Organoselenium Chemistry

Authors: Fateh V. Singh, Thomas Wirth

Address: VIT University, Chennai Campus, Vandalur-Kelambakkam Road,
Chennai-600127, Tamil Nadu, India

Cardiff University, School of Chemistry, Main Building, Park Place,
Cardiff CF10 3AT, United Kingdom

Email: wirth@cf.ac.uk
1. Introduction

Organoselenium chemistry has been established as valuable research area in synthetic and medicinal chemistry.\textsuperscript{1-11} After the discovery of the selenoxide elimination reaction in early 1970s,\textsuperscript{12-14} organoselenium reagents received the great success in organic synthesis including asymmetric synthesis.\textsuperscript{15-18} More commonly, synthetic transformations such as selenenylation, selenocyclizations and 2,3-sigmatropic rearrangements have been successfully achieved using these reagents under mild reaction conditions.\textsuperscript{19-33} The application of these reagents in catalysis makes them more suitable reagents in organic synthesis.\textsuperscript{34-39} Several books,\textsuperscript{1-7, 41-43} book chapters\textsuperscript{8-11, 44-48} and review articles\textsuperscript{49-64} have been published to explain the utility of organoselenium reagents in synthesis. This chapter highlights the application of organoselenium reagents in organic synthesis including asymmetric synthesis.

2. Organoselenium Reagents As Electrophiles

Organoselenium reagents play different roles in organic reactions but mainly known for their electrophilic behaviour. The electrophilic selenium species can be generated by the cleavage of the Se-Se bond of diselenides and can be used to activate the olefinic double bonds. Due to their electrophilic character, selenium electrophiles react with olefinic double bonds to form three membered seleniranium ion intermediate. Furthermore, the seleniranium ion intermediate can be employed to achieve various selenenylation reactions with different nucleophiles.

2.1. Selenenylation Reactions
Selenium electrophiles have been successfully used to achieve various selenylation reactions such as selenylation of olefins, arenes and other organic species. In the section, various selenylation reactions achieved in current decade will be highlighted.

### 2.1.1 Selenenylation of Alkenes

The addition of selenium electrophiles to alkenes is an important reaction after the discovery of selenoxide eliminations. In the beginning, Nicolaou and coworkers introduced two selenenylation agents $N$-phenylselenophtalimide ($N$-PSP) and $N$-phenylselenosuccinimide ($N$-PSS) and employed these for the selenenylation of olefins.\(^{65,66}\) Hydroxyselenation of alkenes was observed with commercially available selenium electrophile PhSeCl under aqueous reaction conditions.\(^{67}\) Furthermore, the conjugated and non-conjugated dienes were selenenylated under similar reaction conditions.\(^{68}\) Phenylselenyl chloride (PhSeCl) was found good carrier to transfer the PhSe functionality but the involvement of a nucleophilic chloride anion in the side reactions limit the scope of this reaction.

Latter on, diphenyl diselenide 2 was oxidized with ammonium peroxydisulphate to generate the electrophilic species which was further used in methoxyselenenylation of functionalized alkenes in good yields.\(^{69}\) In 1991, diphenyl diselenide 2 was oxidized to $m$-nitrobenzenesulfonate 3 with benzeneselenenyl $m$-nitrobenzenesulfonyl peroxide 1 and used as a carrier to transfer the PhSe moiety during the selenenylation of various olefinic substrates in moderate yields (Scheme 1).\(^{70}\) Different nucleophiles 5 were utilized during the selenenylation of olefinic substrates 4 and methanol was found the best nucleophile.
Scheme 1. Selenenylation of alkenes 4 with selenium electrophile \( m \)-nitrobenzenesulfonate 3.

In 1998, an iodine(III)-mediated selenenylation of olefinic substrates 7 was developed by Tingoli and coworkers. In this report, alkenes 7 were reacted with diphenyl diselenide 2 and (diacetoxyiodo)benzene 8 in acetonitrile and acetoxyselenenylation was observed in good yields (Scheme 2).

Scheme 2. Acetoxyselenenylation of alkenes 7 by the reaction with diphenyl diselenide 2 and (diacetoxyiodo)benzene 8.
More probably, the hypervalent iodine(III) reagent (diacetoxyiodo)benzene \(8\) was used to oxidize diselenide \(2\) to the more electrophilic selenium species \(9\), which activates the olefinic double bond to form three membered selenarium ion intermediate. Furthermore, the three membered intermediate reacts with acetate ions to yield the addition product. Additionally, PhI(OCOCF\(_3\))\(_2\) (PIFA) was also used instead of PIDA \(8\) but similar success could not observed probably due the presence of comparatively less nucleophilic triflate species.\(^7\)

Furthermore, same research group reported the synthesis of another selenium electrophile \(N\)-phenylselenosaccharin (NPSSac) \(13\) by the reaction of commercially available phenylselenium halide \(12\) and silver saccharin (AgSac) \(11\) in dichloromethane at room temperature (Scheme 3). Additionally, newly synthesized selenium electrophile \(13\) exhibited good selenylating properties with olefinic substrates.\(^7\)

\[ \text{PhSeX} \xrightarrow{12a: X = Cl; 12b: X = Br} \begin{array}{c} \text{CH}_2\text{Cl}_2, \text{Argon atm., rt, 3 h} \end{array} \begin{array}{c} \text{N} \rightarrow \text{SePh} \\ \text{11} \end{array} \begin{array}{c} \text{N} \rightarrow \text{SePh} \\ \text{13} \end{array} \]

**Scheme 3.** Synthesis of selenium electrophile \(N\)-phenylselenosaccharin (NPSSac) \(9\) by the reaction of phenylselenium halide \(12\) and silver saccharin (AgSac) \(11\).

In 2012, Wirth and coworkers developed an iodine-catalyzed approach for the selenenylation of terminal alkenes \(14\) in good yields by the reaction with diphenyldiselenide \(2\) using catalytic amount of molecular iodine (Scheme 4).\(^7\) Probably, PhSeI \(12c\) was playing the role of active catalytic species generated by the reaction of diphenyldiselenide \(2\) with molecular iodine in dichloromethane. Notably, additional
external nucleophile was not used during the reaction and terminal alkenes 14 were acting as nucleophile.\textsuperscript{73}

\[ \text{Ar} + (\text{PhSe})_2 + \text{I}_2 \text{ (20-mol\%)} \rightarrow \text{Ar} = \text{Ph, 2-MeC}_6\text{H}_4, 3-\text{MeC}_6\text{H}_4, 4-\text{MeC}_6\text{H}_4, 4-\text{PhC}_6\text{H}_4, 2-\text{Nap} \]

**Scheme 4.** Iodine-catalyzed selenenylation of terminal alkenes 14 by the reaction diphenyldiselenide 2 using catalytic amount of molecular iodine.

The catalytic cycle for iodine-mediated selenenylation of terminal alkenes 14 is depicted in scheme 5. According that the catalytic cycle was initiated by the reaction of diphenyl diselenide 2 with iodine to form the active catalytic species phenylselenium iodide 12c. Furthermore, the active catalytic species 12c activates the olefinic double bond of 14 to form three membered seleniranium ion intermediate 16. Latter on, the nucleophilic attack of alkene 14 to intermediate 16 could facilitate the formation of addition product 16. On elimination, the intermediate 16 furnished the final product 15 along with HI. Finally, HI could further react with diphenyldiselenide 2 to regenerate the active catalytic species phenylselenyl iodide 12c to continue the catalytic cycle.
Scheme 5. Catalytic cycle for iodine-catalyzed selenenylation of terminal alkenes 14 by the reaction diphenyldiselenide 2 using catalytic amount of molecular iodine.

Furthermore, the scope of similar iodine-catalyzed reaction was expanded for the methoxyselenenylation of terminal olefinic substrates 14 using methanol of source of nucleophile under microwave conditions. All the reactions were completed in few minutes and selenenylation products 18 were obtained in good yields (Scheme 6).\textsuperscript{74} Notably, the reaction was found to be quite effective for aromatic substrates but could not be applied to aliphatic olefinic substrates under similar reaction conditions. The mechanistic pathway was quite similar to that depicted in scheme 5 and similar active catalytic species PhSeI 12c was generated in situ to activate the double bond of olefinic substrates 14.

\[ \text{R}^1 \text{SeR}^2 + (\text{R}^2 \text{Se})_2 \xrightarrow{\text{I}_2 (20 \text{ mol\%}), \text{MeOH, DMSO}} \text{MW (100 W), 50 °C, 10 min} \xrightarrow{10 \text{ examples}} \text{R}^1 \text{SeR}^2 \text{OMe} \]

\( \text{R}^1 = \text{Ph, 4-MeC}_6\text{H}_4, 4-\text{ClC}_6\text{H}_4, 4-(\text{Me})_3\text{COC}_6\text{H}_4; \text{R}^2 = n-\text{Bu, Ph, 4-MeC}_6\text{H}_4, 4-\text{OMeC}_6\text{H}_4, 4-\text{ClC}_6\text{H}_4, 3-\text{CF}_3\text{C}_6\text{H}_4 } \)
Scheme 6. Iodine-catalyzed microwave-assisted methoxyselenenylation of terminal alkenes 14.

Recently, the electrophilic nature of phenylselenium iodide 12c was explored by Yan and coworkers for the hydroxyselenenylation of similar terminal alkenes 14. In this report, the alkenes 14 were reacted with stoichiometric amount of diaryl diselenide 2 and molecular iodine in MeCN/H$_2$O (1:1) under an oxygen atmosphere. β-Hydroxyselenenides were isolated in good to excellent yields (Scheme 7). The scope of iodine-mediated hydroxyselenenylation of alkenes was expanded with different olefinic substrates having electron withdrawing and donating functionalities on the aromatic ring. Additionally, selenenylation reaction exhibited similar potential with aliphatic olefinic substrates.

\[ \text{Scheme 7. Iodine-mediated hydroxyselenenylation of styrenes 14 with diaryldiselenide 2 in MeCN/H$_2$O (1:1).} \]

In 2015, a similar electrophilic selenium species (PhSeBr) 12b was generated in situ by using a different catalytic system and was employed for the selenenylation of similar terminal olefins 14. In this approach, the acetoxyselelenenylation of alkenes 14 was achieved by the reaction of diaryl diselenide 2 and catalytic amount of KBr using stoichiometric amount of external oxidant m-CPBA (Scheme 8). The role of external oxidant was to oxidize bromide ion to molecular bromine which was further reacted with diphenyldiselenide 2 to generate the active catalytic species 12b. The combination of
KBr and \( m \)-CPBA with diphenyldiselenide 2 was found quite effective catalytic system for the selenenylation of both aliphatic and aromatic olefinic substrates.

