<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Studies on Highly Selective Addition of Group 16 Heteroatom Compounds to Carbon-Carbon Unsaturated Bonds</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author(s)</strong></td>
<td>玉井 太一</td>
</tr>
<tr>
<td><strong>Editor(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Citation</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Issue Date</strong></td>
<td>2016-01</td>
</tr>
<tr>
<td><strong>URL</strong></td>
<td><a href="http://hdl.handle.net/10466/15122">http://hdl.handle.net/10466/15122</a></td>
</tr>
<tr>
<td><strong>Rights</strong></td>
<td></td>
</tr>
</tbody>
</table>
Studies on Highly Selective Addition of Group 16 Heteroatom Compounds to Carbon–Carbon Unsaturated Bonds

Taichi Tamai

January 2016

Doctoral Thesis at Osaka Prefecture University
Preface

This thesis deals with the studies conducted during April 2013 to March 2016 under the guidance of Professor Akiya Ogawa at the Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University.

This thesis is concerned with the development of the highly selective addition of group 16 heteroatom compounds to carbon–carbon unsaturated bonds. One important topic of this thesis is the development of photochemical radical addition using the unique radical reactivity of tellurium compound. The other topics are the novel transition-metal-catalyzed addition of alkene derivatives.

Department of Applied Chemistry
Graduate School of Engineering
Osaka Prefecture University
January 2016

Taichi Tamai
## Contents

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>General Introduction</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Highly Selective Perfluoroalkyltelluration of Alkynes by the Combination of Iodoperfluoroalkanes and Organic Ditelluride upon Photoirradiation</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>Regioselective Hydrothiolation of Heteroatom-Substituted Alkenes with Thiols Catalyzed by Palladium Diacetate</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>Palladium-Catalyzed Markovnikov-Selective Hydroselenation of N-Vinyl Lactams with Selenols Affording N,Se-Acetals</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>Gold-Catalyzed anti-Markovnikov Selective Hydrothiolation of Inactivated Alkenes</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>Conclusion</td>
<td>89</td>
</tr>
</tbody>
</table>

List of Publications  91

List of Awards  94

Acknowledgement
Chapter 1

General Introduction

Organic synthesis, which creates essential chemical products for our lives from fossil and natural resources, is fundamental technology to realize an affluent modern society. In particular, rapid development of high efficient and selective organic reactions in recent decades enables synthesis of a wide variety of fine chemicals. However, the production of large amounts of wastes for synthesis of pharmaceuticals and fine chemicals provides serious problems; for examples, more than ten or hundred amounts of wastes, to the amounts of target molecules, were produced.\(^1\) Therefore, the development of more atom-economical synthetic methods for these compounds without production of wastes is a significant research problem in this decade.

The synthesis of highly functionalized molecules requires not only selective \(\text{C}–\text{C}\) bond forming reactions but also functionalization reactions where heteroatoms are introduced into a particular position of carbon frameworks. Thus, the development of highly selective and efficient methods for introduction of specific element groups into organic molecules is of great importance. Because group 16 heteroatoms, such as sulfur, selenium, and tellurium, are largely produced in industry in Japan, beneficial use of these elements is strongly desired. The recent developed clarification of the characteristic features of group 16 heteroatom compounds clearly shows the utilities of these heteroatom compounds. For example, many group 16 heteroatom compounds exhibit bioactivities, and physical properties.\(^2\) Indeed, pharmaceutical compounds, functional materials, and synthetic intermediates bearing group 16 heteroatoms have been developed in recent years (Scheme 1-1).
Among synthetic reactions, addition reaction to unsaturated bonds is one of the most atom-economical transformations, because addition products can principally involve all elements of reactants in their structures. In general, addition reactions are classified roughly into the following three categories, i.e., ionic addition, radical addition, and transition-metal-catalyzed addition. As to group 16 heteroatoms, classically, a variety of ionic additions under acidic and basic conditions have been developed. In recent decade, the developments of innovative photoinduced radical addition reactions based on characteristic features of group 16 heteroatoms were reported by Professor Ogawa’s research group. Additionally, transition-metal-catalyzed additions of group 16 heteroatom compounds to alkynes also have been developed by overcoming the nature of catalyst poison of group 16 heteroatoms.

Scheme 1-1. Examples of Functional Molecules Containing Group 16 Heteroatoms

In this thesis, the author has developed highly selective addition reactions of group 16 heteroatom compounds to carbon–carbon unsaturated bonds. One important topic of this thesis is the development of photoinduced radical addition based on the unique radical reactivity of tellurium compounds (Chapter 2). The other topics are the novel transition-metal-catalyzed addition of sulfur and selenium compounds to alkene derivatives (Chapters 3–5).

This thesis is consisted of six chapters and the outlines of each chapter are summarized as follows.
Chapter 1 describes the background, general objectives, and the contents of this thesis.

Chapter 2 describes a novel photoinduced perfluoroalkyltelluration of alkynes based on the unique radical reactivity of diphenyl ditelluride (Scheme 1-2). Radical addition to unsaturated bond is one of the most useful methods for introduction of heteroatoms into organic molecules. Organotellurium compounds are known as useful synthetic intermediates for tellurium-lithium exchange reaction and cross-coupling reaction. Organic ditellurides, a representative organotellurium compounds, indicate excellent carbon radical trapping ability. Therefore, combination of ditelluride and other heteroatom compound enables the development of highly efficient and selective radical addition reactions.

On the other hand, recently fluorous chemistry revealed that convenient separation of products and/or reagents (or catalysts) has been attained by extraction with fluorous solvents (FBS: fluorous biphasic system). Perfluoroalkyl iodides have fluorous (perfluoroalkyl) groups in their structures and react with unsaturated bond under photoirradiation. Therefore, perfluoroalkyl iodides are convenient reagents for introduction of fluorous (perfluoroalkyl) groups into organic molecules. Thus, straightforward synthetic methods for compounds bearing telluro and perfluoroalkyl groups can be designed using a diphenyl ditelluride and perfluoroalkyl iodide mixed system. When perfluoroalkyltelluration was conducted under photoirradiation with visible light, the corresponding β-perfluoroalkylalkenyl tellurides were obtained regio- and stereoselectively. Moreover, the obtained adduct could successfully be applied to tellurium-lithium exchange reaction. These results indicated that perfluoroalkyltelluration product has potential as a useful synthetic intermediate to introduce perfluoroalkyl group into organic molecules.

\[
\text{R} \quad \xrightarrow{h\nu \ (>400 \text{ nm})} \quad \text{(PhTe)}_2 - \text{R}_1 \quad \text{mixed system} \quad \xrightarrow{\text{PhTe}} \quad \text{R} - \text{R}_f
\]

*Scheme 1-2. Chapter 2*
Chapter 3 describes a novel Pd-catalyzed Markovnikov-selective hydrothiolation of heteroatom-substituted alkenes (Scheme 1-3). In general, organic sulfur compounds have been known to be incompatible with transition metal catalysts owing to the feature of catalyst poison of organic sulfur compounds. Recently, it was revealed that the coordination of alkyne to transition metal catalyst prevented formation of bridged catalyst complex. However, this method was limited to alkynes and allenes, and the transition-metal-catalyzed reaction of alkene derivatives with organic sulfur compounds has been still undeveloped. Therefore, the author developed the transition-metal-catalyzed addition of organosulfur compounds to alkene derivatives by using heteroatom-substituted alkenes. Pd-catalyzed hydrothiolation of vinyl ethers, where alkoxyl group is bonded directly to C–C double bond, successfully afforded Markovnikov-type adducts selectively in excellent yields. Similarly, Pd-catalyzed hydrothiolation of N-vinyl lactams also proceeded efficiently to afford the corresponding hydrothiolation products with high selectivity. These reactions have tolerance to not only terminal alkene derivatives but also internal alkene derivatives. This hydrothiolation of vinyl ethers and N-vinyl lactams were promising methodology for construction of O,S- and N,S-acetal derivatives.

