Electrochemical Synthesis of Organoselenium Compounds: A Graphical Review

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Abstract
Electrochemical synthesis, due to its environmentally benign, sustainable, and practical nature, has become an appealing and powerful substitute for traditional methods for oxidizing and reducing organic compounds. Thus, numerous valuable changes have been established in the field of organic synthesis through the utilization of electrochemistry. Among these electrochemical transformations, the formation of C–Se bonds stands out as an exceptionally noteworthy reaction type. In this graphical review, we present a succinct summary of the progress in utilizing electrochemical strategies for synthesizing organoselenium compounds.

Key words electrochemistry, organoselenium compounds, selenylation, difunctionalization, cyclization, cross-coupling

Organoselenium chemistry has remained a field of persistent exploration ever since selenium was recognized as an essential trace element within the human body. The significance of organoselenium compounds has experienced a substantial surge, particularly since the 1970s, marked by the discovery of numerous intriguing compounds boasting diverse applications in synthesis and biology. Notably, among these compounds, diselenides have emerged as immensely valuable organic entities. The presence of Se–Se bonds confers their distinctive chemical attributes, enabling their involvement in a range of reactions as electrophilic (RSe⁺), nucleophilic (RSe⁻), or free-radical (RSe•) agents.

Over the past decades, advancements have propelled the synthesis of organoselenium molecules, a field often characterized by the routine utilization of costly catalysts and a variety of transition metals. This has spurred an ongoing quest to unearth more economical and environmentally friendly methodologies for generating selenium-containing compounds. Notably, recent breakthroughs in this pursuit have culminated in the development of an efficient and ecologically sound electrochemical selenylation process.

Electrochemistry has become an important strategy in organic synthesis, leading to the development of a multitude of beneficial transformations. One of its strengths lies in its capacity to induce carbon–carbon and carbon–heteroatom bond formation through anodic oxidation, all within an environment free from external oxidants. Notably, the domain of electrochemical synthesis has witnessed a surge in its utilization within the context of the formation of organoselenium compounds. Within the scope of this graphical review, our aim is to provide readers with an extended collection of instances exemplifying the utilization of electrochemical techniques in the synthesis of organoselenium compounds.
Biographical Sketches

Balati Hasimujiang was born in Xinjiang Province, P. R. of China. He earned his B.S. in 2011 and his M.S. in 2018, both from Xinjiang Normal University in 2011. In 2020, he joined the group of Prof. Ruan at the School of Pharmaceutical Sciences, Guangzhou Medical University, where he performed his graduate studies and obtained his Ph.D. in June 2023. He is currently undertaking postdoctoral research in the laboratory of Prof. Ruan. His research interests focus on new methodologies in electrochemical synthesis, selenium chemistry, and the synthesis of biologically active compounds.

Zhixiong Ruan was born in Guangdong, P. R. of China. After obtaining his B.Eng. in pharmaceutical engineering at Guangdong University of Technology and his M.Sc. in medicinal chemistry at Jinan University, he joined the research group of Prof. Dr Lutz Ackermann at Georg-August-Universität Göttingen, and obtained his Ph.D. in chemistry in 2017. He was subsequently employed as a professor at the School of Pharmaceutical Sciences, Guangzhou Medical University. His current research interests are focused on organic electrochemistry, peptide modification and synthetic medicinal chemistry.
Notable features
- Iodide salts employed as both electrolyte and catalyst.
- Electrochemical regioselective C(sp²)-H selenylation.

Seminal studies:
Electrocatalytic C–H selenylation of indoles

Selected scope

Reaction mechanism:

Graphite anode
Pt plate cathode

1/2 PhSePh

Iodide-ion-catalyzed electrochemical C(sp²)-H selenylation

Selected scope

Electrochemical selenylation/oxidation of N-alkylisoquinolinium salts

Selected scope

Electrochemical C–H selenylation of 1H-pyrazoles

Selected scope

Further reading

Other contributions of KI-mediated electrochemical selenylation:
(1) Chen, ChemistrySelect 2023, 8, 1049.

Figure 1 Electrochemical C–H selenylation (part 1)
Figure 2  Electrochemical C–H selenylation (part 2)\textsuperscript{1m–p}

**Notable features**
- Copper-catalyzed electrochemical C(sp\textsuperscript{3})–H selenylation.
- Direct electrochemical C(sp\textsuperscript{2})–H selenylation.