![Scheme 8: KBr-catalyzed acetoxyselenylation of alkenes 14 by the reaction of diaryl diselenides 2 with \( m \)-CPBA as a catalyst.](image)

\[ \text{R}^1 \quad 14 \quad (\text{R}^2\text{Se})_2 \quad \text{KBr} (20 \text{ mol\%}), \text{m-CPBA} \quad \text{AcOH, rt, 3 h} \quad 14 \text{ examples} \quad \text{20: 44-94\%} \]

**R**\(^1\) = \( n \)-Bu, Me\(_2\)(COH), Ph, 4-Me\(_6\)C\(_6\)H\(_4\), 4-BrC\(_6\)H\(_4\), 4-ClC\(_6\)H\(_4\), 4-FC\(_6\)H\(_4\), 4-AcOC\(_6\)H\(_4\), 4-t-BuC\(_6\)H\(_4\), Py; \( R^2 = \text{Ph or Bn} \)

The catalytic cycle for KBr-catalyzed acetoxyselenylation of alkenes 14 is described in scheme 9. The catalytic cycle initiates with oxidation of bromide ion to bromine using \( m \)-CPBA as an oxidant. Bromine was further reacted with diselenide 2 to form the more electrophilic species phenylselenyl bromide 12b. Electrophilic selenium species 12b activates the double bond of terminal alkene 14 to three membered selenarium ion intermediate 21 along with the formation of bromide ion. Finally, intermediate 21 reacts with acetic acid to yield final product 20 while bromide ion was further oxidized to continue the catalytic cycle.
Scheme 9. The catalytic cycle for KBr-catalyzed acetoxyselenylation of terminal alkenes 14 using m-CPBA as an external oxidant.

2.1.2. Stereoselective Selenenylation of Alkenes

The scope of organoselenium electrophiles is not limited to achieve racemic selenenylation but a number of highly stereoselective selenenylation have been developed extensively using a variety of chiral selenium electrophiles. Various enantiomerically pure chiral diselenides 22-39 have been synthesized and applied to transfer chirality in the stereoselective methoxyselenenylation of alkenes (Figure 1). Some new chiral binaphthyl-cored diselenides 22 were synthesized by Fujita and his research group and used in different stereoselective methoxyselenenylation of styrene 14 (R = H) (Scheme 10).77-82 The methoxyselenenylated product 41 was obtained with up to 49% diastereomeric excess (Table 1, entry 1).79 Furthermore, C2 symmetric chiral diselenides 23 and 24 were synthesized and employed for the methoxyselenenylation of styrene 14 (R = H) at low temperature using methanol as source of nucleophile.83-86 These two chiral auxiliaries 23 and 24 showed up to 77% diastereomeric excess during these methoxyselenenylation (Table 1, entries 2 and 3).84,86
Figure 1. The structures of selective chiral selenium diselenides 22-40.

Furthermore, ferrocenyl-cored chiral diselenides of type 25 were introduced by Uemura and coworkers and showed high selectivities in stereoselective methoxyselenenylation.\textsuperscript{87-92} The reaction products 42 were observed in good yields with upto 97\% diastereomeric excess (Table 1, entry 4).\textsuperscript{87}
Scheme 10. Asymmetric methoxyselenenylation of styrenes 14 using chiral diselenides 22-40.

Table 1. Stereoselective methoxyselenenylation of styrenes 14.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Chiral Diselenide</th>
<th>Counterion</th>
<th>Reaction Conditions</th>
<th>41 de (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22</td>
<td>Br</td>
<td>MeOH, 25 °C</td>
<td>49</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>OTf</td>
<td>Et₂O, –78 °C</td>
<td>77</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>OTf</td>
<td>Et₂O, –78 °C</td>
<td>73</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>Br</td>
<td>CH₂Cl₂, 25 °C</td>
<td>97</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>26</td>
<td>OTf</td>
<td>CH₂Cl₂/MeOH, –78 °C</td>
<td>92</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
<td>PF₆</td>
<td>CH₂Cl₂/MeOH, –78 °C</td>
<td>42</td>
<td>101</td>
</tr>
<tr>
<td>7</td>
<td>28</td>
<td>OTf</td>
<td>MeOH, –78 °C</td>
<td>94</td>
<td>105</td>
</tr>
<tr>
<td>8</td>
<td>29</td>
<td>OSO₃H</td>
<td>MeOH, 25 °C</td>
<td>62</td>
<td>105</td>
</tr>
<tr>
<td>9</td>
<td>30</td>
<td>OTf</td>
<td>MeOH, –114 °C</td>
<td>92</td>
<td>102, 103</td>
</tr>
<tr>
<td>10</td>
<td>31</td>
<td>OTf</td>
<td>MeOH, –114 °C</td>
<td>95</td>
<td>103</td>
</tr>
<tr>
<td>11</td>
<td>32</td>
<td>OTf</td>
<td>MeOH, –100 °C</td>
<td>93</td>
<td>103</td>
</tr>
<tr>
<td>12</td>
<td>33</td>
<td>OTf</td>
<td>CH₂Cl₂/MeOH, –78 °C</td>
<td>92</td>
<td>107</td>
</tr>
<tr>
<td>13</td>
<td>34</td>
<td>OTf</td>
<td>CH₂Cl₂/MeOH, –78 °C</td>
<td>81</td>
<td>109</td>
</tr>
<tr>
<td>14</td>
<td>35</td>
<td>OTf</td>
<td>Et₂O/MeOH, –100 °C</td>
<td>95</td>
<td>110</td>
</tr>
</tbody>
</table>
Additionally, camphor-based chiral diselenide 26 and its derivatives were tested in similar reactions\textsuperscript{93-98} and up to 92% diastereoselectivity was obtained (Table 1, entry 5).\textsuperscript{97} Furthermore, various C2 symmetric chiral diselenides 27 having cyclic amines as chiral moieties were synthesized by Fujita and coworkers and used as an electrophile in stereoselective methoxyselenenylation reactions with different alkenes.\textsuperscript{99-101} It was observed that moderate selectivity was obtained with styrene (Table 1, entry 6) but high selectivity was observed when (E)-β-methylstyrene was used as substrate. The presence of the nitrogen atom at the position segregated by four bonds in diselenides 27 makes them more suitable for strong Se---N interactions which are necessary for a transfer of the chirality in asymmetric selenenylation reactions.\textsuperscript{101}

After knowing the impact of strong Se---N interactions on the selectivity, Wirth and others reported the synthesis of diselenides 28, 29 and 30-32 having nitrogen and oxygen atom respectively at the position segregated by four bonds from the selenium atom.\textsuperscript{102-106} All the synthesized diselenides 28, 29 and 30-32 showed high selectivities (up to 95% \textit{de}) in the methoxyselenenylation of styrene 14 (R = H) (Table 1, entries 7-11). Furthermore, chiral diselenide 33 and its derivatives were synthesized by Tiecco and coworkers where sulfur atom was used at the position segregated by four bonds from the

| 15 | 36 | OTf | MeOH, –78 °C | 40 | 113 |
| 16 | 37 | OTf | MeOH, –78 °C | 72 | 115 |
| 17 | 38 | Br  | MeOH, rt    | 40 | 117 |
| 18 | 39 | OTf | MeOH, CH\textsubscript{2}Cl\textsubscript{2}, –78 °C | 36 | 118 |
| 19 | 40 | OTf | MeOH, –78 °C | 44 | 119 |
selenium atom. The methoxyselenenylation of styrene 14 was achieved in 96% diastereomeric excess when diselenide 33 was used as chiral source (Table 1, entries 7-11). In 2005, the heteroatom sulfur was replaced with selenium by Cox and Wirth to synthesize a new selenium-stabilized diselenide 34. It was used for the stereoselective methoxyselenenylation of styrene and could show up to 81% de which was slightly lower compared with diselenides having other heteroatoms sulfur 33 and oxygen 30, 31 (Table 1, entry 13). In 2009, Uehlin and Wirth reported the synthesis of another novel chiral diselenide 37 having C-2 symmetry and produce methoxyselenenylation of (E)-ethoxystyrenes with up to 95% de (Table 1, entry 14). In the next year, Wirth and coworkers introduced sulfoxide-containing diselenides but could not produce the high selectivities during similar methoxyselenenylation. Additionally, menthane- and terpene-cored chiral diselenides 35 and 36 were also tested in similar reactions but low and moderate selectivities were observed respectively (Table 1, entries 15 and 16). In 2012, Santi and coworkers developed another new chiral diselenide 38 having ester chiral functionality at ortho-position in which exhibited low selectivities in similar methoxyselenenylation (Table 1, entry 17). In 2016, ortho-functionalized optically active diaryldiselenides 39 were prepared by Scianowski and coworkers where similar selenenylation reactions could only achieve with up to 36% diastereomeric excess (Table 1, entry 18). Recently, dipinanyl-cored diselenides 40 were prepared by same research group and induced slightly better selectivity in methoxyselenenylation compared to diselenides 39 (Table 1, entry 19). Additionally, a variety of counterions have been successfully used during these methoxyselenenylation and the nucleophilicity of the counterion plays a crucial role for the selectivity in these reactions. The counterions
having lower nucleophilicity induce the higher selectivity in the methoxyselenenylation of olefins.\textsuperscript{95, 100, 101}

Oxygen nucleophiles can also be replaced with nitrogen and carbon nucleophiles during the oxyselenenylation of alkenes. Furthermore, few stereoselective azidoselenenylation\textsuperscript{120,121} and carboselenenylation\textsuperscript{122-124} have been achieved with high selectivities using nitrogen and carbon nucleophiles respectively.