Scheme 1-3. Chapter 3

Chapter 4 describes a novel Pd-catalyzed hydroselenation of N-vinyl lactams affording N,Se-acetals (Scheme 1-4). Recently, the utilities of organoselenium compounds such as pharmaceuticals and synthetic intermediates have been revealed. Thus, development of selective introduction methods of seleno groups into organic molecules is still desired strongly. Similarly
as sulfur compounds, however, transition-metal-catalyzed reaction of organoselenium compounds is also unexplored. Therefore, hydroselenation of N-vinyl lactams as alkene derivatives was examined in detail. The reactions of terminal N-vinyl lactams with benzeneselenol proceeded smoothly to produce Markovnikov-type adducts selectively without addition of any catalyst. In contrast, the reactions of internal N-vinyl lactams required Pd catalyst to promote hydroselenation.

![Scheme 1-4. Chapter 4](image)

Chapter 5 describes a novel gold-catalyzed hydrothiolation of inactivated alkenes (Scheme 1-5). In chapters 3 and 4, the author describes Pd-catalyzed hydrothiolation and -selenation of heteroatom-substituted alkenes. However, scope and limitations of these reactions are limited to activated alkenes and development of transition-metal-catalyzed addition of organic sulfur compounds to inactivated alkenes is an unresolved problem. Accordingly, the author focused attention on gold catalysts which are known to activate C–C unsaturated bond. When the gold-catalyzed hydrothiolation of inactivated alkenes with thiols were examined, the corresponding anti-Markovnikov-type adducts were obtained selectively.

![Scheme 1-5. Chapter 5](image)
Chapter 1. General Introduction

Chapter 6 describes the conclusion of this thesis.

This thesis describes a series of highly selective addition reactions of group 16 heteroatoms with unsaturated compounds. In particular, frontier works of transition-metal-catalyzed addition of group 16 heteroatom compounds to alkenes will open up eco-friendly refined synthesis of organosulfur compounds.

References


Chapter 2

Highly Selective Perfluoroalkyltelluration of Alkynes by the Combination of Iodoperfluoroalkanes and Organic Ditelluride upon Photoirradiation

2-1 Introduction

Radical addition of heteroatom compounds to unsaturated compounds is one of the most useful methods for introduction of heteroatom functions into organic molecules.\(^1\) Along this line, recently, a series of photoinduced radical addition reactions of organoselenium and tellurium compounds such as organic diselenides and ditellurides to unsaturated compounds were developed.\(^2\) For example, organic diselenides and ditellurides add to alkynes upon photoirradiation under higher concentration of the starting materials to afford the corresponding vicinal diseleno- and ditelluroalkenes, respectively (Eq. 2-1).\(^3\)\(^4\) In addition, carboselenation and -telluration of unsaturated bonds based on radical characteristic feature of organic chalcogenides were also developed (Eqs. 2-2 and 2-3).\(^5\)\(^6\)

\[
\begin{align*}
\text{R} & \quad \text{+ (ArY)}_2 \quad \xrightarrow{\text{hv}} \quad \text{ArY} \quad \text{Y = Se, Te} \\
\text{R} & \quad \text{+ ArSeR'} \quad \xrightarrow{\text{hv}} \quad \text{ArSe} \quad \text{R' = CH}_2\text{(COOEt)}_2 \\
\text{R} & \quad \text{+ R'TeR''} \quad \xrightarrow{\text{AIBN}} \quad \text{TeR''} \\
\end{align*}
\]

(2-1) \quad (2-2) \quad (2-3)

In contrast to the radical addition of organic diselenides and ditellurides to alkynes, the
corresponding radical addition to alkenes is a very inefficient process. However, a series of heteroatom mixed systems, which provide powerful tools to heteroatom compounds having two different heteroatom functions, were developed. For example, a variety of alkenes undergo regioselective thioselenation with (PhS)$_2$ and (PhSe)$_2$ upon photolysis (Eq. 2-4). The excellent regioselectivity observed in this reaction is based on the kinetic control: (i) Thio radicals are much more reactive toward carbon–carbon unsaturated compounds compared with seleno radicals; (ii) Diselenides indicate excellent carbon radical trapping ability compared with disulfides. Therefore, the thio radical formed \textit{in situ} upon photolysis selectively attacks alkenes and the resulting carbon radicals are selectively captured with the diselenide. The photoinduced thioselenation with (PhS)$_2$ and (PhSe)$_2$ can be applied to a wide range of unsaturated compounds such as alkynes, allenes, conjugate dienes, and vinylcyclopropanes. For example, alkynes undergo regioselective thioselenation to give the corresponding $\beta$-phenylthio-substituted vinyl selenides in high yields.

\[ R \xrightarrow{\text{hv} (>300 \text{ nm})} \text{CHCl}_3, 40-45^\circ \text{C} \quad \begin{array}{c} \text{(PhS)}_2 - (\text{PhSe})_2 \\ \text{SPh} \end{array} \]

\[ \xrightarrow{\text{(PhS)}_2 - (\text{PhSe})_2} \text{R} \quad \begin{array}{c} \text{PhSe} \\ \text{SPh} \end{array} \]

The thioselenation methodology can be applied to the photoinduced thiotelluration and selenotelluration of alkynes by use of disulfide–ditelluride and diselenide–ditelluride mixed systems (Eqs. 2-5 and 2-6).

\[ R \xrightarrow{\text{hv} (>400 \text{ nm})} \text{CHCl}_3, 45^\circ \text{C} \quad \begin{array}{c} \text{(PhS)}_2 - (\text{PhTe})_2 \\ \text{SPh} \end{array} \]

\[ \xrightarrow{\text{(PhS)}_2 - (\text{PhTe})_2} \text{R} \quad \begin{array}{c} \text{PhTe} \\ \text{SPh} \end{array} \]

\[ R \xrightarrow{\text{hv} (>400 \text{ nm})} \text{CHCl}_3, 45^\circ \text{C} \quad \begin{array}{c} \text{(PhSe)}_2 - (\text{PhTe})_2 \\ \text{SePh} \end{array} \]

\[ \xrightarrow{\text{(PhSe)}_2 - (\text{PhTe})_2} \text{R} \quad \begin{array}{c} \text{PhTe} \\ \text{SePh} \end{array} \]
Furthermore, photoinduced introduction of two different heteroatom groups to carbon–carbon unsaturated bonds by novel combination of group 16 and group 15 heteroatom compounds was achieved. Thus, photoinduced selenophosphination of alkynes has been attained by the combination of diphenyl diselenide and tetraphenyldiphosphine (Eq. 2-7). In the selenophosphination of terminal alkynes, the seleno and phosphino groups are introduced to the terminal and internal positions of alkynes, regioselectively. Furthermore, the combination of diphenyl ditelluride and tetraphenyldiphosphine leads to novel phosphinotelluration of alkynes. Interestingly, the phosphino and telluro groups are introduced to the terminal and internal carbons of terminal alkynes (Eq. 2-8). Based on these results, it has been estimated that the relative reactivities of heteroatom-centered radicals toward carbon–carbon unsaturated bonds are as follows: \( \text{PhSe} \cdot > \text{Ph}_2\text{P} \cdot > \text{PhTe} \cdot \). These reactions clearly demonstrate the efficacy of the heteroatom mixed systems for the highly selective introduction of two heteroatom functions into organic molecules.