**CuCl\textsubscript{2}-catalyzed electrochemical C(sp\textsuperscript{3})–H selenylation**

**Reaction mechanism:**
\[
\text{CuCl}_2 \text{catalyzed electrochemical C(sp\textsuperscript{3})–H selenylation}
\]

**Selected scope**
- 78%
- 53%
- 43%
- 79%

**Graphite anode**

**Direct electrochemical C–H selenylation of 2H-indazoles**

**Selected scope**
- 85%
- 63%
- 80%
- 68%

**Electrochemical selenylation of sulfoxonium ylides**

**Selected scope**
- 85%
- 74%

**Proposed mechanism:**


The α-keto gem-diselenides showed excellent antimicrobial activity against *Candida albicans*.
Notable features
- Three-component electrochemical aminoselenation and oxyselenation.
- Stereoselective electrochemical selenoalkylation.
- Electrochemical radical carbonsele nation.
- Electrochemical deutero-selenylation.

**Electrochemical aminoselenation and oxyselenation**

\[
\text{R}^1\text{NH}_2 + \text{PhSeSePh} \rightarrow \text{R}^1\text{NHSePh} + \text{PhSeH}.
\]

Selected scope

\[
\begin{align*}
\text{(2a) Lei, Org. Lett. 2019, 21, 1297.} \\
\end{align*}
\]

**Electrochemical radical carbonsele nation**

\[
\text{R}^1\text{CH} + \text{PhSeTi} \rightarrow \text{R}^1\text{CHSePh}.
\]

Selected scope

\[
\begin{align*}
\text{(2d) Lei, Org. Lett. 2021, 23, 7724.} \\
\text{(2c) Xu, Asian J. Org. Chem. 2020, 9, 1760.}
\end{align*}
\]

**Electrochemical deutero-selenylation**

\[
\text{R}^1\text{H} + \text{R}^2\text{SeSeR} \rightarrow \text{R}^1\text{HSeD} + \text{R}^2\text{D}.
\]

Selected scope

\[
\begin{align*}
\text{(2e) Wang, Org. Chem. Front. 2022, 9, 2815.} \\
\end{align*}
\]
Notable features
- Electrochemical cyclization of N-arylacrylamides.
- Electrochemical radical selenylation.
- Electrochemical synthesis of selenylbenzo[b]furans.

Electrochemical oxidative cyclization of activated alkynes

\[ R^1\text{C}R^2 + n\text{-Bu}_4\text{BF}_4 (15 \text{ mA}) \quad \text{undivided cell} \]

Selected scope

\[ \begin{array}{ccc}
\text{MeSe} & \text{MeSe} & \text{Se} \\
\text{Me} & \text{PhSe} & \text{Me} \\
\text{Ph} & \text{Se} & \text{Ph} \\
\end{array} \]

83% 85%

(3a) Guo, Green Chem. 2019, 21, 4706.

Electrochemical cyclization of N-arylacrylamides

\[ R^1\text{N}R^2 + n\text{-Bu}_4\text{BF}_4 (2.0 \text{ equiv}) \quad \text{undivided cell, 18 mA} \]

Selected scope

\[ \begin{array}{ccc}
\text{Me} & \text{Me} & \text{N} \\
\text{Me} & \text{Me} & \text{N} \\
\text{Bn} & \text{N} & \text{Me} \\
\end{array} \]

80% 85% 84%


Electrochemical selenylation/cyclization of quinones

\[ R^1\text{OH} + n\text{-Bu}_4\text{NPF}_6 (1.0 \text{ M}) \quad \text{MeCN, rt, 10 mA} \]

Selected scope

\[ \begin{array}{ccc}
\text{Me} & \text{Me} & \text{Se} \\
\text{Me} & \text{Me} & \text{Se} \\
\text{Ph} & \text{Se} & \text{Ph} \\
\end{array} \]

93% 91%


Electrochemical oxidative selenolactonization of alkenoic acids

\[ R\text{Se} + \text{LiClO}_4 (0.1 \text{ M}), \text{MeCN} \]

Selected scope

\[ \begin{array}{ccc}
\text{Me} & \text{Me} & \text{Se} \\
\text{Me} & \text{Me} & \text{Se} \\
\text{Ph} & \text{Se} & \text{Ph} \\
\end{array} \]

88% 60% 70%


Electrochemical synthesis of selenylbenzo[b]furans

\[ R\text{Se} + \text{LiClO}_4 (0.1 \text{ M}), \text{MeCN} \]

Selected scope

\[ \begin{array}{ccc}
\text{Ph} & \text{Se} & \text{Ph} \\
\text{Ph} & \text{Se} & \text{Ph} \\
\text{Me} & \text{Se} & \text{Me} \\
\end{array} \]

96% 65% 76%

(3h) Ruan, Molecules 2022, 27, 6314.

See also:
(3i) Braga, Front. Chem. 2022, 10, 88099.
Notable features

- Electrochemical selenylation/cyclization.
- Electrochemical selenocyclization of alcohols.
- Electrochemical tandem cyclization of unsaturates.