\subsection*{2.1.3. Selenocyclizations}

Selenocyclizations are an important approach in organic chemistry which are frequently used to construct various bioactive heterocyclic compounds.\textsuperscript{30,31,125} Several reaction products such as selenolactones obtained from selenocyclization reactions have been successfully used as substrates in selenium-catalyzed cyclization reactions.\textsuperscript{37} In addition, the selenocyclization reaction has been applied in the total synthesis of natural products.\textsuperscript{126-129} The selenocyclization process is quite similar to the oxyselenenylation of alkenes as shown in scheme 11. The reaction begins with activation of the double bond in 43 with the selenium electrophile 44 to form seleniranium ion intermediate 45. The seleniranium ion intermediate 45 then reacts with an internal nucleophile to lead the formation of a selenocyclization product. The formation of cyclic product 46 occurs through \textit{endo}-cyclization while the other cyclic product 47 occurs via \textit{exo}-cyclization. This is depend on ring-size of newly formed product and reaction conditions applied (Scheme 11). Additionally, the selenium moiety in the products 46 and 47 can be oxidized to develop selenium-catalyzed cyclization reactions.
Scheme 11. Selenocyclization of olefins 43 to endo- and exo-cyclization products 46 and 47 using selenium electrophiles 44.

A variety of alkenes bearing internal nucleophile have been successfully cyclized to different selenocyclic products such as selenolactone and selenoethers using various selenium electrophiles. Initially, different benzene selenenyl sulphates were used as electrophiles to achieve the selenocyclization of unsaturated alcohols and unsaturated carboxylic acids under mild reaction conditions.\textsuperscript{130-132} In 1991, benzeneselenenyl \textit{m}-nitrobenzenesulfonate 3 was used to achieve thecyclization of unsaturated alcohols 48 and 49 to the corresponding five- and six-membered cyclic ethers 50 and 51 respectively in high yields (Scheme 12).\textsuperscript{70} The cyclization reactions were completed in short reaction times and proceeded via an \textit{exo}-cyclization process. Interestingly, the cyclization of unsaturated alcohol 48 (n = 1) produced the \textit{exo}-cyclic product 50 exclusively at \(-40\) °C while the \textit{endo}-cyclic product was only observed as minor product at 0 °C. Additionally, only the \textit{exo}-cyclic product 51 was obtained during the cyclization of olefinic alcohol 49 even at 0 °C.
Scheme 1. Selenocyclization of unsaturated alcohols 48 and 49 to generate O-heterocyclic compounds 50 and 51 using selenium electrophiles 3.

In a similar vein, the unsaturated carboxylic acids 52 and 53 were cyclized to five- and six-membered lactones 54 and 55 respectively using the same selenium electrophile 3 in excellent yields (Scheme 13). During these cyclizations, only exo-cyclic products were obtained and the selenocyclizations could not proceed via endo-cyclization process.

Scheme 13. Selenocyclization of unsaturated carboxylic acids 52 and 53 to lactones 54 and 55 respectively using the selenium electrophile 3.

In 1998, the oelfinic substrates 48 and 49 were cyclized to corresponding cyclic ethers 50 and 51 by Tingoli and coworkers. In this report, more electrophilic selenium species 9 was generated in situ by the oxidation of diselenide 2 with iodine(III) reagent 8 and used to activate the double bond of the unsaturated alcohol (Scheme 14). The cyclization reactions proceeded via an exo-cyclization process and reaction products 50 and 51 were obtained in good yields.
Scheme 14. Iodine(III)-mediated selenocyclization of unsaturated alcohols 48 and 49 to selenocyclic ethers 50 and 51 by the reaction of diphenyl diselenide 2 with PIDA 8 as an oxidant.

The selenocyclization of 2-(cyclopent-2-en-1-yl)acetic acid 56 under reaction conditions also proceeded by an exo-cyclization reaction. The fused bicyclic compound 6-(phenylselanyl)hexahydro-2H-cyclopenta[b]furan-2-one 57 was obtained in 76% yield (Scheme 15). Additionally, similar exo-cyclizations were observed during the selenocyclization of unsaturated ketonic substrates 58 and 59 (Scheme 15).
Scheme 15. Iodine(III)-mediated selenocyclization of unsaturated carboxylic acid 56 and ketones 58 and 59 to cyclic compounds 57, 60 and 61 respectively using selenium electrophile 9.

Furthermore, the similar selenocyclizations of unsaturated alcohol 49 and acid 52 were achieved by Tingoli and coworkers.\(^{72}\) In this report, active selenium electrophilic species \(N\)-phenylselenosaccharin (NPSSac) 13 was generated \textit{in situ} and used during these cyclization reactions. Cyclic ether 50 and lactone 54 were obtained as the reaction products in excellent yields (Scheme 16).

\[
\text{CH}_2\text{Cl}_2, \text{rt}, 1 \text{ h} \quad \begin{array}{c}
\text{PhSe} \quad \text{O} \\
\text{50: 92%}
\end{array}
\]

Scheme 16. Selenocyclization of the unsaturated alcohol 49 and acid 52 to the corresponding cyclic ether 50 and lactone 54 respectively using \(N\)-phenylselenosaccharin (NPSSac) 13 as an electrophile.

In 2010, Wirth and co-workers developed an approach for intermolecular selenocyclization of alkenes 14 and \textit{in situ} generated aryl selenium triflate by the reaction of diselenide 62 and bromine followed by the addition of silver triflate in THF at 0 °C (Scheme 17).\(^{111}\)
Scheme 17. Intermolecular selenocyclization of alkenes 14 and the electrophilic species aryl selenyl triflate 62.

Interestingly, an external nucleophile was not used during this selenocyclization approach and the formation of the cyclic product was achieved by the activation of the double bond to form a selenarium ion followed by subsequent cyclization involving the sulfoxide moiety of an in situ generated electrophile (Scheme 17). Notably, the reaction worked with terminal styrenes albeit in low yields, but β-substituted styrenes could not be utilized as substrate during these cyclizations.\(^{111}\)

In 2012, Menichetti and coworkers reported an intermolecular selenocyclization of 2-N-sulfonylamino diselenides 63 with alkenes 14 via copper(II)-catalyzed activation of the Se-Se bond in the presence of triethylamine. All the reactions were found to be quite slow and took 2-3 days to complete yielding benzo[b] [1,4]selenazines 64 in 43-79% yields (Scheme 18).\(^{133}\)
Scheme 18. Cu(II)-catalyzed intermolecular selenocyclization of 2-N-sulfonylamino diselenides 63 with alkenes 14 to form benzo[b][1,4]selenazines 64.

Additionally, cyclic alkenes 65 and 66 were found to be suitable substrates for the cyclization reaction under similar conditions and Se-containing tricyclic compound 67 and 68 were obtained in 60% and 59% yields respectively (Scheme 19).\textsuperscript{133}

Scheme 19. Cu(II)-catalyzed intermolecular selenocyclization of 2-N-sulfonylamino diselenides 63 with cyclic olefinic substrates 65 and 66 to Se-containing tricyclic compounds 67 and 68 respectively.

The catalytic cycle for the Cu(II)-catalyzed intermolecular selenocyclization of 2-N-sulfonylamino diselenides 63 with alkenes 14 to Se-containing heterocyclic compounds 64 is depicted in scheme 20.\textsuperscript{133} According the proposed catalytic cycle, Cu(II)-species activates the diselenide 63 in the presence of a base and the formation of
intermediate 69 occurs. The activated diselenide 69 reacts with alkene 14 forming the episelenarium ion intermediate 71 which is probably in equilibrium with the open carbocationic intermediate 72. Intermediate 72 can then undergo an intramolecular cyclization to yield the final product 64. Finally, selenolate ion intermediate 70 generated during the formation of episelenarium ion intermediate 71 can then be oxidized to regenerate the diaryl diselenide 63 to continue the catalytic cycle.

Scheme 20. Catalytic cycle for the Cu(II)-catalyzed intermolecular selenocyclization of 2-N-sulfonylamino diselenides 63 with alkenes 14 to benzo[b] [1,4]selenazines 64.

In 2016, Viglianisi and coworkers expanded the scope of the selenocyclization reaction of p-methoxystyrene 14 with 2-N-sulfonylamino diselenides 63 which have different electron-withdrawing and donating functionalities. The reactions were observed to be quite slow and took 1-10 days to complete but benzo[b] [1,4]selenazines 64 could produce in good yields (Scheme 21).
Scheme 21. Cu(II)-catalyzed synthesis of benzo[b] [1,4]selenazines 64 by the reaction of 2-N-sulfonylamino diselenides 63 with p-methoxystyrene 15.

Additionally, the denosylation of synthesized benzo[b] [1,4]selenazines 64 was performed with thioacetic acid and LiOH in dry DMF. The course of reaction was found to be relatively slow once again and N-unsubstituted selenazines 73 were obtained in good yield (Scheme 22).134 Recently, the selenocyclization approach was applied by Wang and Bates for the synthesis of one intermediate during the total synthesis of natural productallahabadolactone A.135

Scheme 22. Denosylation of compound 64 with with thioacetic acid and LiOH in DMF.

2.1.4. Stereoselective Selenocyclizations

Various chiral diselenides have been successfully used to achieve different stereoselective selenocyclization reactions of olefins bearing internal nucleophiles. In 1995, Uemura and coworkers achieved the distereoselective selenocyclization of unsaturated alcohol 49 and carboxylic acid 52 using chiral ferrocene-based selenium
electrophiles 74. The cyclized products 75 and 76 were obtained with high diastereomeric excess (Scheme 23).\textsuperscript{135} As usual, the selenium electrophile 74 was generated \textit{in situ} by the reaction of chiral diselenide 25 with bromine in dichloromethane at low temperature.

\textbf{Scheme 23.} Stereoselective selenocyclization of unsaturated alcohol 49 and carboxylic acid 52 using chiral ferrocene-based selenium electrophiles 74.

