]

Scheme 9. The mechanism for the selenium-catalysed oxidation of aldehydes 33 to carboxylic acids 36.

Figure 2: Structures of organoselenium catalysts 24, 37 and 38.

In 2001, Sheldon and co-workers developed Baeyer–Villiger oxidations of ketones 5 using 1 mol\% of bis(trifluoromethyl)phenyl diselenide 24 in the presence of hydrogen peroxide. The cyclic ketones 5 were oxidized to cyclic esters 39 in excellent yields while acyclic ketones could produce their corresponding esters in quite poor yields under similar reaction conditions (Scheme 10).\(^{45}\) Various diaryl diselenide-based selenium-catalysts were tested during these
oxidations and diselenides bearing electron-withdrawing groups showed better selectivity and reactivity compared to other diselenides. Probably, in situ generated selenenic and perselenenic acids are working as an active catalytic species. The electron-withdrawing nature of diselenides promotes the nucleophilic attack by the oxygen of hydrogen peroxide to form selenenic and perselenenic acid intermediates. Moreover, aldehydes were successfully oxidized into corresponding carboxylic acids in high yields using similar conditions.

![Scheme 10](image)

**Scheme 10.** Baeyer-Villiger oxidations ketones 5 to lactones 39 using 1.0 mol% of bis[trifluoromethyl]phenyl diselenide 24 in the presence of hydrogen peroxide.

Other cyclic ketones 5 were successfully converted to the corresponding lactones 39 in high yields using 5 mol% diselenide 37 in the presence of hydrogen peroxide. Moreover, Baeyer-Villiger oxidation products 39 were also obtained in excellent yields using selenoxide 38 as catalyst. α,β-Unsaturated ketones can also be used as substrates in selenium-catalysed Baeyer-Villiger oxidations to achieve various substituted vinyl esters in moderate yields. The recycling nature and reusing ability of selenium-catalyst makes this approach more attractive for synthetic organic chemists. Additionally, the selenium-catalysed approach was successfully applied in the synthesis of butanoldisulfides by Baeyer-Villiger oxidation of cyclobutanones.

Yu and others investigated an interesting selenium-catalysed approach for the oxidation of β-ionone where the selectivity of products was switchable according the choice of organoselenium catalyst. During these oxidations, diaryl diselenide 24 and dibenzyl diselenide 41 were used as catalyst and oxidation of β-ionone with 24 could furnish to epoxide 43 while catalyst 41 leads the formation of corresponding Baeyer-Villiger oxidation product 42 (Scheme 11). Additionally, oxidation reactions were performed up to 40 mmol scale and yields was remained high in both reactions (86% for ester 42 and 70% for epoxide 43). Moreover, the *in situ* generated benzyl selenenic acid was further used as catalyst in next four cycles of Baeyer-Villiger oxidation reaction although a significant decrease in the yield was observed in each cycle. Abiet the *in situ* generated catalytic species was peroxyxylselenin in both reactions.

![Scheme 11](image)

**Scheme 11.** Selenium-catalysed approach for the oxidation of β-ionone 40 to epoxide 43 and ester 42 using selenium-catalysts 24 and 41, respectively.

Selenium-catalysed oxidation of sp³ C–H bonds

Oxidation of sp³ C–H bonds to carbonyl compounds is an important synthetic protocol in organic chemistry. Recently, a selenium-catalysed oxidation approach benzyl C–H bond was developed where benzylpyridines 44 were treated with 5 mol% of PhSeBr 45 in DMSO/H₂O under oxygen atmosphere (1 atm). Additionally, 1.0 equivalent of AcOH was required to activate the sp³ C–H bond and oxidation products 46 were obtained in poor to excellent yields (Scheme 12). The wide range of functional groups on aromatic substrates were successfully tolerated and the selenium-catalytic oxidation approach follow the free radical mechanism.

![Scheme 12](image)

**Scheme 12.** Selenium-catalysed oxidation of benzylpyridines 44 to benzophenones 46 using PhSeBr 45 as catalyst.

Selenium-catalysed oxidation of oximes

The oxidation of oximes is another quite useful reaction in synthetic organic chemistry. Selenium-catalysed oxidation of aldoximes lead variety of oxidation products. Aldoximes 47 can be dehydrated to their corresponding organonitriles 49 using catalytic amounts of diaryl diselenide (3-FC₆H₅Se)₂ 48 and hydrogen peroxide as an oxidant (Scheme 13). The effect of different aliphatic and aromatic substituents in the substrates was studied and the reaction would not work well with most of the aldoximes having aliphatic substituents.