**Figure 5** Electrochemical selenylation/cyclization (part 2)

**Electrochemical selenylation/cyclization**

Selected scope


**Electrochemical tandem cyclization of unsaturates**

Selected scope


**Electrochemical multicomponent synthesis of 4-selanylpizazoles**

Selected scope

Figure 6  Electrochemical selenylation/cyclization (part 3)²f,3t–z

Notable features

- Electrochemical synthesis of significant selenoheterocycles.
- Electrochemical selenylation involving RSe⁺ or RSeSe⁺ intermediates.

Electrochemical radical selenylation/1,2-carbon migration

**Selected scope**

<table>
<thead>
<tr>
<th>Compound</th>
<th>SEPh</th>
<th>SEPh</th>
<th>SEPh</th>
<th>SEPh</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>90%</td>
<td>70%</td>
<td>75%</td>
<td>54%</td>
</tr>
</tbody>
</table>


Electrochemical synthesis of selenylated chromones

**Selected scope**

<table>
<thead>
<tr>
<th>Compound</th>
<th>SEPh</th>
<th>CO₂+ [Cu] (20 mol%), K₂CO₃ (2.0 equiv)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>95%</td>
<td>81%</td>
</tr>
</tbody>
</table>


Electrochemical synthesis of selenylated oxazolidine-2,4-diones

**Selected scope**

<table>
<thead>
<tr>
<th>Compound</th>
<th>SEPh</th>
<th>Me</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>87%</td>
<td>83%</td>
</tr>
</tbody>
</table>


Electrochemical synthesis of seleno-benzo[b]azepines

**Selected scope**


Proposed mechanism:

Glassy carbon anode

- PhSe⁺ + PhSe⁺

Glassy carbon cathode

- 1/2 PhSeSePh

Electrooxidative selenylation of alkynes

**Selected scope**

<table>
<thead>
<tr>
<th>Compound</th>
<th>SEPh</th>
<th>PhSe⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>83%</td>
<td>79%</td>
</tr>
<tr>
<td></td>
<td>97%</td>
<td></td>
</tr>
</tbody>
</table>

See also: (3y) Lee, Org. Biomol. Chem. 2023, 21, 3002.
Notable features
- Electrochemical radical selenylation of boronic acids.
- Electrochemical oxidative cross-coupling.
- Electrochemical selenylation of phosphonates.

Electrochemical radical selenylation of boronic acids

\[
\text{RSeSeR} + n-Bu_4\text{NBr} \rightarrow \text{RSe} + \text{RSe}^+ \\
\text{RSe}^+ + \text{RSe} \rightarrow \text{RSeSeR}
\]

Selected scope
- MeOSeMe 94%
- PhSeSePh 89%
- PhSeSePh 98%
- PhSeSePh 90%

Proposed mechanism:

\[
\text{PhSeSePh} \xrightarrow{\text{Mn}^2+} \text{PhSe}^+ \xrightarrow{1/2 \text{PhSeSePh}} \text{PhSe}^+ + \text{PhSe}^+ \\
\text{PhSe}^+ + \text{PhSe}^+ \rightarrow \text{PhSeSePh}
\]

Electrochemical oxidative cross-coupling

\[
\text{R}^1\text{OH} + \text{RSeSeR} \xrightarrow{\text{LiClO}_4} \text{R}^1\text{SePh} + \text{PhSe}^+ \\
\text{PhSe}^+ + \text{PhSe}^+ \rightarrow \text{PhSeSePh}
\]

Selected scope
- PhSeSePh 94%
- MeOSeSeMe 95%
- MeOSeSeMe 95%

Proposed mechanism:

\[
\text{PhSe} \xrightarrow{\text{Mn}^2+} \text{PhSe}^+ \xrightarrow{1/2 \text{PhSeSePh}} \text{PhSe}^+ + \text{PhSe}^+ \\
\text{PhSe}^+ + \text{PhSe}^+ \rightarrow \text{PhSeSePh}
\]

Electrochemical selenylation of phosphonates

\[
\text{PhSeSePh} \xrightarrow{\text{MeCN/HOAc}} \text{PhSePh} + \text{AcO-PhSe} \\
\text{PhSePh} + \text{AcO-PhSe} \rightarrow \text{PhSeSePh}
\]

Selected scope
- PhSePhOEt 90%
- PhSePhPh 90%

Proposed mechanism:

\[
\text{PhSeSePh} \xrightarrow{\text{Mn(OAc)}_3 \cdot \text{H}_2\text{O}} \text{PhSePh} + \text{AcO-PhSe} \\
\text{PhSePh} + \text{AcO-PhSe} \rightarrow \text{PhSeSePh}
\]

Figure 7 Electrochemical cross-coupling reactions\(^{4a-e}\)
Conflict of Interest

The authors declare no conflict of interest.

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References


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