The camphor-based chiral selenium electrophiles 77 and 78 were synthesized \textit{in situ} and tested in the diastereoselective selenofunctionalizations of alkenols and alkenoic acids by Back and coworkers (Figure 2). Selenoetherifications were achieved with up to 90\% diastereoselectivity while poor selectivities were observed in case of selenolactonizations.\textsuperscript{96,98,136} Interestingly, the selenocyclization reactions proceeded quite efficiently with high selectivities using camphorselenenyl chlorides unlike the asymmetric oxyselelenenylation reactions.\textsuperscript{98}

\textbf{Figure 2.} Structures of camphor-based chiral selenium electrophiles 77, 78 and 79.
Furthermore, the chiral camphor-derived diselenide 25 was transferred into the corresponding camphorslenenyl sulfate 79 by in situ oxidation with ammonium persulfate in the presence of a stoichiometric amount of trifluoromethanesulfonic acid. Additionally, the newly generated selenium electrophile 79 was successfully employed during the synthesis of enantiomerically pure trisubstituted perhydrofuro[2,3-b]furans138 and 1,6-dioxaspiro[4.4]nonane derivatives (spiroacetals).139

In 1997, Tomoda and coworkers synthesized selenium electrophile 81 with hexafluorophosphate as the counter ion in situ by the reaction of chiral cyclic amine-based diselenide 27 with bromine at low temperature followed by the addition of silver hexafluorophosphate. Selenium electrophile 81 was then applied in the selenocyclization of different di- and trisubstituted olefins of type 80 containing oxygen nucleophiles with cyclized products 82 being obtained in excellent diastereoselectivities (Scheme 24). Notably, poor selectivities were observed during the cyclization of terminal alkenes.101

![Scheme 24](image)

Scheme 24. Asymmetric selenocyclization of different di- and trisubstituted olefins of type 80 using chiral selenium electrophile 81.

Furthermore, C2-symmetrical chiral diselenide 24 was converted into corresponding arylselenyl triflate 84 and used in stereoselective selenolactonization of
unsaturated carboxylic acids 83. Five-membered selenolactones 85 were obtained with more than 98% diastereomeric excess (Scheme 25). Once again, terminal alkenes could not show the promising selectivities under similar reaction conditions. Chiral selenium electrophile 84 has selenium and oxygen atoms in close proximity, allowing a Se···O intramolecular interaction. The stereochemistry of lactone 85 was assigned by the formation of lactone 86 by deselenenylation and comparison of the optical rotation of the resulting lactone 86 with the literature value.83 The element of C2 symmetry was another vital factor for obtaining high facial selectivity during these cyclization reactions.83,84 The same electrophilic species 84 was also applicable for the selenoetherifications of unsaturated alcohols but comparatively lower diastereoselectivities were observed.

**Scheme 25.** Stereoselective selenocyclization of unsaturated carboxylic acid 83 using chiral selenium electrophiles 84.

Some highly stereoselective selenolactonizations of unsaturated carboxylic acids of type 87 (dr up to 92:8, product 90) were developed by Wirth and coworkers using chiral selenium electrophiles 88 and 89 (Scheme 26).106 Additionally, polymer-bound chiral selenium electrophilic reagents were introduced by Uehlin and Wirth and were used in stereoselective selenofunctionalizations. However, the cyclized products were unfortunately observed in moderate selectivities.140 Sulfur-containing
aryl selenylbromides were investigated by Tiecco and coworkers in the stereoselective selenocyclizations of γ-alkenyl oximes.\textsuperscript{141}

\textbf{Scheme 26.} Stereoselective selenocyclization of unsaturated carboxylic acid 87 using chiral selenium electrophiles 88 and 89.

In the past few years, various terpene-derived chiral diselenides have been converted into corresponding selenium electrophiles and have been tested in different stereoselective selenocyclizations.\textsuperscript{113,115,119} Notably, these chiral electrophiles could achieve only limited success in the stereoselective cyclizations compared with the other electrophiles.

There are few selenocyclization reactions reported in the literature where olefins containing nitrogen nucleophiles were successfully cyclized to enantiomerically rich nitrogen-containing heterocycles using chiral selenium electrophile. In 1998, Wirth and coworkers introduced different chiral selenium reagents (Figure 3) and compound 91 was used to develop stereoselective aminoselenocyclizations.\textsuperscript{142} Furthermore, the carbamate 95 was cyclized by using different electrophile 88, 92-94 and the cyclized nitrogen-containing product 96 was obtained in the highest \textit{de} with electrophile 94 (Scheme 27).\textsuperscript{143}
Figure 3. The structures of chiral selenium electrophiles 88 and 91-94.

Finally, cyclized product 96 was converted into naturally occurring compound salsolidine 97 with 90% enantiomeric excess following deselenylation and deprotection of the Boc functionality (Scheme 27).\textsuperscript{143}

Scheme 27. Stereoselective Synthesis of salsolidine 97 by aminoselenocyclization of carbamate 95 followed by deselenylation and deprotection.

In 2000, Tiecco and coworkers used a camphor-derived chiral selenium electrophile (not shown here) to achieve aminocyclizations with high selectivities.\textsuperscript{144} Furthermore, the sulfur containing chiral selenium electrophile 99 was generated \textit{in situ} from corresponding diselenide and used to achieve the synthesis of isoxazolidines 100 with up to 86\% \textit{de} by aminoselenocyclization of olefinic substrates 98 (Scheme 28). The chiral isoxazolidine 100 was subsequently converted into 1,3-amino alcohol 101 in three chemical steps with 86\% enantiomeric excess.\textsuperscript{145}
Scheme 28. Stereoselective synthesis of enantiomerically enriched \(1,3\)-amino alcohol \(100\) by aminoselenocyclization of oximes \(98\) using chiral selenium electrophile \(99\).

Additionally, same chiral selenium electrophile \(99\) was used to achieve cyclic nitrones \(103\) by the aminoselenocyclization of olefinic oximes \(102\) with up to 64%. The cyclic nitrones \(103\) were then converted into the bicyclic compounds \(105\) through a dipolar cycloaddition with methyl propiolate (Scheme 29).^{146}

Scheme 29. Stereoselective synthesis of cyclic nitrones \(103\) by aminoselenocyclization of oximes \(102\) using chiral selenium electrophile \(99\).

There are few selenocyclization reactions reported in the literature where alkenes bearing carbon nucleophiles have been successfully employed as substrates. The chemistry of carboselenocyclization is already matured^{147, 148} In the beginning, various functionalized cyclic products were obtained by carboselenocyclization of \(\beta\)-dicarbonyl compounds using selenium electrophiles.^{149, 150} The first report on stereoselective
carboselenocyclizations was introduced in 1998 by Déziel and coworkers.\textsuperscript{151} In this report, olefinic substrates \textbf{107} were cyclized into tetrahydronaphthalene scaffolds \textbf{109} using chiral selenium electrophile \textbf{84}. Initially, the methoxyselenenylation product \textbf{108} (with 98\% de) and the cyclized product \textbf{109} were obtained in a 1:1 ratio. Treatment on 108 with triflic acid resulted in a complete conversion to \textbf{109} via the seleniranium intermediate \textbf{110} (Scheme 30).

![Scheme 30](image-url)

\textbf{Scheme 30}. Stereoselective synthesis of tetrahydronaphthalene scaffolds \textbf{109} by carboselenocyclization of alkene \textbf{107} using chiral selenium electrophile \textbf{84}.

\textbf{2.1.5. Selenenylation of C-H Bonds}

\textbf{2.1.5.1. Selenenylation of Aliphatic C-H}

In the past few years, selenium electrophiles have been successfully applied for the selenenylation of both aliphatic and aromatic C-H bonds. The selenenylation of C-H bonds is now a useful reaction in organic synthesis. The selenenylation of 1-indanone \textbf{111} at \(\alpha\)-position was achieved in 2006 by Tingoli and coworkers using selenium electrophile \(N\)-phenylselenosaccharin (NPSSac) \textbf{11}. The \(\alpha\)-selenenylated product of 1-indanone \textbf{112}
was obtained in 72% yield (Scheme 31). The same reaction was also applied for the selenenylation of acyclic ketones at \( \alpha \)-position in high yields.

![Scheme 31](image)

**Scheme 31.** Functionalization of 1-indanone 111 at \( \alpha \)-position using \( N \)-phenylselenosaccharin (NPSSac) 13 as an electrophile.

Furthermore, the selenenylation of cyclic amides 113 was achieved by Kumar and coworkers using diphenyldiselenide 2 as source of electrophile in the presence of potassium tert-butoxide in DMSO. \( \alpha \)-Selenenylated cyclic amides 114 were obtained in moderate to good yields (Scheme 32). The scope of this approach was not limited to cyclic amide and acyclic amides were found to be potential substrates for this reaction.

![Scheme 32](image)

**Scheme 32.** Selenenylation of cyclic amides 113 at the \( \alpha \)-position using diphenyldiselenide 2 in the presence of potassium tert-butoxide in DMSO.

Notably, expected selenenylation product 116 was not obtained when \( \alpha \)-tetralone 115 was used as substrate in the same reaction under similar reaction conditions. In this reaction, the formation of 2-phenylselanyl-1-naphthol 117 occurred by concomitant chalcogenation and aromatization (Scheme 33).
Scheme 33. Conversion of $\alpha$-tetralone 115 to 2-phenylselanyl-1-naphthol 117 using diphenyldiselenide 2 in the presence of potassium tert-butoxide in DMSO.

2.1.5.2. Selenenylation of Aromatic C-H

There are few reports in which selenium electrophiles have been used for the selenenylation of aromatic C-H bonds. In few approaches, transition metals have been used to initiate the reaction while few reactions proceeded without using any transition metal.