![Reaction Scheme](image)

Recently, the photoinduced radical addition of perfluoroalkyl iodides to a series of unsaturated compounds such as alkynes, allenes, alkenes, conjugated dienes, methylenecyclopropanes, vinylcyclopropanes, and isocyanides, and their application to radical cyclization reactions were investigated (Scheme 2-1). The obtained perfluoroalkyliodination products are useful as synthetic intermediates, because the obtained iodides can be replaced conveniently by a variety of carbon and heteroatom groups. In addition, perfluoroalkyl (fluorous) groups make it possible to isolate the products easily by fluorous/organic/aqueous
Chapter 2. Perfluoroalkyltelluration of Alkynes upon Photoirradiation

extraction technique.

**Scheme 2-1.** Photoinduced Perfluoroalkyliodination to Unsaturated Compounds

During the course of studies on the radical addition reactions of heteroatom compounds to unsaturated compounds, the combination of group 16 and group 17 heteroatoms was examined. Photoinduced perfluoroalkylselenation of terminal alkynes has been achieved by use of the mixed system of diphenyl diselenide and perfluoroalkyl iodide (Eq. 2-9).\textsuperscript{17}

\[
\text{R} = \text{PhTe} \quad \text{(PhSe)\textsubscript{2}–R\textsubscript{f}I} \quad h\nu (>300 \text{ nm}) \quad \text{BTF, 40 °C} \quad \text{Ph–R\textsubscript{f}} 
\]

In this chapter, the author wishes to report a highly selective photoinduced perfluoroalkyltelluration of terminal alkynes by the novel combination of organic ditelluride and perfluoroalkyl iodide.

2-2 Photoinduced Perfluoroalkyltelluration of Alkynes

First, the reaction conditions of the perfluoroalkyltelluration were optimized using phenylacetylene as the substrate (Table 2-1). The perfluoroalkyltelluration of phenylacetylene
requires the use of excess amounts (ca. 8~10 equivalents) of the alkyne. When the reaction of phenylacetylene with diphenyl ditelluride and tridecafluoro-n-hexyl iodide was conducted in CH$_3$CN upon irradiation with high pressure Hg lamp through Pyrex, the desired perfluoroalkyltelluration product was obtained in 12% yield (entry 1). Table 2-1 indicates the results of the photoinduced perfluoroalkyltelluration of phenylacetylene by varying the molar ratios of phenylacetylene/(PhTe)$_2$/nC$_6$F$_{13}$I. As the results, when the molar ratio of phenylacetylene/(PhTe)$_2$/nC$_6$F$_{13}$I is 0.91(0.1 mL)/0.02/0.01, the perfluoroalkyltelluration product was obtained in good yield (entry 3). The perfluoroalkyl and phenyltelluro groups are introduced to the terminal and internal positions of phenylacetylene, respectively, and (E)-isomer was obtained stereoselectively. Under the conditions of entry 3 in Table 2-1, the yields of the perfluoroalkyltelluration vs. the times of photoirradiation were as followed: 41% (4 h); 57% (8 h); 68% (13 h); 64% (15 h). This perfluoroalkyltelluration product is promising as a synthetic intermediate because vinyl tellurides are useful starting materials for the formation of vinyl anions by tellurium-lithium exchange reaction.$^{18}$ Moreover, transition-metal-catalyzed cross-coupling reaction using vinyl tellurides are reported.$^{19}$

### Table 2-1. Varying Molar Ratio of Perfluoroalkyltelluration

<table>
<thead>
<tr>
<th>entry</th>
<th>phenylacetylene, mL</th>
<th>(PhTe)$_2$, mmol</th>
<th>nC$<em>6$F$</em>{13}$I, mmol</th>
<th>yield, % $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.10</td>
<td>0.01</td>
<td>0.01</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>0.10</td>
<td>0.01</td>
<td>0.02</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>0.10</td>
<td>0.02</td>
<td>0.01</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>0.05</td>
<td>0.02</td>
<td>0.01</td>
<td>37</td>
</tr>
<tr>
<td>5</td>
<td>0.10</td>
<td>0.03</td>
<td>0.01</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>0.10</td>
<td>0.03</td>
<td>0.02</td>
<td>31</td>
</tr>
</tbody>
</table>

$^a$ Determined by $^1$H NMR.
Next, the perfluoroalkyltelluration of phenylacetylene in several solvents was conducted, and the results are shown in Scheme 2-2. The perfluoroalkyltelluration proceeded in various solvents such as protic solvents, aprotic & polar solvents, and aprotic & nonpolar solvents. Among the solvents employed, acetonitrile is the best solvent for the perfluoroalkyltelluration.

**Scheme 2-2. Perfluoroalkyltelluration in Several Solvents**

Under the optimized reaction conditions, the perfluoroalkyltelluration of phenylacetylene was conducted using several perfluoroalkyl iodides (Scheme 2-3). Both light and heavy fluorous iodides (perfluoroalkyl iodides) can be utilized for perfluoroalkyltelluration. However, pentafluorophenyl iodide did not afford the corresponding adduct at all. The relatively stronger C–I bond energy of pentafluorophenyl iodide may contribute to the inefficiency in radical addition reaction.

**Scheme 2-3. Perfluoroalkyltelluration Using Several Perfluoroalkyl Iodides**

\[
\text{Ph} \quad + \quad \text{PhTe} \quad + \quad \text{(PhTe)}_2 \quad + \quad n\text{C}_n\text{F}_{13} \quad + \quad \text{solvent} \quad \overset{h\nu (>400 \text{ nm})}{\longrightarrow} \quad \text{Ph} \quad + \quad \text{PhTe} \\
0.1 \text{ mL} \quad 0.01 \text{ mmol} \quad 0.02 \text{ mmol} \quad \text{solvent (0.5 mL)} = \text{ neat} \quad 23\% \\
\text{CH}_3\text{OH} \quad 22\% \\
\text{CH}_2\text{CN} \quad 68\% \\
\text{DMF} \quad 45\% \\
\text{acetone} \quad 24\% \\
\text{CHCl}_3 \quad 26\% \\
\text{BTF*} \quad 41\% \\
\text{THF} \quad 41\% \\
\text{benzene} \quad 7\% \\
\]

* BTF: benzo trifluoride (PhCF₃).
Chapter 2. Perfluoroalkyltelluration of Alkynes upon Photoirradiation

The photoinduced perfluoroalkyltelluration of various terminal alkynes using \((\text{PhTe})_2/R_f\) mixed systems was examined, and the results are shown in Table 2-2. A variety of aromatic alkynes underwent regio- and stereoselective perfluoroalkyltelluration. In the cases of aromatic alkynes having strong electron-withdrawing groups such as nitro and cyano groups at the \(p\)-position, the yields of the desired perfluoroalkyltelluration products were lower (entries 6 and 7). Aliphatic alkynes also underwent perfluoroalkyltelluration to give the corresponding fluorous vinylic tellurides in moderate yields (entries 8 and 9). In the cases of electron-deficient alkynes such as ethyl propiolate, small amounts of the perfluoroalkyltelluration product were obtained regio- and stereoselectively (entry 10). The difference in the reactivity of aromatic and aliphatic alkynes is most probably owing to the difference in the stability of the corresponding vinylic radical intermediates. In general, vinylic radicals generated from aliphatic alkynes form \(\sigma\)-radicals (which are very fast equilibrium between \((E)\)- and \((Z)\)-isomers),\(^{20}\) whereas \(\alpha\)-aryl-substituted vinylic radicals are assumed to be \(\pi\)-radicals,\(^{21}\) which are more stable compared with the \(\sigma\)-radicals formed from aliphatic alkynes. The regioselectivity of the perfluoroalkyltelluration products could be determined unambiguously by the coupling constant \(J_{\text{H-F}}\) of vinylic proton. The vinylic proton at the \(\alpha\)-position of \(R_f\) group appears triplet \((J_{\text{H-F}} = 14.2\ \text{Hz})\), whereas the vinylic proton at the \(\beta\)-position of \(R_f\) group becomes singlet. On the other hand, determination of the stereochemistry of the perfluoroalkyltelluration products was performed based on NOE experiments, as shown below (Figure 2-1).