![Scheme 13](image)

**Scheme 13.** Selenium-catalysed oxidation of aldoximes 47 to organonitriles 49 using (3-FC₆H₅Se)₂ 48 as catalyst.

Additionally, the reactions were performed at large scale also and catalyst residue was reused in similar reactions up to 5-6 times without losing much catalytic efficiency. The possible catalytic cycle for the selenium-catalysed dehydration of aldoximes 47 to organonitriles 49 is shown in Scheme 14. According to the catalytic cycle, the reaction was initiated with the formation of selenenic acid intermediate 50 by *in situ* oxidation of catalytic species 48 with H₂O₂. Subsequently, the acid intermediate 50 undergoes dehydration and formed corresponding selenenic anhydride intermediate 51. Furthermore, the anhydride intermediate 51 reacts with aldoxime 47 to form another intermediate 52, which subsequently rearranged to its selenoxide isomer 53. Finally, the selenoxide isomer 53 facilitates the syn-elimination to form final product 49 and selenenic acid 50 to continue the catalytic cycle.
Scheme 14. Mechanism for the selenium-catalysed dehydration of aldoximes 47 to organonitriles 49 using diselenide 48 as catalyst.

In 2015, Yu and co-workers modified the same approach by using seleninic acid as pre-catalyst and air as an oxidant. A similar selenium-catalysed dehydration reaction was achieved under solvent free conditions. Recently, the same research group explored the catalytic utility of dibenzyl diselenide 41 in deoxyamination of oximes 54 to carbonyl compounds 5 in the presence of hydrogen peroxide (Scheme 15). Notably, the reaction was scaled-up up to 50 mmol and recycled catalyst was reused more five times but slight lowering was observed in the yields. Interestingly, both aldoximes and ketoximes exhibited the same potential in this reaction and oxidation products were obtained in good yields. Notably, peroxyselenenic acid was probably working as an active catalytic species. This reaction provides an opportunity to organic chemist for the deprotection of oximes.

Scheme 15. Deoxyamination of oximes 54 to carbonyl compounds 5 using dibenzyl diselenide 41 as catalyst.

**Selenium-catalysed Halogenation**

Few organoselenium catalysts have been successfully used to achieve halogenation of alkenes using halide ions in the presence of hydrogen peroxide. This chemistry began in 1979 when organoselenium catalysts were used for the chlorination of olefins using N-chlorosuccinimide (NCS) as chlorine source and hydrogen peroxide as an oxidant. The same chlorine source was employed to achieve selenium-catalysed allylic chlorination and chloroamidation of olefins. In 2013, polymer supported selenenyl bromide was developed as a catalyst for chlorinations. The importance of organoselenium catalysts is not limited to chlorination and catalysed few other halogenation reactions also. In 2015, Detty and co-workers synthesized few xerogel-sequestered silanated organoselenides which showed effective catalytic activity towards the bromination of alkenes using sodium bromide as bromine source. Furthermore, the diarylselenides have been used as co-catalyst with DMAP to achieve bromolactonizations. Recently, Zhao and co-workers introduced an organoselenium-catalysed approach for the allylic fluorination of functionalized alkenes 54 using 10 mol% of dibenzyl diselenide 41 using 

**Scheme 16. Selenium-catalysed allylic fluorination of alkenes 54 with 10 mol% of dibenzyl diselenide 41 using TMFP-OTf 55 as an oxidant and fluorine source.**

The catalytic cycle for the fluorination of alkenes 54 is depicted in Scheme 17. The catalytic cycle was initiated by the oxidative cleavage of diselenide 41 to more electrophilic selenium species BnSeF by the reaction with TMFP-OTf 55. The newly generated electrophile 58 activates the olefinic double bond of substrate 54 to form seleniranium ion intermediate 59. Furthermore, intermediate 59 is attacked by fluorine anion to form fluoroselenenylated intermediate 60. Then, another molecule of TMFP-OTF 55 oxidizes the selenium functionality of intermediate 60 to facilitate its elimination and form intermediate 61. On elimination of a proton and the selenium moiety, the intermediate 61 forms fluorinated product 57 and regenerates the electrophilic species BnSeF 58 which continues the catalytic cycle.
Scheme 17. The catalytic cycle for the fluorination of alkenes 54 to 57 with catalyst 41 using TMFP-OTf 55 as an oxidant and fluorine source.