2.1.5.2.1. Metal-mediated Selenenylation of Aromatic C–H

Various metals have been successfully introduced into the selenenylation of aromatic C-H bonds. In 1995, Kim and Lee achieved the selenenylation of pyrimidones using diphenyldiselenide 2 as source of electrophile in the presence of catalytic amount of Mn(OAc)$_3$ in DMSO. The approach however could only provide selenenylaion products in low yields.\(^{153}\)

2.1.5.2.1.1. Copper-Mediated Selenenylation of Aromatic C–H

In 2014, Cu(I)-catalyzed approach for the selenenylation of 3-(4-methoxyphenyl)imidazo[1,5-\textit{a}]pyridine 118 was reported by Shibahara and coworkers using diphenyldiselenide 2 as an electrophile in the presence of catalytic amounts of CuBr. The reaction product 119 was obtained in quantitative yields (Scheme 34).\(^{154}\) Additionally, 1-methylindole was tested as substrate under similar reaction conditions. Selenenylation was observed at C-2 position but reaction product 121 was obtained in
low yield compared to the selenenylation of 3-(4-methoxyphenyl)imidazo[1,5-\textit{a}]pyridine 118 (Scheme 32).^{154}

![Scheme 34. Cu(I)-catalyzed selenenylation of 3-(4-methoxyphenyl)imidazo[1,5-\textit{a}]pyridine 118 and 1-methylindole 120 using diphenyldiselenide 2 as an electrophile.](image)

Selenenylation of 8-aminoquinolones 122 was achieved at the C-5 position by using various diselenides of type 2 as electrophilic source and 1.5 equivalents of CuBr$_2$ in DMSO under an oxygen atmosphere. Notably, the selenenylation reactions were found to be slightly sluggish and require higher temperature to precede while corresponding diarylselenides 123 were obtained in good yields (Scheme 35).^{155} This approach was found to have equal potential to selenenylate substrates having both electron-donating and withdrawing groups.
Scheme 35. Cu(II)-Mediated selenenylation of 8-aminoquinolones 122 to corresponding diarylselenides 123 using diaryldiselenides 2.

In 2016, the diselenenylation approach was developed where benzamides 124 (X = CH) or nicotinamides 124 (X = N; R² = H) were used as substrates by Baidya and coworkers. In this report, diselenenylation of benzamides 124 was achieved by the reaction with different diaryldiselenides 2 in the presence of Cu(OAc)₂ in DMSO. The selenenylation occurred at the C-2 and C-6 positions on the benzene ring and 2,6-bis(phenylselanyl)-N-(quinolin-8-yl)benzamides 125 were obtained in good yields (Scheme 36). In case of N-(quinolin-8-yl)isonicotinamides 124 (X = N; R² = H) the diselenenylation occurred at the C-3 and C-5 position on the pyridine ring and 3,5-bis(phenylselanyl)-N-(quinolin-8-yl)isonicotinamides were obtained in useful yields. The course of reaction was not to found change much when using different electron-donating and withdrawing groups on aromatic ring on the substrate.

\[ \text{Scheme 36. Cu(II)-Mediated diselenenylation of benzamides 124 using diaryldiselenides 20 and Cu(OAc)₂ in DMSO.} \]

Monoselenenylation was observed in case of N-(quinolin-8-yl)thiophene-2-carboxamide 126 as a substrate by using various diaryldiselenides 2 under similar reaction conditions. The selenenylation was occurred at the C-3 position on the thiophene
ring and 3-(arylselanyl)-N-(quinolin-8-yI)thiophene-2-carboxamides 127 were obtained 55-92% yields (Scheme 37).

![Scheme 37](image)

**Scheme 37.** Cu(II)-Mediated selenenylation of \(N\)-(quinolin-8-yI)thiophene-2-carboxamide 126 using diaryldiselenides 2 and Cu(OAc)\(_2\) in DMSO.

Other selenenylation were also achieved using Cu(OAc)\(_2\) as catalyst in same report. Similar amide substrates 124 were treated with diphenyldiselenide 2, 20 mol\% of Cu(OAc)\(_2\), KF as an additive and silver carbonate as an oxidant in DMSO. The diselenenylated products 125 were obtained in moderate to good yields (Scheme 38).

Unlike \(N\)-(quinolin-8-yI)thiophene-2-carboxamide 126, selenenylation was observed when \(N\)-(quinolin-8-yI)thiophene-3-carboxamide 126 (3-thienyl) was used as substrate. Probably, silver carbonate was used to regenerate the Cu(II) species *in situ* by oxidation of the reduced Cu(I) species.

![Scheme 38](image)

**Scheme 38.** Cu(II)-Catalyzed mono-/diselenenylation of benzamides 124 using diphenyldiselenides 2 and Cu(OAc)\(_2\) as catalyst and Ag\(_2\)CO\(_3\) as an oxidant.
2.1.5.2.1.2. Palladium-Catalyzed Selenenylation of Aromatic C–H

Recently, the selenenylation of aromatic species have been developed using selenium electrophiles in the presence of a palladium catalyst. In 2015, the selenenylation of arenes 128 was developed by Law and others using N-(phenylseleno)phthalimide (N-PSP) 129 as an electrophile and [PdCl₂(MeCN)₂] 130 as catalyst in an environmentally friendly solvent water. Monoselenenylated products 131 were obtained in low yields as major reaction products while diselenenylated products 132 were isolated as minor product in few of the reactions (Scheme 39).¹⁵⁷

![Scheme 39](image)

**Scheme 39.** Pd-Catalyzed selenenylation of arenes 128 using N-(phenylseleno)phthalimide (N-PSP) 129 and 10 mol% of [PdCl₂(MeCN)₂] 130.

Furthermore, interesting observations were seen when two parallel reactions were performed with similar arenes 128 and electrophilic selenium species 129 in the presence of same catalyst 130 using different ratios of same solvent (DMSO/H₂O) combination (Scheme 40).¹⁵⁸ Monoselenenylated products 131 were obtained when reactions were attempted in a 1:1 ratio of DMSO and water as the solvent while diselenenylation products 132 were achieved where a 4:1 ratio of the same solvent combination was used (Scheme 40). The other reaction conditions were kept the same in both cases and the products 131 and 132 were both isolated in high yields.
Scheme 40. Pd-Catalyzed mono-/diselenenylation of arenes 128 using N-(phenylseleno)phthalimide (N-PSP) 129 and 10 mol% of [PdCl₂(MeCN)]₂ 130.

2.1.5.2.1.3. Iridium-Mediated Selenenylation of Aromatic C–H

Recently, iridium-complex (FlrPic) 134 was found as an efficient catalyst for the selenenylation of functionalized indoles 133. The selenenylation of indoles 133 were performed with diaryldiselenides 2 using 2.0 mol% of catalyst 134 in the presence of visible-light. Selenenylation occurred at the C-3 position and the unsymmetrical diarylselenides 135 were obtained in high yields (Scheme 41).\(^{159}\) Notably, reaction products 135 were obtained in comparatively lower yields with diheteroaryldiselenides 2 (\(R^7 = \) Pyridyn-4-yl, thiophene-2-yl and thiophene-3-yl). Additionally, the selenenylation reactions were unsuccessful when \(R^5 = \) Ts and \(R^6 = 2\)-methoxycarbonyl were used as substrates 133.

Scheme 41. Ir-Catalyzed selenenylation of functionalized indoles 133 using diaryldiselenides 2 and 2 mol% of FlrPic 134.
2.1.5.2.2. Metal-Free Selenenylation of Aromatic C–H

There are few reports where the selenenylation of aromatic C–H bonds have been achieved without using toxic metals. Initially, a metal-free selenenylation of aromatic species was developed by Yoshida and coworkers using benzeneselenenyl m-nitrobenzenesulfonate 3 as source of selenium electrophile.\(^2\) In 2006, (NPSSac) 13 was used as source of selenium electrophile to develop the similar selenenylation of aromatic species 136a and 136b (Scheme 42).\(^7\) Notably, both approaches were suitable only for the selenenylation of electron-rich arenes and electron-deficient arenes were found to be unsuccessful in this reaction.

Scheme 42. Metal-free selenenylation of electron-rich arenes 136a and 136b using N-phenylselenosaccharin (NPSSac) 13 as an electrophile.

In 2016, Braga and coworkers used molecular iodine as a catalyst to develop the selenenylation of imidazo[1,2-a]pyridines 138 using diaryldiselenides 2 in the presence of DMSO as an oxidant under solvent free conditions. The selenenylation of substrates 138 occurred at the C-3 position selectively and unsymmetrical diarylselenides 139 were isolated in high yields (Scheme 43).\(^1\) Additionally, this approach was successfully applied to the selenenylation of aromatic substrates having both electron-donating and withdrawing substituents.
Scheme 43. Iodine-catalyzed selenenylation of imidazo[1,2-a]pyridines 138 using diaryldiselenides 2.

In 2017, a NH₄I-mediated approach for the selenenylation of chromones 140 was investigated by the reaction of electrophilic selenium species 2 and ammonium iodide in the presence of air. The selenenylation of chromones 140 occurred at the C-3 position selectively and chromone-based unsymmetrical diarylselenides 141 were isolated in moderate to good yields (Scheme 44). Additionally, quinolin-4(1H)-one 140 (R¹ = R² = H; X = NH) was successfully used as a substrate and the corresponding selenenylation product 141 was obtained in 53% yield.
Regarding the reaction mechanism, NH₄I decompose to NH₃ and HI at 135 °C which gets further oxidized to iodine in the presence of atmospheric oxygen. Molecular iodine then reacts with diselenide species 2 to form active selenium electrophilic species PhSeI 12c that can be used for selenenylation of the substrates.

2.2. Cyclization Reactions

2.2.1. Metal-Free Cyclization Reactions

Selenium electrophiles have been involved in different cyclization reactions with or without using transition metals. In 2009, Amosova and coworkers developed an SeCl₂-mediated cyclization of divinyl sulfide 142 to 2,6-dichloro-1,4-thiaselenane 144 in quantitative yield (Scheme 45). In addition, the synthesized compound 144 was used as key precursor during the synthesis of selenium-containing heterocycles.

![Scheme 45. SeCl₂-mediated cyclization of divinyl sulfide 142 to 2,6-dichloro-1,4-thiaselenane 144.](image)

2.2.2. Metal-Mediated Cyclization Reactions

2.2.2.1. Iron-Mediated Cyclization Reactions

Various metals have been used either in stoichiometric or catalytic amounts to achieve different cyclization reactions using selenium electrophiles. During these cyclizations, neither metal nor diselenide species were able to activate the triple bond. Generally, the metal salt reacts with the diselenide to form a complex which further activates the triple bond. In 2015, Zeni and coworkers reported the synthesis of selenophenes 146 in good yields by the cyclization of functionalized 1,3-diynes 145 with
2.0 equivalents of dibutyldiselenide 2 and 2.0 equivalents of FeCl₃ (Scheme 46). Additionally, the cyclization reaction was attempted with catalytic amounts of FeCl₃ but this proved unsuccessful. Probably, the FeCl₃ reacts with diselenide species to form a more electrophilic species which can further activate the triple bond of substrates 145.