![Figure 2-1. Determination of Regio- and Stereochemistry of Perfluoroalkyltelluration](image-url)
Table 2-2. Perfluoroalkyltelluration of Terminal Alkynes

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>product</th>
<th>2</th>
<th>yield, %(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="1a" /></td>
<td><img src="image" alt="2a" /></td>
<td>2a</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="1b" /></td>
<td><img src="image" alt="2b" /></td>
<td>2b</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="1c" /></td>
<td><img src="image" alt="2c" /></td>
<td>2c</td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="1d" /></td>
<td><img src="image" alt="2d" /></td>
<td>2d</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="1e" /></td>
<td><img src="image" alt="2e" /></td>
<td>2e</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="1f" /></td>
<td><img src="image" alt="2f" /></td>
<td>2f</td>
<td>11</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="1g" /></td>
<td><img src="image" alt="2g" /></td>
<td>2g</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="1h" /></td>
<td><img src="image" alt="2h" /></td>
<td>2h</td>
<td>26</td>
</tr>
<tr>
<td>9</td>
<td><img src="image" alt="1i" /></td>
<td><img src="image" alt="2i" /></td>
<td>2i</td>
<td>19</td>
</tr>
<tr>
<td>10</td>
<td><img src="image" alt="1j" /></td>
<td><img src="image" alt="2j" /></td>
<td>2j</td>
<td>6</td>
</tr>
</tbody>
</table>

\(^a\): \(n\text{C}_6\text{F}_{13}\) (0.01 mmol), acetylene (excess), (PhTe)\(_2\) (2 equiv), \(h\nu\): high pressure
A possible pathway for the present perfluoroalkyltelluration may involve the following:

(i) \((\text{PhTe})_2\) mainly undergoes homolytic cleavage upon visible light irradiation to generate \(\text{PhTe}^\cdot\), because the absorption of \((\text{PhTe})_2\) is stronger than that of \(\text{R}_f\text{I}\) (Figure 2-2); (ii) The formed telluro radical abstracts iodine atom from \(\text{R}_f\text{I}\) to generate \(\text{R}_f^\cdot\); \(^{22}\) (iii) \(\text{R}_f^\cdot\) attacks the terminal carbon of alkynes to form vinylic radical intermediates; (iv) The formed vinyl radical intermediates are trapped selectively by \((\text{PhTe})_2\) to give the perfluoroalkyltelluration products (Scheme 2-2). The stereochemistry is determined when vinyl radical intermediates are trapped by \((\text{PhTe})_2\). The steric effect between \(\text{R}_f\) group and \((\text{PhTe})_2\) in the transition state to give \((Z)\)-isomer may contribute to the excellent \(E\) selectivity. As can be seen from Figure 2-3, diphenyl ditelluride has its absorption maximum in visible region, and therefore the perfluoroalkyltelluration was conducted upon visible light irradiation. Compared with the perfluoroalkylselenation, the corresponding perfluoroalkyltelluration is somewhat difficult to take place, because the relatively lower stability of the product tellurides toward photoirradiation.

\begin{center}
\includegraphics[width=\textwidth]{figure2_2.png}
\end{center}

\textbf{Figure 2-2. A Plausible Pathway of Perfluoroalkyltelluration}
In summary, the highly selective perfluoroalkyltelluration of terminal alkynes has been attained by using a mixed system of diphenyl ditelluride and perfluoroalkyl iodide. The formed vinylic tellurides are useful precursors for generation of vinylic anions and vinylic organometallics. Furthermore, perfluoroalkyl groups ($R_f$) are important fluorous tags, and make it possible to separate products easily by extraction.

2-3 Conclusion

In summary, the highly selective perfluoroalkyltelluration of terminal alkynes has been attained by using a mixed system of diphenyl ditelluride and perfluoroalkyl iodide. The formed vinylic tellurides are useful precursors for generation of vinylic anions and vinylic organometallics. Furthermore, perfluoroalkyl groups ($R_f$) are important fluorous tags, and make it possible to separate products easily by extraction.
2-4 Experimental Section

General Comment

Unless otherwise stated, all starting materials and catalysts were purchased from a commercial source and used without further purification. \(^1\)H NMR spectra (400 MHz) and \(^{13}\)C NMR spectra (100 MHz) were taken in CDCl\(_3\) with Me\(_4\)Si as an internal standard. Chemical shifts in \(^1\)H NMR were measured relative to CDCl\(_3\) and converted to \(\delta\) (Me\(_4\)Si) values by using \(\delta\) (CDCl\(_3\)) 7.26 ppm. Chemical shifts in \(^{13}\)C NMR were measured relative to CDCl\(_3\) and converted to \(\delta\) (Me\(_4\)Si) values by using \(\delta\) (CDCl\(_3\)) 77.00 ppm. IR spectra are reported in wave numbers (cm\(^{-1}\)). FAB mass spectra were obtained by employing double focusing mass spectrometers.

General Procedure for the Synthesis of (E)-Perfluoro-1-(phenytelluro)-1-aryl-1-octene.

In a NMR tube were placed alkyne (0.1 mL), perfluoroalkyl iodide (0.01 mmol) and diphenyl ditelluride (8.2 mg, 0.02 mmol) in CH\(_3\)CN (0.5 mL). The mixture was irradiated with a high pressure Hg lamp through a glass filter \((h\nu > 400 \text{ nm})\) at room temperature for 13 h. After the reaction was complete, the corresponding perfluoroalkyltelluration product as a single stereoisomer \((E\)-isomer), was formed in moderate yield. Products were purified by extraction with FC-72 (C\(_6\)F\(_{14}\)).

\((E)-3,3,4,4,5,5,6,6,7,7,8,8,8\text{-Tridecafluoro-1-(phenytelluro)-1-phenyl-1-octene} \ (2a)\). Pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm): \(\delta\) 5.53 (t, \(J_{H-F} = 14.2 \text{ Hz}, 1\text{H}\)), 7.22–7.32 (m, 5H), 7.36–7.57 (m, 3H), 7.83–7.85 (d, \(J = 6.7 \text{ Hz}, 2\text{H}\)); \(^{13}\)C\{_\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm): \(\delta\) 98.9, 115.1, 126.8, 127.8, 128.2, 128.7, 129.7, 130.1, 132.5, 141.0; \(^{19}\)F NMR (373 MHz, CDCl\(_3\), ppm): \(\delta\) -126.1, -123.1, -122.9, -121.6, -103.2, -80.7; IR (NaCl): 3055, 2927, 2854, 1242, 1200, 1142, 1961, 737, 691 cm\(^{-1}\); HRMS (FAB) calcd for C\(_{20}\)H\(_{12}\)F\(_{13}\)Te \([\text{M+H}]^+\): 628.9794, 629.9794.
Chapter 2. Perfluoroalkyltelluration of Alkynes upon Photoirradiation