Selenium-catalysed Amination of C-H Bonds

The amination of C-H bonds is an important synthetic tool for the formation of new C-N bonds in different organic compounds. In the past, various synthetic strategies have been used to construct such C-N bonds including transition-metal-catalysed protocols,62 hypervalent iodine63 and selenium(IV)-mediated amination of alkenes.64 In 2013, Breder and co-workers achieved the first selenium-catalysed amination of alkenes.65 In this reaction, various unactivated olefins 54 were aminated to allylic amides 64 in good to excellent yields. Interestingly, phenylselenenyl bromide was found to be an inefficient catalyst for the amination reaction in the presence of NFSI 63 under similar reaction conditions. Additionally, diphenyl diselenide 9 was found to be an attractive catalyst for the amination of unactivated cyclic olefins under similar reaction conditions.

Scheme 18. Selenium-catalysed amination of alkenes 54 using NFSA 63 as an oxidant and source of nitrogen.

The same catalyst/oxidant [(PhSe)2 9/NFSI 63] combination was employed for the amination of terminal alkenes 65 in the presence of a base and the amination occurred selectively at position C-3. 3-Amino allyl alcohols 66 were isolated in good to high yields (Scheme 19). Interestingly, the reaction site was switched completely from terminal to the other side of double bond when the reaction performed with substrates without an alcoholic group. A mixture of amination products was observed when substrates bearing protected alcohols were employed under similar reaction conditions. Notably, the presence of hydroxyl groups is mandatory to achieve a selective amination at the C-3 position. Moreover, the same catalytic system was able to aminate disubstituted alkenes at C-3 position with similar catalytic potential.

Scheme 19. Selenium-catalysed amination of terminal alkenes 65 using diphenyl diselenide 9 as catalyst and NFSI 63 as oxidant and nitrogen source.

Recently, Zhao and co-workers developed a selenium-catalysed direct C-H pyridination of 1,3-dienes.66 In this report, 1,3-dienes 67 were treated with N-fluoropyridinium triflate 68 in the presence of 20 mol% (BnSe)2 41 and pyridinium triflates of 1,3-dienes 69 were obtained in good to excellent yields (Scheme 20). N-Fluoropyridinium triflate 69 was used as an oxidant and pyridine source in this reaction.

Scheme 20. Selenium-catalysed C-H pyridination of 1,3-dienes 67 using (BnSe)2 41 as catalyst and N-fluoropyridinium triflate 68 as oxidant and pyridine source.

Furthermore, the impact of N-fluoropyridinium salts on pyridination of 1,3-dienes was also studied. It was found that the reaction did not work with sterically hindered salts. Notably, the yields were slightly lowered when N-fluoropyridinium tetrafluoroborates was replaced with the oxidant 69. Additionally, the same C-H pyridination was successfully performed with both acyclic and cyclic olefins. The catalytic cycle is based on usual selenenylation–deselenenylation pathway.

Phenylselenenyl bromide 45 was found to catalyse the amination of N-aryloxyacetamides 70 N-acetyl p-aminophenols 71 under mild reaction conditions. The amination occurred at para position and N-acetyl p-aminophenols 71 were obtained in good to excellent yields (Scheme 21). Moreover, dearomatization occurred when para-substituted N-aryloxyacetamides were treated under similar reaction conditions.67

Scheme 21. Selenium-catalysed conversion of N-aryloxyacetamides 70 N-acetyl p-aminophenols 71 using phenylselenenyl bromide 45 as catalyst.

Selenium-catalysed Cyclisation Reactions

Various selenium-catalysed cyclisation reactions have been successfully achieved under different reaction conditions. Usually, functionalized olefinic acids, amines or amides are found attractive substrates to develop diverse selenium-catalysed cyclisation reactions.

Selenium-catalysed Lactonisation
The chemistry of selenium-catalysed lactonization is quite new compared to other selenium-catalysed reactions. The first report on the application of selenium catalyst in lactonization was in 2002 but detailed studies were carried out in 2007 by Wirth and co-workers. The combination of diphenyl diselenide as catalyst and [bis(trifluoroacetoxy)iodo]benzene (PIFA) was used to achieve the lactonization of \( \beta,\gamma \)-unsaturated carboxylic acids to butenolides in good yields (Scheme 22). Other iodine(III) reagents such as PIDA and Koser’s reagents can be used oxidant but PIFA showed superiority probably due to its better solubility in acetonitrile and the higher electrophilic nature compared to other iodine(III) oxidants.