![Scheme 46. FeCl₃-Mediated cyclization of functionalized 1,3-diynes 145 to selenophenes 146 using dibutyldiselenide 2 and FeCl₃.](image)

The cyclization of substituted o-alkynylbenzamides 147 to 4-(phenylselanyl)-1H-isochromen-1-imines 148 was also developed by the reaction diaryldiselenide 2 with FeCl₃. The cyclized products 4-(phenylselanyl)-1H-isochromen-1-imines 148 were obtained in good yields (Scheme 47). In few a reactions, the exocyclic products (functionalized isobenzofuran-1(3H)-imines 149) were observed as a minor product.

![Scheme 47. The cyclization of functionalized o-alkynylbenzamides 147 using dibutyldiselenide 2 and FeCl₃ in dichloromethane.](image)
Furthermore, functionalized quinolines 151 could be synthesized in good yields by the cyclization of 2-aminophenylprop-1-yn-3-ols 150 using similar reagent combinations (a diaryldiselenide 2 and FeCl₃) in dichloromethane (Scheme 48). It was observed that Selenocyclizations worked well with substrates bearing both electron-donating and withdrawing substituents.

![Scheme 48](image)

Scheme 48. The synthesis of functionalized quinolines 151 from the cyclization of functionalized 2-aminophenylprop-1-yn-3-ols 150 with diaryldiselenides 2 and FeCl₃.

Recently, the same reagent combination (diaryldiselenide 2 and FeCl₃) was explored to achieve the carbocyclization of benzylic-substituted propargyl alcohols 152 to 2-organoselenyl-naphthalenes 153 (Scheme 49). The reactions were performed in dichloroethane (DCE) and cyclized products 153 were isolated in moderate to good yields.

![Scheme 49](image)

R¹ = H, Me, OMe, Cl; R² = iBu, Ph, 2-O2MeC₆H₄, 4-O2MeC₆H₄, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 4-F₂C₆H₄, 4-Cl₂C₆H₄, 1-Nap, 2-Nap; R³ = iBu, Ph, 2-Py, 4-BrC₆H₄, 3-CF₃C₆H₄, 4-ClC₆H₄, 4-MeC₆H₄, 4-O2MeC₆H₄, 4-FC₆H₄, 2-Nap
Scheme 49. The cyclization of propargyl alcohols 152 to 2-organoselenyl-naphthalenes 153 using diaryl diselenides 2 and FeCl₃.

In 2016, 1,3-diynyl derivatives 154 were cyclized to benzo[b]furan-fused selenophenes (114: X = O) by using similar reagents. The cyclic products 155 were obtained in moderate to good yields (Scheme 50). Additionally, this approach was successfully applied for the synthesis of benzo[b]thiophene-fused selenophenes (155: X = S) or benzo[b]seleno-fused selenophenes (155: X = Se).

Scheme 50. The cyclization of 1,3-diynyl chalcogen derivatives 154 to benzo[b]chalcogen-fused selenophenes 155 by the reaction with diaryldiselenides 2.

In 2015, Zeni and coworkers developed a high yielding Fe(III)-catalyzed approach for the synthesis of 3,4-bis(organoselanyl)-2,5-dihydrofurans 157 by the cyclization of 1,4-butyne-diols 156 with diaryldiselenides 2 using 20 mol% of FeCl₃·6H₂O in DCE in the presence of an oxygen atmosphere (Scheme 51). Additionally, the same catalytic approach was found to be useful for the synthesis of 3,6-dihydro-2H-pyrans and 2,5-dihydro-1H-pyrroles. It is important to note that neither the selenium species nor the iron salt alone was sufficient to promote these cyclizations and both reagents were required for the reaction to proceed. The diselenide species 2 reacts
with FeCl$_3$ to form more electrophilic species which occur further coordinate with one of hydroxyl group to initiate the catalytic reaction.

![Scheme 51](image)

**Scheme 51.** Fe(III)-catalyzed cyclization of 1,4-butyne-diols 156 to 3,4-bis(organoselanyl)-2,5-dihydrofurans 157.

### 2.2.2.2. Copper-Mediated Cyclization Reactions

Recently, Zeni and coworkers developed similar cyclizations using CuI as catalyst. In this report, functionalized 2-(phenylselanyl)indolizines 159 were synthesized in good yields by the cyclization of substituted propargylpyridines 158 with diaryldiselenides 2 using 20 mol% of CuI in the presence of Na$_2$CO$_3$ base (Scheme 52). Like FeCl$_3$, CuI coordinates with diselenide species 2 and formed a complex which activates the triple bond in substrates 158. In addition, the similar cyclization reaction was tested by using dibutyldiselenide 2 (R = "Bu) as source of electrophile but could not promote these cyclizations successfully.

![Scheme 52](image)

**Scheme 52.** copper-mediated cyclization of 2-propargylpyridines 158 to 2-(phenylselanyl)indolizines 159.

\[ R^1 = H, \text{Me}; R^2 = H, \text{Ph, 4-MeC}_6\text{H}_4, 4-\text{OMeC}_6\text{H}_4; R^3 = \text{OAc, COOEt}; R^4 = \text{Ph, 2-MeC}_6\text{H}_4, 4-\text{MeC}_6\text{H}_4, 4-\text{ClC}_6\text{H}_4, 2-\text{OMeC}_6\text{H}_4, 4-\text{OMeC}_6\text{H}_4, 3-\text{CF}_3\text{C}_6\text{H}_4 \]
Scheme 52. Cu(I)-catalyzed cyclization of functionalized propargylpyridines 158 to 2-(phenylselanyl)indolizines 159 using diselenide 2 as an electrophile.

2.2.3 Lewis Acid-Mediated Cyclization Reactions

The combination of Lewis acid with phenylselenyl chloride 12a was found an efficient reagent system to achieve the carbocyclization of stilbenes 160 to dihydronaphthalenes 161. The cyclized products 161 were obtained in moderate to high yields (Scheme 53). Two different Lewis acids SnCl₄ and BF₃·OMe₂ were used during these cyclizations with BF₃·OMe₂ was found superior over SnCl₄.

Scheme 53. Selenium-mediated approach for the carbocyclization of stilbenes 160 to dihydronaphthalenes 161.

Benzo[b]fluorenes 163 were synthesized in useful yields by double carbocyclization of stilbenes 162 under similar reaction conditions using BF₃·OMe₂ as a Lewis acid (Scheme 54). Most of the reactions were found to be quite slow and a few of them took 3 days to complete. The reaction products 163 were observed in slightly lower yields when electron-donating substituents were used at the aromatic ring in the substrates.
Scheme 54. Selenium-mediated synthesis of benzo[b]fluorenes 163 by double carbocyclization of stilbenes 162.

2.3. Metal-Catalyzed Coupling Reactions

Organoselenium reagents have received attention due to their applications as electrophilic partners in metal-catalyzed coupling reactions with different organonucleophiles. The coupling reactions of organoselenium reagents provide access to symmetrical and unsymmetrical diorganoselenides. In 2007, the Cu(I)-catalyzed cross-coupling reaction of diaryldiselenides 2 was achieved with alkyl- or arylboronic acids 164 using 5.0 mol% of CuI-bpy (bpy = 4,4'-bipyridine) 165 (1:1) in DMSO:H₂O (2:1) at 100 °C under an oxygen atmosphere. The approach provides symmetrical and unsymmetrical diorganoselenides 166 in high yields (Scheme 55). This approach showed the tolerance to different electron-donating and withdrawing functionalities at the aromatic ring on the organoboronic acid substrates.

Scheme 55. Cu(I)-catalyzed coupling reaction of diaryldiselenides 2 with alkyl- or arylboronic acids 164 using 5.0 mol% of CuI-bpy 165 (1:1) in DMSO:H₂O (2:1).
In 2009, the similar cross-coupling reaction was developed by Alves and other using CuO nanoparticles (CuO Nps) as catalyst and various diarylselenides 166 were obtained in excellent yields.172 The recyclable nature of the catalyst makes this approach more advantageous over other cross-coupling approaches. Furthermore, CuI was used as catalyst by Alves and other to achieve similar reactions in high yields.173 Interestingly, glycerol was used as solvent and the mixture of CuI-glycerol was reused in similar cross-coupling reactions.173 In 2013, the combination of 3.0 mol% of CuSO\textsubscript{4} and 3.0 mol% of 1,10-Phen.H\textsubscript{2}O (Ph = phenanthroline) was used by Xu and coworkers as new catalytic system to catalyze the similar coupling reactions in good yields.174

In 2009, Wang and coworkers showed that 10 mol% of Fe powder could be efficient catalyst to achieve similar coupling reaction of diaryldiselenides 2 and arylboronic acids 164.175 In the same year, 10 mol% of InBr\textsubscript{3} was introduced by similar research group as an efficient catalyst to achieve similar coupling reactions.176 Recently, Alves and coworkers developed similar coupling reactions in good yields by using 10 mol% of AgNO\textsubscript{3} as catalyst.177

2.3.1. Coupling Reactions Using Ionic Liquids

In past few years, ionic liquids have received a particular attention in organic synthesis due to applications as versatile solvent in several organic reactions. In 2011, Alves and coworkers reported the cross-coupling reaction of organoselenyl chloride 12 with arylboronic acids 164 in an ionic liquid [bmim][PF\textsubscript{6}] (bmin = 1-butyl-3-methylimidazolium) 167 without using any metal catalyst. This approach provides the accessibility of both unsymmetrical and symmetrical diaryldiselenides 166 in moderate to excellent yields (Scheme 56).178 The course of similar reaction was tested in other
imidazolium ionic liquids such as [bmim][BF$_4$] and [bmim][NTf$_2$] but cross-coupling products 166 could obtain in lower yields compare to [bmim][PF$_6$] 167. Additionally, arylselenyl bromides 12 were successfully used electrophilic partners with arylboronic acids under similar coupling reaction conditions.