(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(4-methylphenyl)-1-octene (2b). Pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm): \(\delta 5.48 (t, J_{H-F} = 14.2 \text{ Hz}, 1\text{H}), 7.08–7.25 (m, 5\text{H}), 7.29–7.45 (m, 2\text{H}), 7.83–7.88 (d, J = 7.9 \text{ Hz}, 2\text{H}); ^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm): \(\delta 21.3, 115.3, 117.5, 123.8, 126.8, 128.4, 128.6, 129.7, 130.1, 136.1, 140.9; ^{19}\)F NMR (373 MHz, CDCl\(_3\), ppm): \(\delta -126.1, -123.1, -122.9, -121.6, -103.1, -80.7; \text{IR (NaCl): 3055, 2920, 2851, 1362, 1238, 1238, 1200, 1142, 1119, 841, 813, 775.3, 736.8 687 cm}^{-1}; \text{HRMS (FAB) calcd for C}_{21}\text{H}_{14}\text{F}_{13}\text{Te [M+H]}^+: 642.9950, \text{found: 642.9942.}

(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(4-methoxyphenyl)-1-octene (2c). Pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm): \(\delta 3.80 (s, 3\text{H}), 5.51 (t, J_{H-F} = 14.2 \text{ Hz}, 1\text{H}), 6.81 (d, J = 7.8 \text{ Hz}, 2\text{H}), 7.12–7.35 (m, 5\text{H}), 7.84 (d, J = 7.8 \text{ Hz}, 2\text{H}); ^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm): \(\delta 55.3, 113.0, 118.0, 123.5, 126.7, 128.3, 128.8, 130.0, 130.1, 140.4, 144.5; ^{19}\)F NMR (373 MHz, CDCl\(_3\), ppm): \(\delta -126.1, -123.1, -122.9, -121.4, -102.9, -80.7; \text{IR (NaCl): 3055, 2928, 2855, 1604, 1508, 1439, 1242, 1203, 1141, 1110, 1033, 833, 806, 779, 732 cm}^{-1}; \text{HRMS (FAB) calcd for C}_{21}\text{H}_{14}\text{F}_{13}\text{OTe [M+H]}^+: 658.9899, \text{found: 658.9885.}

(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(4-chlorophenyl)-1-octene (2d). \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm): \(\delta 5.61 (t, J_{H-F} = 14.6 \text{ Hz}, 1\text{H}), 7.19–7.29 (m, 4\text{H}), 7.38–7.44 (m, 3\text{H}), 7.94 (d, J = 8.2 \text{ Hz}, 2\text{H}).

(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(4-fluorophenyl)-1-octene (2e). Pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm): \(\delta 5.58 (t, J_{H-F} = 14.2 \text{ Hz}, 1\text{H}), 6.93–7.03 (m, 2\text{H}), 7.20–7.31 (m, 2\text{H}), 7.40–7.50 (m, 3\text{H}), 7.81 (d, J = 8.2 \text{ Hz}, 2\text{H}); ^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm): \(\delta 114.9, 118.2, 125.7, 128.8, 129.0, 129.8, 129.9, 130.2, 140.8, 141.0; ^{19}\)F NMR (373 MHz, CDCl\(_3\), ppm): \(\delta -126.1, -123.1, -121.6, -113.1, -107.0, -103.1, -80.7; \text{IR (NaCl): 3059, 2959, 2924, 2851, 1635, 1596, 1504, 1434, 1365, 1234, 1199, 1141, 837, 736, 690 cm}^{-1}; \text{HRMS}

- 20 -
(FAB) calcd for C$_{20}$H$_{11}$F$_{14}$Te [M+H]$^+$: 646.9699, found: 646.9667.

**(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(4-nitrophenyl)-1-octene (2f).**

$^1$H NMR (400 MHz, CDCl$_3$, ppm): δ 5.91 (t, $J_{H-F}$ = 14.2 Hz, 1H), 7.38–7.42 (m, 3H), 7.62–7.77 (m, 2H), 7.89 (d, $J$ = 7.8 Hz, 2H), 8.10–8.31 (m, 2H).

**(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(4-cyanophenyl)-1-octene (2g).**

$^1$H NMR (400 MHz, CDCl$_3$, ppm): δ 5.85 (t, $J_{H-F}$ = 14.2 Hz, 1H), 7.37–7.41 (m, 3H), 7.51–7.70 (m, 4H), 7.97 (d, $J$ = 8.2 Hz, 2H).

**(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(3-methylbutyl)-1-octene (2i).**

Pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$, ppm): δ 0.86 (d, $J = 6.0$ Hz, 6H), 1.24 (m, 1H), 1.46 (m, 2H), 2.54 (t, $J = 8.0$ Hz, 2H), 5.50 (t, $J_{H-F}$ = 14.2 Hz, 1H), 7.25–7.41 (m, 3H), 7.83 (d, $J = 7.8$ Hz, 2H); $^{13}$C($^1$H) NMR (100 MHz, CDCl$_3$, ppm): δ 22.3, 28.1, 34.9, 39.6, 112.9, 119.0, 129.5, 130.0, 141.0, 142.1; $^{19}$F NMR (373 MHz, CDCl$_3$, ppm): δ -126.1, -123.4, -122.8, -121.6, -104.3, -80.7; IR (NaCl): 3070, 2958, 2891, 2341, 1663, 1616, 1477, 1438, 1361, 1238, 1203, 1145, 1099, 1064, 1022, 736, 690, 667 cm$^{-1}$.

**(E)-3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-(phenyltelluro)-1-(ethoxycarbonyl)-1-octene (2j).**

$^1$H NMR (400 MHz, CDCl$_3$, ppm): δ 1.23 (t, $J = 6.9$ Hz, 3H), 4.35 (q, $J = 7.3$ Hz, 2H), 5.86 (t,
$J_{H-F} = 14.2$ Hz, 1H), 7.26–7.39 (m, 3H), 8.00 (d, $J = 8.2$ Hz, 2H).

2-5 References


22. During the photoirradiated reactions of alkynes with $R_f$I and $(\text{PhTe})_2$, PhTeI and $R_f$TePh may be formed in situ. To get some information about these species, the author examined the photoirradiated reaction of $R_f$I with $(\text{PhTe})_2$ in the absence of alkynes, and the reactions were monitored by $^{125}$Te and $^{19}$F NMR. In the case of $(\text{PhTe})_2$, the signal of $(\text{PhTe})_2$ disappeared within 3 h, but no new peak was observed in $^{125}$Te NMR. This was probably due to the formation of aggregated mixture of PhTeI.

23. Generation of vinyl anions from vinyl tellurides can be performed upon treatment with $^n$BuLi in THF at $-78$ °C, and the stereochemistry of the formed vinyl anions retains at the temperature.
Chapter 3

Regioselective Hydrothiolation of Heteroatom-Substituted Alkenes with Thiols Catalyzed by Palladium Diacetate

3-1 Introduction

Chapter 2 deals with radical addition of heteroatom compounds to carbon–carbon unsaturated bonds. Besides the radical addition, transition-metal-catalyzed addition of heteroatom compounds to unsaturated compounds are practically useful synthetic methods of heteroatom compounds because good atom economy, high efficiency, and high selectivity can be attained by the methods. Along this line, highly selective transition-metal-catalyzed addition reactions of organosulfur compounds to unsaturated bonds have been developed recently. Organosulfur compounds are known as valuable feedstock chemicals, finding utility in applications such as synthetic intermediates, bioactive compounds, and functional materials. However, examples of the transition-metal-catalyzed addition reaction of organosulfur compounds have been mostly limited to alkynes; thus, the development of a transition-metal-catalyzed addition to alkenes is strongly desired. The difficulties associated with the catalytic addition of organosulfur compounds to alkenes can be attributed to the lower coordination ability of alkenes compared with that of alkynes, which in turn may contribute to catalyst poisoning. However, functionalized alkenes bearing heteroatom are expected to coordinate to catalyst strongly by assistance of the heteroatom.