It is important to discuss the mechanistic pathway of this reaction to understand the role of hypervalent iodine species. The possible catalytic cyclic for selenium-catalysed lactonization of \( \beta,\gamma \)-unsaturated carboxylic acids to butenolides is presented in scheme 23. Initially, PIFA reacts with catalytic species to form another hypervalent iodine species, which converts into more electrophilic species phenylselenenyl trifluoroacetate. Furthermore, the phenylselenenyl trifluoroacetate activates the double bond of \( \beta,\gamma \)-unsaturated carboxylic acid to form selenolactone. The selenide functionality of lactone was oxidized by another molecule of PIFA to facilitate its elimination via intermediate. Finally, intermediate transforms to the butenolides and regenerated iodine(III) species to continue the catalytic cycle.

In 2015, \( \beta,\gamma \)-unsaturated acids were treated under similar reaction conditions (Scheme 24). In 2012, Kumar and others developed the synthesis of isoselenazolone and dihydropyranones equipped with different electron-withdrawing and donating functionalities. Later on, Braga and others achieved similar selenium-catalysed lactonizations with the NaBr/H\(_2\)O\(_2\) combination. Recently, Breder and others replaced hypervalent iodine based oxidants with air in similar selenium-catalysed lactonizations. Additionally, the selenium-catalysed cyclisation approach was used during the synthesis of naturally occurring Greek tobacco lactone.

Selenium-catalysed Aminocyclisations

In the previous section, we have discussed the selenium-catalysed amination reactions using different nitrogen sources as an external nucleophile in the presence of terminal oxidants. There are few reports in the literature where selenium-catalysed aminocyclisations have been achieved using substrates having internal nitrogen nucleophiles. In 2015, Ortgies and Breder developed selenium-catalysed aminocyclisation of ortho-vinyl anilines 84 using 2.5 mol% of diphenyl diselenide 9 in the presence of NFSI 63 as oxidant. The aminocyclisation reactions were performed in toluene and functionalized indoles 85 were obtained in good yields (Scheme 26).

Scheme 26. Selenium-catalysed aminocyclisation of ortho-vinyl anilines 84 to indoles 85 using diphenyl diselenide 9 as catalyst in the presence of NFSI 63.

Moreover, the reaction conditions were modified slightly and similar cyclisations were obtained in dioxane at 30 °C but required 10 mol% catalytic loading. Surprisingly, 1,2-phenyl migration product 87 with cyclisation was obtained exclusively when trisubstituted alkene 86 was used as the substrate (Scheme 27).

Scheme 27. Selenium-catalysed 1,2-phenyl migration with cyclisation of trisubstituted alkene 86 using diphenyl diselenide 9 as catalyst in the presence of NFSI 63.

Zhao and co-workers developed the selenium-catalysed cyclisation of olefinic sulphonamides 88 to five- and six-membered tosyl amines 89 in good to excellent yields using catalyst 9 and N-fluoropyridinium triflate 69 (Scheme 28). Surprisingly, seven-membered amines 91 were isolated in 45-82% yields under slightly modified reaction conditions (Scheme 28). Moreover, the same catalytic approach was applicable for the cycloetherification of olefinic alcohols.

The reductive carbonylation of ortho-nitrobenzamides 92 was successfully used to achieve aminocyclisations. In 2010, Wu and Yu developed selenium-catalysed carbonylation of ortho-nitrobenzamides 92 to 1H-quinazoline-2,4-diones 93 using Se powder as catalyst with CO at 2.0 MPa in the presence of triethylamine. The carbonylation reactions were performed in stainless steel autoclave at 170 °C and cyclic products 93 were isolated in good to excellent yields (Scheme 29). Notably, neither 1.0 MPa nor 3.0 MPa pressure of CO was suitable to achieve these cyclisations.