\[
\text{ArB(OH)$_2$ + RSeCl} \xrightarrow{\text{[bmim][PF$_6$] 167}} \text{ArSeR} \\
\text{rt, N$_2$, 2-6 h} \\
\text{17 examples} \\
\text{166: 84-96%}
\]

\[
\text{Ar} = \text{Ph, 2-MeC$_6$H$_4$, 3-MeC$_6$H$_4$, 4-MeC$_6$H$_4$, 2-OMeC$_6$H$_4$,} \\
\text{3-OMeC$_6$H$_4$, 4-OMeC$_6$H$_4$, 3-CF$_3$C$_6$H$_4$, 4-FC$_6$H$_4$, 2-} \\
\text{ClC$_6$H$_4$, 4-ClC$_6$H$_4$, 2-BrC$_6$H$_4$, 4-BrC$_6$H$_4$, 2-Nap; R = }^{\text{n}}\text{Bu,} \\
\text{Ph, 2-Py, 2-MeC$_6$H$_4$, 4-MeC$_6$H$_4$, 4-FC$_6$H$_4$, 4-ClC$_6$H$_4$, 3-} \\
\text{CF$_3$C$_6$H$_4$, 2,4,6-Me$_3$C$_6$H$_2$, 4-OMeC$_6$H$_4$}
\]


2.4. Carbene Insertion Reactions

In 2016, a metal-free approach for insertion of carbene in Se-Se bonds was introduced by Arunprasatha and Sekar. This carbene-insertion approach was used for the synthesis of bis(phenylseleno)acetals 169 in good yields by the reaction of $N$-tosylbenzylidenehydrazines 168 with diphenyldiselenide 2 in the presence of potassium tert-butoxide
Scheme 57. Metal-free and base-mediated approach for carbene insertion in Se-Se bonds.

All the carbene-insertion reactions were performed in DMSO at 100 °C and proceeded well (Scheme 57). In addition, the same carbene-insertion approach was successfully applied for the synthesis of thioacetals via insertion of carbenes in S-S bonds.

The possible reaction mechanism for carbene insertion reaction is depicted in Scheme 57. According that the reaction was initiated with the formation of diazo intermediate [A] by heating of tosylhydrazone 168 in the presence of a base. The diazo intermediate [A] converts to free carbene intermediate [B] with elimination of nitrogen. Furthermore, free carbene intermediate [B] reacts with diselenide 2 to form ylide intermediate [C]. Finally, intermediate [C] undergo 1,2-migration and form desired product 169.

2.5. Rearrangements
In 2010, Wirth and coworkers investigated the role of PhSeCl 12a in rearrangement reactions. In this report, the synthesis of functionalized naphth-1-ols 171 was developed by the cyclization of stilbenes 170 (R = Ar) having β-keto ester functionality with phenylselenyl chloride 12a followed by the 1,2-migration of aryl group (Scheme 58). Interestingly, this approach was not suitable for the substrates 170 (R = 4-OMeC₆H₄) bearing electron-donating groups at the benzene ring. The cyclization of stilbene 170 (R = 4-OMeC₆H₄) could be achieved only by using in situ generated more electrophilic selenium species such as phenylselenenyl trifluoroacetate. In addition, styrene 170 (R = Me) was also used as substrate and the mixture of cyclic product with 1,2-methyl migration 171 (R = Me) and without migration 172 (R = Me) was obtained in overall 50% yield with 2:1 ratio (Scheme 56).

![Scheme 58](image)

Scheme 58. The cyclization of stilbenes 170 to cyclic products 171.

Tancock and Wirth also explored the same reagent combination (FeCl₃ and PhSeCl 12a) to synthesize tetrasubstituted naphthalenes 174 by the cyclization of stilbenes 173 bearing β-keto ester moiety (Scheme 59). The course of the reaction is similar to the reaction described in Scheme 58.
Scheme 59. The cyclization of stilbenes 173 to cyclic products 174 with 1,2-aryl migration.

Various chiral selenides undergo stereoselective [2,3]-sigmatropic rearrangements in the presence of different terminal oxidants. These stereoselective [2,3]-sigmatropic rearrangements provide access to a variety of allyl alcohols and amines with high selectivities. There are several review articles and a book chapter available in the literature where different stereoselective [2,3]-sigmatropic rearrangements are covered.

3. Organoselenium Reagents as Nucleophiles

There are few reactions available in the literature where organoselenium reagents have been used as a nucleophile. The utility of these reagents as nucleophile was developed in 1970s. Since then various organoselenium reagents have been used as nucleophiles to develop several organic transformations. There are various inorganic selenium nucleophiles such as Li₂Se₂, Na₂Se, Na₂Se₂ and KSeCN which can be used to introduce a selenium atom in organic molecules. KSeCN is commercially available while others can be synthesized easily in situ by starting from metallic selenium.

Diaryldiselenides 2 reacts with Zn in the presence of AlCl₃ or RuCl₃ and form the nucleophilic zinc selenolate Zn(SeAr)₂ that can used for the synthesis of selenoethers, selenol esters and carboxylic acids. In 2009, Braga and coworkers developed the
synthesis of chiral β-seleno amines 177 in useful yields by the using in situ generated zinc selenolate species Zn(SeR)\(_2\) 176 in a biphasic system (Scheme 60).\(^{195}\) Both electron-withdrawing and donating groups at the aromatic ring in diaryldiselenides 2 were used and substrates installed with an electron-withdrawing group were found to be more effective. Additionally, different type of zinc selenolate species PhSeZnX could be prepare by the reaction of metallic zinc with phenylselenyl chloride or bromide and has been successfully applied as a nucleophile for the ring opening of epoxides.\(^{196}\) Additionally, aryl zinc selenolates were successfully used for the synthesis of diarylselenides 166 with the reaction of hypervalent iodine salts in aqueous media.\(^{197}\)

Scheme 60. The synthesis of chiral β-seleno amines 177 by the reaction with zinc selenolate species Zn(SeR)\(_2\) 176 in biphasic system.

The chemistry of these reagents as nucleophiles was began with nucleophilic substitution reactions\(^{188}\) but the main focus has been in their application in the synthesis of symmetrical and unsymmetrical diarylselenides via metal-catalyzed C-Se bond forming reactions. In 2002, Nishiyama and Sonoda introduced the application of these reagenets as a nucleophilic partner in Pd(0)-catalyzed cross-coupling reactions.\(^{198}\) In this reaction, phenyl tributylstannyl selenide 178 was treated with aryl iodides 179 in the
presence of 5 mol% of Pd(PPh₃)₄ 180 in toluene and diarylselenides 166 were isolated in good yields (Scheme 61).  

\[
\text{SeSnBu}_3 \quad + \quad \begin{array}{c} \text{I} \\ \text{R} \end{array} \quad + \quad \text{CO} \quad \xrightarrow{\text{Pd(PPh₃)₄ 180 (5 mol%) \, \text{toluene, 80 °C, 5 h}}} \quad \begin{array}{c} \text{R} \\ \text{Se} \end{array} 
\]

R = H, 2-Me, 3-Me, 4-Me, 4-OMe, 4-Cl, 4-NO₂

**Scheme 61.** Pd(0)-catalyzed coupling reaction of phenyl tributylstannyl selenide 178 with aryl iodides 179 using 5.0 mol% of Pd(PPh₃)₄ 180 in toluene.

Furthermore, Gujadhur and Venkataraman replaced phenyl tributylstannyl selenide 178 with phenyl selenol and achieved the coupling reaction with electron-rich aryl iodides 179 using CuI as catalyst. In 2004, phenyl selenol was used in Pd-catalyzed cross-coupling reactions with bromoporphyrins under mild reaction conditions. In the next year, Tanoka and coworkers developed the Rh-catalyzed reductive coupling of diselenides 2 with alkyl halides 181 in the presence of triethylamine using hydrogen as a reducing agent. The reaction products 183 were obtained in excellent yields (Scheme 62). The role of hydrogen is to generate Rh-SeR species by the reaction with catalyst RhCl(PPh₃)₃.

\[
\text{PhSeSePh} \quad + \quad \begin{array}{c} \text{R-X} \\ \text{X} \end{array} \quad \xrightarrow{\text{RhCl(PPh₃)₃ 182 (3 mol%), H₂ (1.0 atm)}} \quad \text{PhSeR} 
\]

\[
\text{PhSeSePh} \quad + \quad \begin{array}{c} \text{R-X} \\ \text{X} \end{array} \quad \xrightarrow{\text{THF-Et₃N (5:1), 50 °C, 24 h \, 8 examples}} \quad \text{PhSeR} 
\]

R = Bn, PhCO, Me(CH₂)₄; X = Cl, Br

**Scheme 62.** Rh(I)-catalyzed reductive coupling of diphenyldiselenide 2 with alkyl halides 181 using 3.0 mol% of Pd(PPh₃)₄ 182 in the presence of triethylamine using hydrogen as a reducing agent.
Recently, Pace and coworkers developed synthesis of α-aryl- and α-alkyl seleno methylketones 186 in excellent yields by the reaction of Weinreb amides 184 with diselenoacetals 185 in the presence of "BuLi in ether or THF at -78 °C (Scheme 63). The diselenoacetals 185 provide corresponding seleno carbanions on selenium/lithium exchange with "BuLi. Furthermore, the in situ generated selenocarbanions added to Weinreb amides 185 to form final products 186. In addition, several chiral organoselenium reagents have been used as nucleophile to develop different stereoselective reactions.

\[
\begin{align*}
\text{R}^1\text{N}^\text{OMe} + \text{R}^2\text{SeCH}_2\text{SeR}^2 & \xrightarrow{\text{"BuLi (1.25 equiv)}} \text{Et}_2\text{O or THF, -78 °C, 1 h}} \\
\text{184} & \text{185} \\
\text{R}^1 = \text{alkyl, aryl, Bn; R}^2 = \text{alkyl, aryl} \\
\text{186: 84-93%}
\end{align*}
\]

Scheme 63. The synthesis of α-aryl- and α-alkyl seleno methylketones 186 by the reaction of Weinreb amides 184 with diselenoacetals 185 in the presence of "BuLi.