Thus, the author has focused attention on alkenes bearing heteroatom group, and has
developed a novel Pd-catalyzed addition reaction of thiols with heteroatom-substituted alkenes, which proceeds with excellent regioselectivity to afford the corresponding Markovnikov adducts in good yield (Scheme 3-1). Therefore, the present Pd-catalyzed addition is a regiocomplemented methods to the radical addition (thiol-ene reaction), which provides anti-Markovnikov adducts.\textsuperscript{9}

\textit{Previous work:}

\[ R=\equiv + R^2SH \xrightarrow{Pd(OAc)_2 (5 \text{ mol\%})} R\equiv SR^2 \quad (3-1) \]

\textit{This work:}

\[ R^1\equiv R + R^2SH \xrightarrow{Pd(OAc)_2 (5 \text{ mol\%})} R^1\equiv SR^2 \quad (3-2) \]

\[ R\equiv R + R^2SH \xrightarrow{Pd(OAc)_2 (5 \text{ mol\%})} R\equiv SR^2 \quad (3-3) \]

Scheme 3-1. Palladium-Catalyzed Hydrothiolation

3-2 Pd-Catalyzed Hydrothiolation of Vinyl Ethers

Firstly, the optimization of the addition of benzenethiol (2a) to \textit{n}-butyl vinyl ether (1a) in the presence of Pd(OAc)$_2$ as catalyst was examined (Table 3-1). When the reaction of \textit{n}-butyl vinyl ether (1a) with benzenethiol (2a) was conducted at 45 °C for 20 h using 5 mol\% of Pd(OAc)$_2$, the Markovnikov-type hydrothiolation product (3aa) was regioselectively obtained in 95\% yield without formation of \textit{anti}-Markovnikov-type adduct (entry 1). When the amount of Pd(OAc)$_2$ decreased to 1 mol\%, the desired hydrothiolation proceeded inefficiently (entry 2). In the absence of the Pd catalyst, a complex reaction mixture was formed, including 7\% of Markovnikov-type adduct 3aa and 18\% of the corresponding \textit{anti}-Markovnikov-type adduct.
Next, the optimization of reaction times and temperatures was examined. The results indicated that hydrothiolation proceeded well in shorter times under mild conditions (entries 4–7).

**Table 3-1. Optimization of Hydrothiolation of Vinyl Ether**

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>time, h</th>
<th>temp., °C</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd(OAc)$_2$ (5 mol%)</td>
<td>20</td>
<td>45</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>Pd(OAc)$_2$ (1 mol%)</td>
<td>20</td>
<td>45</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>20</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>Pd(OAc)$_2$ (5 mol%)</td>
<td>14</td>
<td>45</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>Pd(OAc)$_2$ (5 mol%)</td>
<td>5</td>
<td>45</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>Pd(OAc)$_2$ (5 mol%)</td>
<td>20</td>
<td>reflux</td>
<td>77</td>
</tr>
<tr>
<td>7</td>
<td>Pd(OAc)$_2$ (5 mol%)</td>
<td>20</td>
<td>30</td>
<td>83</td>
</tr>
</tbody>
</table>

*a* Reaction conditions: *n*-butyl vinyl ether (1a, 0.5 mmol), benzenethiol (2a, 0.5 mmol), THF (0.3 mL). *b* Determined by $^1$H NMR analysis. *c* Accompanied by 18% of the anti-Markovnikov hydrothiolation adduct in the reaction mixture. In other entries, no formation of anti-Markovnikov adducts was observed.

Next, the Pd-catalyzed hydrothiolation of several vinyl ethers was performed, and the results are summarized in Table 3-2. In the cases of branched vinyl ethers 1b and 1c, the desired Markovnikov hydrothiolation products were obtained in 85% and 87% yields, respectively (entries 2 and 3). The reaction of vinyl ethers 1d and 1e bearing chloro and hydroxyl groups, respectively, afforded the corresponding hydrothiolation products 3da and 3ea in good to moderate yields (entries 4 and 5). Interestingly, the reaction of internal vinyl ether 1f also proceeded efficiently to yield the corresponding hydrothiolation product despite the generally
known difficulty of transition-metal-catalyzed reaction of internal alkenes (entry 6). Furthermore, cyclic vinyl ethers \textbf{1g} and \textbf{1h} were also tolerant to the hydrothiolation (entries 7 and 8).

\begin{table}
\centering
\caption{Hydrothiolation of Several Vinyl Ethers \textsuperscript{a}}
\begin{tabular}{cccc}
\hline
entry & substrate & 1 & product \& 3 & yield, \% \textsuperscript{b} \\
\hline
1 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1a & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3aa & 95 \\
2 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1b & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3ba & 85 \\
3 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1c & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3ca & 87 \\
4 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1d & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3da & 90 \\
5 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1e & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3ea & 57 \\
6 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1f & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3fa & 87 \\
7 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1g & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3ga & 88 \\
8 & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\end{tikzpicture} & 1h & \begin{tikzpicture}
\draw (0,0) -- (1,0) -- (1.5,0.5) -- (1,1) -- (0,1) -- (0,0);
\draw (2,0) -- (2,1);
\end{tikzpicture} & 3ha & 84 \\
\hline
\textsuperscript{a} Reaction conditions: vinyl ether (1, 0.5 mmol), benzenethiol (2a, 0.5 mmol), Pd(OAc)$_2$ (5 mol%), THF (0.3 mL), 45 $^\circ$C, 20 h. \textsuperscript{b} Isolated yield.
\end{tabular}
\end{table}
Next, the scope and limitations of this Pd-catalyzed hydrothiolation of vinyl ethers by using several thiols were examined. The results of the reaction of *n*-butyl vinyl ether 1a with several thiols 2 are summarized in Table 3-3. In the cases of benzenethiols bearing electron-donating or electron-withdrawing groups, such as methyl, methoxy, fluoro, and chloro...
substituents on the aryl groups, the Pd-catalyzed Markovnikov hydrothiolation took place, affording the corresponding products 3ab, 3ac, 3ad, and 3ae, respectively, in good yields (entries 2–5). However, aliphatic thiols, such as phenylmethanethiol 2f and cyclohexanethiol 2g, gave low yields of the corresponding hydrothiolation products 3af and 3ag, respectively (entries 6 and 7).10

3-3 Pd-Catalyzed Hydrothiolation of N-Vinyl Lactams

Highly selective hydrothiolation of alkenes bearing nitrogen functional groups is also of great interest as an application of the vinyl ether hydrothiolation to other functionalized alkenes. The author chose N-vinyl lactams as alkenes bearing nitrogen functional group for the Pd-catalyzed hydrothiolation. The lactam skeleton is a prominent structural feature found in a number of biologically active natural products.11 Some of bioactive lactam compounds containing N,S-acetal unit, such as penicillin, exhibit remarkable antibiosis. Therefore, the development of highly selective methods for introduction of sulfur group to lactam units is strongly desired.