The catalytic cycle for the selenium-catalysed carbonylation of ortho-nitrobenzamides 92 to 1H-quinazoline-2,4-diones 93 is described in Scheme 30. The catalytic cycle was initiated with the in situ generation of carbonyl selenide (SeCO) 94 by the reaction of elemental selenium with CO. After that the carbonyl selenide species 94 reacts with ortho-nitrobenzamide 92 to form nitrene intermediate 95. The nitrene intermediate 95 reacts with another molecule of carbonyl selenide (SeCO) 94 and forms isocyanate intermediate 96 along with Se. Finally, the isocyanate intermediate 96 undergoes intramolecular hydrogen transfer to yield the final cyclic product 93. Probably, the role of triethylamine was to stabilize the in situ generated carbonyl selenide species.
The selenium-catalysed synthesis of highly functionalized pyrroles was achieved by the reaction of γ-nitro substituted carbonyl compounds with carbon monoxide using selenium as catalyst and N-methylpyrrolidine as a base (Scheme 31).

Scheme 31. Selenium-catalysed synthesis of pyrroles by the reaction of γ-nitro substituted carbonyl compounds with CO using Se as catalyst in the presence of a base.

Selenium-catalysed Esterification

In 1992, organoselenium catalysts were used for the first time in esterification reactions by Iwaoka and Tomoda. The next report on selenium-catalysed esterification was published only in 2012 by Kumar and co-workers. In this report, the catalytic potential of isoselenazolone was explored for the bromoesterification of cyclic olefins in good to excellent yields (Scheme 33). N-Bromosuccinimide (NBS) was used as bromine source and bromoesters were obtained in single trans-isomer. Notably, the mixture of both trans- and cis-isomers was obtained when acyclic alkenes were used as substrates in this reaction.

Scheme 33. Selenium-catalysed bromoesterification of cyclic olefins using NBS as bromine source.

In 2016, the combination of diphenyl diselenide catalyst with photocatalyst was used to develop the esterification of functionalized olefins. In order to achieve these esterification reactions, the mixture of alkenes with different aliphatic carboxylic acids in acetonitrile was irradiated in the presence of 10 mol% diphenyl diselenide and 5.0 mol% of photocatalyst. In most of the reactions, allylic esters were obtained in high yields except aromatic alkenes (Scheme 34). Probably, the photocatalyst was activated on irradiation at 465 nm and initiates the formation of more electrophilic active organoselenium species.
Selenium-catalysed Trifluoromethylthiolation

The selenium-catalysed trifluoromethylthiolation is a relatively new reaction compared to other selenium-catalysed reactions. The aminotrifluoromethylthiolation of styrene 27 (R¹ = Ph and R² = H) was achieved by the reaction with 20 mol% of di[4-methylphenyl]selenide 112 in water/acetonitrile using N-CF₃S-saccharin 111 as source of SCF₃. The trifluoromethylthiolated product 113 was obtained in 94% yield (Scheme 35). Various electron-rich and electron-withdrawing diarylselenides 112 were used as catalyst and electron-rich diarylselenides exhibited high catalytic efficiency. Notably, the selenide catalyst activates the CF₃S reagents to generate more reactive CF₃S⁺ cation and stabilizes the trifluoromethylthiiranium ion intermediate. The electronic properties of selenide catalyst play a vital role in this aminotrifluoromethylthiolation reaction.85


Furthermore, the same research group developed the hydroxytrifluoromethylthiolation of alkenes 21 using a similar reagent combination in nitromethane under oxygen atmosphere.86 Notably, 10 mol% of di[4-methylphenyl]selenide 112 catalyst was found sufficient to catalyse this reaction. The hydroxytrifluoromethylthiolated products 114 were isolated in moderate to excellent yields (Scheme 36). The scope of reaction was further expanded with variety of olefinic substrates and reaction products were obtained in higher yields with electron-withdrawing aromatic olefins compared to other substrates. The same catalytic combination was successfully applied for the trifluoromethylthiolactonizations of nucleophile-tethered alkenes.


The possible catalytic cycle for the selenium-catalysed trifluoromethylthiolation of alkenes 21 is depicted in Scheme 37. The catalytic cycle is initiated with oxidation of catalytic selenide species 112 to diaryl selenoxide 117 by oxygen in nitromethane. After that the selenoxide 117 is further reduced to 112 by N-CF₃S-saccharin 111 along with the formation of TIOH. Furthermore, the formation of an intermediate 115 occurs by the co-activation of selenide 112 and in situ generated TIOH. The intermediate 115 further reacts with alkenes 21 to form episulfonium ion intermediate 116. Finally, the intermediate 112 reacts with H₂O to form final product 114 and regenerates catalyst 112 to continue the catalytic cycle.

Scheme 37. The possible catalytic cycle for the selenium-catalysed trifluoromethylthiolation of alkenes 21.