4. Catalytic Reactions

The popularity of organoselenium reagents have been enhanced dramatically in past two decades especially due to their utility in organic synthesis as a catalyst. In the past, several review articles and book chapter have covered different aspects of selenium-catalyzed organic reactions. In this section, catalytic transformations using organoselenium reagents are described.

4.1. Selenium-Catalyzed Oxidations of Alcohols

The first report on selenium-catalyzed the oxidation of alcohols to carbonyl compounds was reported in 1996 by Onami and his coworkers. After that, similar
oxidations were achieved by using the combination of bis[2-(2-pyridyl)phenyl] diselenide as catalyst and N-chloro-4-chlorobenzenesulfonamide sodium salt as terminal oxidant.\textsuperscript{206} In 2009, Arends developed the oxidation of benzyl alcohol by replacing the N-chloro-4-chlorobenzenesulfonamide sodium salt with tert-butyl hydroperoxide (TBHP).\textsuperscript{207}

In 2012, the secondary alcohols \textbf{187} were oxidized to corresponding ketones \textbf{189} in good yields by reacting secondary alcohols \textbf{187} with bromine in the presence of catalytic amount of isoselenazolone \textbf{188} (Scheme 64).\textsuperscript{208} Notably, the oxidation reaction was equally useful for the oxidation of both cyclic and acyclic alcohols. Additionally, organoselenium reagents have been successfully used as catalyst for the oxidation of thiol substrates.\textsuperscript{209}

\begin{center}
\textbf{Scheme 64.} Selenium-catalyzed oxidation of secondary alcohols \textbf{187} to corresponding ketones \textbf{189} using catalytic amount of isoselenazolone \textbf{188} with bromine.
\end{center}

\textbf{4.2. Selenium-Catalyzed Oxidation of Alkenes}

Oxidation of alkenes is more commonly leads the synthesis of different epoxides and diols. Various selenium-catalyzed oxidations of alkenes are existing in the literature which provides corresponding epoxides and diols in useful yields. The application of these reagents in catalysis was begun with the epoxidation of alkenes and first report came in 1978 by Hori and Sharpless.\textsuperscript{210} Later, similar selenium-catalyzed epoxidation of
alkene was came after long wait in 1999. In this report, the 2,4-bisperfluoroctylphenyl butylselenide 191 was used to catalyze the epoxidation of cyclic and acyclic alkenes 190 using 60% H2O2 as an oxidant in a fluorous biphasic system and functionalized epoxides 192 were isolated in high yields (Scheme 65). Notably, the catalyst was recovered by phase separation and could be reused without losing its catalytic activity. The similar oxidations were achieved by using aryl benzyl selenoxides with the combination of same oxidant. Furthermore, glycerol-based recyclable solvents were used as as green reaction media and found significant success in similar oxidations.

![Scheme 65](image-url)

**Scheme 65.** Selenium-catalyzed epoxidation of alkenes 190 to epoxides 192 using catalytic amount of butylselenide 191.

Like selenium-catalyzed epoxidation reactions, the chemistry of selenium-catalyzed hydroxylation of alkenes is quite old and first report came in 1999. Furthermore, the olefinic substrates 14 were treated with combination of catalyst SeO2 and H2O2 oxidant and functionalized trans-diols 195 were obtained in moderate to good yields (Scheme 66). The catalytic cycle of these oxidations suggested that the perselenic acid was working as the active catalytic species.
Scheme 66. Selenium-catalyzed hydroxylation of alkenes 14 to trans-diols 195 using 10 mol% of SeO₂.

In 2008, 10 mol% of diphenyl diselenide 2 with hydrogen peroxide was also used to achieve hydroxylations alkene 14 in good yields but most of the reactions required longer time to consume the starting material.²¹⁵ Furthermore, selenium catalysts 2, 196 and 197 were used for the dihydroxylation of cyclohexene 196 and 1.0 mol% of catalyst 2 required 42 h to achieve full conversion.²¹⁶ On the other hand, more electrophilic diselenide catalyst 196 at same loading required only 5 h to achieve the complete conversion.²¹⁶ Additionally, full conversion was observed in 3 h at 10 mol% catalytic loading of polymer-supported selenium catalyst 197 in water.²¹⁷

Figure 4. The structures of organoselenium catalysts 2, 196 and 197.

In 2007, Konwar and coworkers introduced the first selenium-catalyst for the cleavage of olefinic double bond to carbonyl compounds.²¹⁰ Recently, Yu and co-workers developed another selenium-catalyzed oxidation of terminal alkenes 14 to corresponding carbonyl compounds 189 using dialkyl diselenide 2 as catalyst and hydrogen peroxide as oxidant in ethanol. The cleavaged products 189 were obtained in useful yields (Scheme 67).²¹⁸
Scheme 67. Selenium-catalyzed oxidation of terminal alkenes 14 to ketones 189 using dialkyl diselenides 2 as catalyst.

### 4.3. Selenium-Catalyzed synthesis of Allylic Alcohols

In 2015, Zhao and coworkers employed diphenyldiselenide 2 as catalyst to achieve the synthesis of 3-amino allylic alcohols 201 in high yields by reaction of terminal alkenes 198 using NFSI 199 as oxidant and NaF as an additive (Scheme 68). It was found that the presence of hydroxyl group was essential to achieve the synthesis of compounds 201.

Scheme 68. Selenium-catalyzed synthesis of 3-amino allylic alcohols 201 by the reaction of terminal alkenes 198 using diphenyldiselenide 2 as catalyst and NFSI 199 as an oxidant.

The alkenes 198 were found as useful substrates for the synthesis of α,β-unsaturated aldehydes 202 when same reaction was performed in EtOAc without using any base and additive. Carbonyl compounds 202 were isolated in moderate to high yields (Scheme 69).
Scheme 69. Selenium-catalyzed synthesis of α,β-unsaturated aldehydes 202 by the reaction of alkenes 198 using diphenyldiselenide 2 as catalyst and NFSI 199 as an oxidant.

4.4. Selenium-Catalyzed Cyclization Reactions

4.4.1. Selenium-Catalyzed Lactonization Reactions

In past decade, organoselenium reagents have been successfully introduced as catalysts in lactonization reactions. In 2007, Wirth and coworkers reported selenium-catalyzed lactonization of carboxylic acids 203 to butenolides 205 using diphenyl diselenide 2 as catalyst and [bis(trifluoroacetoxy)iodo]benzene (PIFA) 204 as an oxidant. The cyclized products 205 were isolated in moderate to high yields (Scheme 70). Other iodine(III) reagents such as PIDA and Koser’s reagents were tested also as an oxidant but best result was obtained with PIFA 204. The role of hypervalent iodine species is to activate the selenium functionality (SePh) of corresponding selenolactone intermediate for selenoxide elimination process. Additionally, efforts were made to develop the asymmetric version of same catalytic lactonization but low selectivites were observed. Furthermore, the same catalytic approach was expanded for the synthesis of functionalized dihydropyranones and isocoumarins by same research group.
Scheme 70. Selenium-catalyzed lactonization of $\beta,\gamma$-unsaturated carboxylic acids 203 to butenolides 205 using diphenyl diselenide 2 as catalyst and [bis(trifluoroacetoxy)iodo]benzene (PIFA) 204 as an oxidant.

In 2012, the bromolactonization of substituted $\gamma,\delta$-unsaturated acids 206 was achieved in excellent yields by using isoselenazolone 188 as catalyst with bromine or N-bromosuccinimide (NBS) in the presence of a base. Notably, $\gamma,\delta$-unsaturated acids 206 undergo exo-cyclization while endo-cyclization products were observed when $\gamma,\delta$-unsaturated acids 203 were treated under similar reaction conditions (Scheme 71).\textsuperscript{208}
Scheme 71. Selenium-catalyzed lactonization of alkenoic acids 206 and 203 to five-membered lactones 207 and 208 respectively using 1.0 mol% isoselenazolone 188 with bromine or NBS.

4.4.2. Selenium-Catalyzed Stereoselective Lactonization Reactions

In 2016, Maruoka and coworkers developed the synthesis of indane-cored chiral selenide 209 and used as catalyst in enantioselective lactonizations β,γ-unsaturated acids 203. The lactonization of acids 203 were performed with 10 mol% of chiral catalyst 209 in the presence of oxidant NFSI 199. The cyclized products 211 were obtained in high yields with up to 96% enantiomeric excess (Scheme 72).

![Scheme 70](image)

**Scheme 70.** Enantioselective lactonizations β,γ-unsaturated acids 203 using 10 mol% of chiral catalyst 209 in the presence of oxidant NFSI 199.

4.4.3. Selenium-Catalyzed Aminocyclizations

In 2015, Ortgies and Breder reported an aminocyclization of styrenes or stilbenes 211 bearing amino functionality at ortho-position using using diphenyldiselenide 2 as catalyst. The aminocyclization reactions of substrates 211 were performed using selenium catalyst 2 in the presence of N-fluorobenzenesulfonimide 199 in toluene and cyclized compounds 212 were obtained in good yields (Scheme 73).
Scheme 73. Selenium-catalyzed aminocyclization of styrenes or stilbenes 211 to indoles 212 using diphenyldiselenide 2 as catalyst and NFSI 199 as an oxidant.

5. Conclusion

This book chapter summarizes the key applications of organoselenium reagents in organic synthesis. Several synthetic transformations such as addition reactions with alkenes and selenocyclizations, selenenylation of aliphatic and aromatic species, metal-catalyzed C-C bond formation reactions, carbene-insertion and rearrangement reactions are discussed. The developments of catalytic reactions using catalytic amounts are described in detail. Additionally, the asymmetric variants of various synthetic transformations using stoichiometric or catalytic amounts organoselenium reagents are also covered. Several reaction products obtained during these reactions would be important synthetic intermediates for the synthesis of various biologically active synthetic and natural products.

6. References