The optimization of the reaction conditions of hydrothiolation by using N-vinylpyrrolidinone as the manageable N-vinyl lactam was examined (Table 3-4). When the reaction of N-vinylpyrrolidinone (4a) with benzenethiol (2a) was conducted at 45 °C for 20 h using 5 mol% or 1 mol% of Pd(OAc)$_2$, the Markovnikov-type hydrothiolation product (5aa) was obtained in 94% or 80% yields (entries 1 and 2). In the absence of Pd(OAc)$_2$, the desired hydrothiolation of N-vinyl lactam proceeded inefficiently (entry 3). The reaction using other palladium catalysts, such as Pd(PPh$_3$)$_4$, PdCl$_2$(PhCN)$_2$ and PdCl$_2$(cod), was examined (entries 4–6). PdCl$_2$(PhCN)$_2$- and PdCl$_2$(cod)-catalyzed hydrothiolation yielded the desired Markovnikov-type adduct in moderate yield, whereas Pd(PPh$_3$)$_4$ did not catalyze hydrothiolation.
of $N$-vinyl lactam. Next, the hydrothiolation was conducted varying temperature and time (entries 7–9). These results clearly indicate that the hydrothiolation of $N$-vinyl lactam can proceed under mild conditions.

### Table 3-4. Optimization of Hydrothiolation of $N$-Vinyl Lactam

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>time, h</th>
<th>temp., °C</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd(OAc)$_2$</td>
<td>20</td>
<td>45</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>Pd(OAc)$_2$ (1 mol%)</td>
<td>20</td>
<td>45</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>20</td>
<td>45</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>Pd(PPh$_3$)$_4$</td>
<td>20</td>
<td>45</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>PdCl$_2$(PhCN)$_2$</td>
<td>20</td>
<td>45</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>PdCl$_2$(cod)</td>
<td>20</td>
<td>45</td>
<td>77</td>
</tr>
<tr>
<td>7</td>
<td>Pd(OAc)$_2$</td>
<td>20</td>
<td>30</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>Pd(OAc)$_2$</td>
<td>14</td>
<td>45</td>
<td>81</td>
</tr>
<tr>
<td>9</td>
<td>Pd(OAc)$_2$</td>
<td>5</td>
<td>45</td>
<td>87</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: $N$-vinylpyrrolidinone (4a, 0.5 mmol), benzenethiol (2a, 0.5 mmol), catalyst (5 mol%), THF (0.3 mL). $^b$ Determined by $^1$H NMR analysis.

Next, under the optimized reaction conditions, the scope and limitation of hydrothiolation of $N$-vinyl lactams was investigated (Table 3-5). When internal $N$-vinyl lactams 4b and 4c were used for the catalytic hydrothiolation, the corresponding $N,S$-acetals 5ba and 5ca were obtained in 73% and 69% yields, respectively (entries 2 and 3). In the case of branched and aromatic internal $N$-vinyl lactams 4d and 4e, the desired hydrothiolation proceeded in good to mo-
Table 3-5. Hydrothiolation of Several N-Vinyl Lactams

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>4</th>
<th>product</th>
<th>5</th>
<th>yield, % b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="4a" /></td>
<td>4a</td>
<td><img src="image" alt="5aa" /></td>
<td>5aa</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="4b" /></td>
<td>4b</td>
<td><img src="image" alt="5ba" /></td>
<td>5ba</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="4c" /></td>
<td>4c</td>
<td><img src="image" alt="5ca" /></td>
<td>5ca</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="4d" /></td>
<td>4d</td>
<td><img src="image" alt="5da" /></td>
<td>5da</td>
<td>71</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="4e" /></td>
<td>4e</td>
<td><img src="image" alt="5ea" /></td>
<td>5ea</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="4f" /></td>
<td>4f</td>
<td><img src="image" alt="5fa" /></td>
<td>5fa</td>
<td>87</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="4g" /></td>
<td>4g</td>
<td><img src="image" alt="5ga" /></td>
<td>5ga</td>
<td>ND</td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="4h" /></td>
<td>4h</td>
<td><img src="image" alt="5ha" /></td>
<td>5ha</td>
<td>ND</td>
</tr>
<tr>
<td>9</td>
<td><img src="image" alt="4i" /></td>
<td>4i</td>
<td><img src="image" alt="5ia" /></td>
<td>5ia</td>
<td>ND</td>
</tr>
</tbody>
</table>

*a* Reaction conditions: *N*-vinyl lactams (4, 0.5 mmol), benzenethiol (2a, 0.5 mmol), Pd(OAc)$_2$ (5 mol%), THF (0.3 mL), 45 °C, 20 h. *b* Isolated yield.
derate yields (entries 4 and 5). The reaction of \( N \)-vinylcaprolactam 4f took place efficiently to get Markovnikov adduct regioselectively (entry 6). In the case of 1-(2-methylpropenyl)-2-pyrrolidinone 4g and 1-cyclohexylidene-2-pyrrolidinone 4h, however, the desired reaction did not proceed at all. This is probably because the bulkiness of alkene interrupted the approach of Pd-sulfide complex to the alkenes. Moreover, the hydrothiolation using \( N \)-vinylphthalimide 4i as substrate did not take place owing to the lower coordination ability of nitrogen atom.

Furthermore, Pd-catalyzed hydrothiolation of \( N \)-vinyl lactam using several thiols was performed, and the results are summarized in Table 3-6. Benzenethiols bearing electron-donating and electron-withdrawing groups, such as methyl, methoxy, fluoro, and chloro group, afforded the corresponding hydrothiolation products 5ab, 5ac, 5ad, and 5ae, respectively (entries 2–5). In the case of aliphatic thiols, such as phenylmethanethiol 2f and cyclohexanethiol 2g, the desired hydrothiolation products were obtained in moderate to good yields (entries 6 and 7). This results indicated that hydrothiolation of \( N \)-vinyl lactams proceeded more efficiently owing to the effect of their amide unit compared with the hydrothiolation of vinyl ethers.

To obtain insight into the present Pd-catalyzed hydrothiolation reaction, the author examined the catalytic hydrothiolation of a vinyl ether using a preformed Pd-sulfide complex (Scheme 3-2). Initially, the Pd-sulfide complex was prepared by reaction of Pd(OAc)\(_2\) with benzenethiol (2a) according to the literature.\(^6\) The reaction of \( n \)-butyl vinyl ether (1a) with benzenethiol (2a) in the presence of 5 mol\% of Pd-sulfide complex A as a catalyst afforded the corresponding Markovnikov hydrothiolation product (3aa) in 85% yield. Furthermore, when the equimolar reaction of Pd-sulfide complex A with a vinyl ether was conducted, no hydrothiolation product was obtained at all. These results strongly suggest that thiol is essential for the hydrothiolation, and also Pd-sulfide complex A is a highly effective catalyst for the hydrothiolation of vinyl ethers.
Table 3-6. Pd-Catalyzed Hydrothiolation of N-Vinyl Lactams Using Several Thiols $^a$

\[ \text{4a} \ + \ RSH \xrightarrow{\text{Pd(OAc)}_2, \text{THF, } 45^\circ \text{C, } 20 \text{ h}} \text{5} \]

<table>
<thead>
<tr>
<th>entry</th>
<th>RSH, 2</th>
<th>product</th>
<th>5</th>
<th>yield, % $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \text{Ph-SH} )</td>
<td>( \text{5aa} )</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>( \text{Me-Ph-SH} )</td>
<td>( \text{5ab} )</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>( \text{MeO-Ph-SH} )</td>
<td>( \text{5ac} )</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>( \text{F-Ph-SH} )</td>
<td>( \text{5ad} )</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>( \text{Cl-Ph-SH} )</td>
<td>( \text{5ae} )</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>( \text{Ph-SH} )</td>
<td>( \text{5af} )</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>( \text{Cyclohexane-SH} )</td>
<td>( \text{5ag} )</td>
<td>59</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: \( N\text{-vinylpyrrolidinone (4a, 0.5 mmol), thiol (2, 0.5 mmol), Pd(OAc)}_2 \) (5 mol%), THF (0.3 mL), \( 45^\circ \text{C, 20 h.} \) $^b$ Isolated yield.