Selenium-catalysed Ring Expansions

Recently, several research groups have identified the application of organoselenium catalysts in rearrangements. In 2015, ring expansion was achieved during the oxidation of functionalized isatins 118 using catalytic amount of diphenyl diselenide 9 in the presence of terminal oxidant H₂O₂.87 The oxidation reactions were found quite slow and isatoic anhydrides 119 (ring expansion products) were obtained in high yields (Scheme 38). Moreover, the reaction was scaled-up with up to 50 mmol and rearranged products 119 were obtained in healthy yields. Furthermore, the catalytic species was recovered simply by filtration of reaction mixture and catalyst was recovered in its mother liquid. The mother liquid was further charged up with the substrate 118 and hydrogen peroxide and process was successfully repeated up to seven times. Surprisingly, a significant increase in the yield of rearranged products 119 was observed in first five cycles while slightly lowered in remaining two cycles. An easy work-up procedure and recyclability of the catalyst makes this procedure more suitable for industrial purpose.

Scheme 38. Selenium-catalysed ring expansions.
Scheme 38. Selenium-catalysed ring expansion of isatins 118 to isatoic anhydrides 119 using diphenyl diselenide 9 as catalyst and H₂O₂ as an oxidant.

Another approach to organoselenium-catalysed oxidative ring expansions was developed by Yu and co-workers. In their report, various highly active disubstituted methylenecyclopropanes 120 were treated with 5 mol% of (2-FC₆H₄Se)₂ 121 in the presence of hydrogen peroxide and substituted cyclobutanones 122 (ring expansion products) were obtained in moderate yields (Scheme 39). Various diaryl diselenides bearing electron-rich and electron-deficient moieties but diselenides catalyst with electron-deficient moiety exhibited better catalytic activities compared to electron-rich species. Notably, monosubstituted methylenecyclopropanes could find the suitable substrates under oxidative reaction conditions used in this reaction.

Scheme 39. Selenium-catalysed ring expansion of cyclopropanes 120 to cyclobutanones 122 using diselenide 121 as catalyst and H₂O₂ as oxidant.

The catalytic cycle for the selenium-catalysed ring expansion of methylenecyclopropanes 120 to cyclobutanones 122 is described in Scheme 40. According to the catalytic cycle, the reaction was initiated with the oxidation of catalytic species 121 to seleninoperoxoic acid species 123 by hydrogen peroxide. The intermediate 123 activates the double bond of methylenecyclopropane 120 to form cationic intermediate 124. After that, the cationic intermediate 124 rearranged to another cationic intermediate 125. Furthermore, the intermediate 125 undergoes an intramolecular rearrangement to form another reaction intermediate 126. Finally, intermediate 126 decomposes to the ring expansion product 122 along with the formation of organoselenenic acid [E]. The organoselenenic acid species [E] oxidizes to selenoperoxoic acid [A] to continue the catalytic cycle.

Scheme 40. The catalytic cycle. Selenium-catalysed ring expansion of cyclopropanes 120 to cyclobutanones 122 using diselenide 121 as catalyst and H₂O₂ as oxidant.

Selenium-catalysed Stereoselective Reactions

The chemistry of selenium-catalysed stereoselective reactions is particularly less developed research area compared to its racemic reactions but the history of these reactions is become quite old now. The first report on the application of chiral selenium catalyst in asymmetric synthesis was introduced by Uemura and co-workers in 1994. Since this report, various chiral organoselenium catalysts have been successfully employed during the development of a wide range of stereoselective reactions. In 2006, Braga and his research group compiled a review article where they covered various aspects of selenium-catalysed asymmetric reactions including selenium-ligated reactions. Wirth and co-workers employed various nitrogen containing chiral diselenides to achieve the synthesis of enantiomerically enriched secondary alcohols via the addition of diethylzinc to aldehydes. Moreover, the other research groups have discovered few more chiral selenium catalysts for similar reactions. Note that the catalytic amount of few chiral organoselenium reagents have been used as ligand in transition metal-catalysed reactions. Few selenium-based chiral ligands have been used to achieve the Cu-catalysed enantioselective conjugate addition of organometallic reagents to enantiomerically rich enones. Some selenium-based ligands have received a wide range of applications in Pd-catalysed stereoselective allylic alkylations. Additionally, few other organoselenium reagents have been identified as successful catalysts for different stereoselective reactions such as aldol reaction, Darzen reaction and Baeyer-Villiger oxidations. High selectivities were obtained in case of aldol and Darzen reactions while Baeyer-Villiger oxidations could only be achieved in low yields.
Chiral diselenides 128-131 were used as catalysts in stereoselective dihydroxylation of cyclohexene (Figure 3). Dihydroxylation was achieved in 20% enantiomeric excess when reaction was performed using sulfur-containing chiral diaryl diselenide 128 at room temperature.\(^\text{109}\) Moreover, the high selectivities were obtained at low temperature with the same chiral catalyst.\(^\text{95}\) Selenium-catalysts 129-131 were used in the hydroxylation of cycloalkenes and L-selenocystine based-catalyst 129 exhibited superior catalytic activity over catalysts 130 and 131.\(^\text{110}\) Unexpectedly, poor or no selectivity was observed when acyclic alkenes were hydroxylated using similar catalysts.\(^\text{110}\)

**Figure 3.** The structures of various chiral selenium reagents 128-131.

In 1998, Wirth and co-workers developed a selenium-catalysed asymmetric reaction based on stereoselective selenenylation-elimination reaction sequence.\(^\text{111}\) In this report, they developed a sequence of methoxyselenylation and oxidative β-hydride elimination of alkenes 132 using nitrogen-containing chiral diselenide 133 as catalyst and sodium persulfate as terminal oxidant (Scheme 41). The reaction products 136 were obtained in low yields with up to 75% enantiomeric excess.\(^\text{111}\) Initially, the diselenide species 133 activates the olefinic double bond of alkene 132 to form selenide intermediate 134. Furthermore, the selenium functionality of intermediate 134 was oxidized to intermediate 135 by sodium peroxodisulfate. Finally, the intermediate 135 undergo β-hydride elimination and form final product 136 along with the regeneration of catalytic species. Later on, the asymmetric electrochemical selenenylation-elimination reaction sequence was developed with moderate enantiomeric excess using catalytic amount of chiral diselenides.\(^\text{112}\)

**Scheme 41:** Selenium-catalysed asymmetric reaction based on the stereoselective selenenylation-elimination reaction of β-methyl styrene 132.

The same selenenylation-elimination sequence was utilized to achieve enantioselective lactonization of β,γ-unsaturated carboxylic acids 72 to γ-butenolides 74 using different enantiomerically pure diaryl diselenides. Notably, the limited success was achieved in terms of enantiomeric excess during these lactonizations.\(^\text{59,113}\) In 2016, Maruoka and coworkers reported the first highly enantioselective lactonization of β,γ-unsaturated carboxylic acids 72 to enantioenriched γ-butenolides 74 using indane-based chiral selenide 137. During these lactonizations NFSI 63 was used as terminal oxidant and γ-butenolides were obtained in excellent yields with up to 96% enantiomeric excess (Scheme 42).\(^\text{114}\)

![Image of selenium-catalysed asymmetric reaction](image)

**Scheme 42.** Selenium-catalysed enantioselective lactonizations β,γ-unsaturated acids 72 using 10 mol% of chiral catalyst 137 in the presence of oxidant NFSI 63.

Probably, the rigidity of an indane-based chiral selenium catalyst 138 was playing a vital role in achieving γ-butenolides 74 with high enantiomeric excess. Moreover, the synthesized γ-butenolides 74 were reduced to chiral (Z)-allyl alcohols without any notably decrease of optical purity.\(^\text{114}\)

Furthermore, the indane-based chiral selenide 138 was used to catalyse the lactonization of (E)-4-phenylbut-3-enio acid 71 using N-CF<sub>3</sub>S-saccharin 111 as source of SCF<sub>3</sub> in the presence of triflic acid (TIOH). The trifluoromethylthiolated lactone 139 was obtained in excellent yield with 72% enantiomeric excess (Scheme 43).\(^\text{115}\) Notably, the indane-based chiral sulfide catalysts showed better selectivity compare to selenide 138. Triflic acid was used to make the salt of catalytic species which activates the SCF<sub>3</sub> reagent.

**Scheme 43:** Selenium-catalysed enantioselective trifluoromethylthiolating lactonizations (E)-4-phenylbut-3-enio acid 71 using 20 mol% of indane-based chiral catalyst 138 and N-CF<sub>3</sub>S-saccharin 111 as source of SCF<sub>3</sub>.

Recently, menthane-based selenium catalyst 141 was used to transfer the chiral information during the catalytic oxylactonization of β,γ-unsaturated acids 140.\(^\text{116}\) The cyclised product 142 was obtained in 95% yield with up to 28% enantiomeric excess (Scheme 44). Moreover, the structurally similar catalyst 143 could produce only the racemic mixture, probably due to the steric hindrance on the selenium atom (Scheme 44).\(^\text{116}\)
Scheme 44: Selenium-catalysed enantioselective oxylactonizations of \( \beta,\gamma \)-unsaturated acids 140 using 5.0 mol% of menthane-based chiral catalyst 141 and 143 in the presence of \( \text{H}_2\text{O}_2 \).

In 2013, Yeung and co-workers synthesized new chiral \( C_2 \)-symmetric mannitol-derived cyclic selenium catalyst 145 in four chemical steps starting from mannitol.\(^{117}\) This catalyst 145 was used to develop enantioselective bromocyclisation of trisubstituted olefinic amines 144 as bromine source.\(^{117}\) The cyclisation reactions proceeded via an endo-cyclic process and the resulting functionalized pyrrolidines 147 were obtained with up to 95% enantiomeric excess (Scheme 45). Interestingly, the nature bromine source and position of attachment with nosylamide influence the selectivity. The presence of \( N \)-bromophthalimide (NBP) exhibited the superiority over other bromine source while the 3-nitrobenzenesulfonamide showed far better selectivity compare to its 2- and 4-nosyl analogues.

Scheme 45: Selenium-catalysed enantioselective bromocyclisation of trisubstituted olefinic amines 144 using 20 mol% of \( C_2 \)-symmetric mannitol-derived cyclic selenium catalyst 145 and NBP.

Recently, Zhao and co-workers modified the indane-based selenium catalyst 145 to 149 and applied for the catalytic trifluoromethylthiolating aminocyclisation of \( \gamma,\delta \)-unsaturated nosylated amines 148 in the presence of Lewis acid.\(^{118}\) During these cyclisations, \( \text{PhOSO}_2\text{NSCF}_3 \) was used as source of \( \text{SCF}_3 \) and the trifluoromethylthiolated pyrrolidines 151 were obtained in high yields with up to 95% enantiomeric excess (Scheme 46).\(^{124}\) Additionally, indane-based chiral sulfides were also explored in this reaction but could produce only low enantiomeric excess. Expectedly, the cyclisations were proceeded via an exo-cyclic process when reactions were performed with substrates having one more carbon atom.

Scheme 46: Selenium-catalysed enantioselective trifluoromethylthiolating aminocyclisation of \( \gamma,\delta \)-unsaturated nosylated amines 148 using 20 mol% of indane-based chiral catalyst 149 in the presence of a Lewis acid.

Very recently, the same indane-based selenium catalyst 149 was further explored by Zhao and co-workers to develop highly enantioselective desymmetrization and carbotrifluoromethylthiolation approach.\(^{119}\) In this approach, various gem-diaryl-tethered alkenes 152 were cyclised to tetrahydronaphthalenes 153 using catalytic species 149 in the presence of \( \text{TMSOTf} \). The same \( \text{SCF}_3 \) source was used and enantiomerically pure trifluoromethylthiolated tetrahydronaphthalenes 153 were isolated in >99% enantiomeric excess (Scheme 47).\(^{119}\)

Scheme 47: Selenium-catalysed enantioselective carbotrifluoromethylthiolation of gem-diaryl-tethered alkenes 152 using indane-cored chiral catalyst 149 in the presence of \( \text{TMSOTf} \).

Conclusions

In this review, we have covered various synthetically important organic transformations using variety of achiral and chiral organoselenium catalysts (Scheme 48). Various synthetic transformations such as oxidation of alcohols, olefins and carbonyl compounds, cyclisations and ring expansions have been successfully achieved using different organoselenium catalysts in the presence of mild oxidants. Few of these selenium-catalysed reactions have been successfully achieved at large scale with high yields and catalysts were recovered and reused several times without losing much catalytic efficiency. These catalytic approaches would be more suitable for industrial purpose. Recently, few chiral organoselenium
catalysts have been investigated to achieve different stereoselective cyclisations including carbocyclisations with prodigious selectivity. Moreover, few products obtained during these catalytic transformations are important synthetic intermediates for the construction of biologically active synthetic and natural products.

Conflicts of interest
There are no conflicts to declare.

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Notes and references