Further investigations were conducted to acquire information on the hydrothiolation reaction. When a Lewis acid catalyst such as Sc(OTf)$_3$ was introduced to the reaction instead of the Pd catalyst, the desired hydrothiolation product was not obtained at all. This result indicates that the Pd catalyst did not serve in a Lewis-acid capacity to catalyze the hydrothiolation. As
another possibility, it was considered that AcOH generated from the reaction of Pd(OAc)$_2$ and benzenethiol might catalyze this hydrothiolation as a Brønsted acid. Thus, the reaction using AcOH as a protic acid was examined. However, the hydrothiolation reaction did not proceed.

Although the detail of the reaction mechanism is not clear at present, a possible reaction pathway for the Pd-catalyzed hydrothiolation of heteroatom-substituted alkene with thiol 2 is shown in Scheme 3-3. The author thinks heteroatoms on the alkene are of great importance for making it possible to take place the hydrothiolation, because Pd-catalyzed hydrothiolation of normal (heteroatom-unsubstituted) alkenes did not proceed at all. Therefore, the Pd(OAc)$_2$ catalyst reacts with thiols to form Pd-sulfide complex A. Then, vinyl ether 1 coordinates to Pd-sulfide complex A, providing Pd-sulfide-alkene complex B, where heteroatoms might coordinate to the palladium, stabilizing the complex B. Subsequent insertion generates $\beta$-thio-substituted palladium intermediate C. The following protonation of palladium intermediate

Scheme 3-2. Examination of the Effects of Pd Catalyst
C with thiol provides the Markovnikov hydrothiolation product regioselectively, with regeneration of Pd-sulfide complex A.\textsuperscript{12}

**Scheme 3-3.** A Possible Reaction Pathway of Pd-Catalyzed Hydrothiolation of Heteroatom-Substituted Alkenes

### 3-4 Conclusion

In summary, a novel and highly selective Pd-catalyzed Markovnikov hydrothiolation of alkenes bearing heteroatom functional groups under mild conditions has been developed. The nature of the thiol substrate is general and includes thiols previously reported as problematic in transition-metal-catalyzed reactions of alkenes. Internal and cyclic alkenes bearing heteroatom are also shown to be compatible. In addition, the present hydrothiolation could produce $O,S$-acetals or $N,S$-acetals, and new stereogenic center in their structure. Therefore, application of
this methodology toward the enantioselective hydrothiolation will be next explored, because these acetal derivatives are known as useful synthetic intermediates and bioactive products.\textsuperscript{11, 13} The author believes that this catalytic hydrothiolation will open up a new field of transition-metal-catalyzed reactions of alkenes.

### 3-5 Experimental Section

#### General Comment

Unless otherwise stated, all starting materials and catalysts were purchased from a commercial source and used without further purification. The following substrates were prepared by using dehydration condensation of pyrrolidinone and the corresponding aldehydes with \textit{p}-TsOH: \textit{(E)}-1-(1-pentenyl)-2-pyrrolidinone\textsuperscript{14}, \textit{(E)}-1-(3-phenyl-1-propenyl)-2-pyrrolidinone\textsuperscript{15}, \textit{(E)}-1-(3,3-dimethyl-1-butenyl)-2-pyrrolidinone\textsuperscript{15}, \textit{(E)}-1-styryl-2-pyrrolidinone\textsuperscript{14}, 1-(2-methylpropenyl)-2-pyrrolidinone\textsuperscript{15}, 1-cyclohexylidene-2-pyrrolidinone\textsuperscript{15}. Tetrahydrofuran (THF) as solvent and benzenethiol were used after distillation. \textsuperscript{1}H NMR spectra (400 MHz) and \textsuperscript{13}C NMR spectra (100 MHz) were taken in CDCl\textsubscript{3} with Me\textsubscript{4}Si as an internal standard. Chemical shifts in \textsuperscript{1}H NMR were measured relative to CDCl\textsubscript{3} and converted to \(\delta\) (Me\textsubscript{4}Si) values by using \(\delta\) (CDCl\textsubscript{3}) 7.26 ppm. Chemical shifts in \textsuperscript{13}C NMR were measured relative to CDCl\textsubscript{3} and converted to \(\delta\) (Me\textsubscript{4}Si) values by using \(\delta\) (CDCl\textsubscript{3}) 77.00 ppm. IR spectra are reported in wave numbers (cm\textsuperscript{-1}). FAB mass spectra were obtained by employing double focusing mass spectrometers. Elemental analyses and EI mass spectra were performed in the analytical section of Osaka University.

#### General Procedure for Hydrothiolation of Heteroatom-Substituted Alkenes.

In a two-necked 10 mL flask with a magnetic stirring bar under N\textsubscript{2} atmosphere were
placed Pd(OAc)$_2$ (0.025 mmol), freshly distilled THF (0.3 mL), heteroatom-substituted alkene (0.5 mmol), and thiol (0.5 mmol), in that order. The reaction was conducted at 45 °C for 20 h, and then the resulting solution was filtered through Celite with ethyl acetate as an eluent. Concentration in vacuo, and purification by preparative TLC (silica gel, eluent: hexane) provided the hydrothiolated product.

1-(Phenylthio)ethyl butyl ether (3aa). This compound was prepared from n-butyl vinyl ether (64.7 μL, 0.5 mmol) and benzenethiol (51.1μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (105.1 mg, 95%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.92 (t, $J = 7.3$ Hz, 3H), 1.38 (sext, $J = 7.3$ Hz, 2H), 1.50 (d, $J = 6.3$ Hz, 3H), 1.54−1.61 (m, 2H), 3.43 (td, $J = 6.3$ Hz, 9.0 Hz, 1H), 3.88 (td, $J = 6.3$ Hz, 9.0 Hz, 1H), 4.88 (q, $J = 6.3$ Hz, 1H), 7.24−7.31 (m, 3H), 7.46−7.48 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 14.0, 19.5, 22.7, 31.6, 67.9, 84.8, 127.5, 128.8, 133.3, 133.8; IR (NaCl) 3071, 2959, 2932, 2870, 1582, 1481, 1439, 1369, 1315, 1261, 1111, 1026, 972, 910, 744 cm$^{-1}$; HRMS (EI) Calcd for C$_{12}$H$_{18}$OS: 210.1078, Found: 210.1080; Anal. Calcd for C$_{12}$H$_{18}$OS: C, 68.52; H, 8.63. Found: C, 68.41; H, 8.67.

1-(Phenylthio)ethyl 2-methylpropyl ether (3ba). This compound was prepared from 2-methylpropyl vinyl ether (65.0 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (89.6 mg, 85%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.92 (dd, $J = 6.9$ Hz, 8.2 Hz, 6H), 1.50 (d, $J = 6.4$ Hz, 3H), 1.86 (sept, $J = 6.9$ Hz, 1H), 3.21 (dd, $J = 6.9$ Hz, 9.2 Hz, 1H), 3.63 (dd, $J = 6.9$ Hz, 9.2 Hz, 1H), 4.89 (q, $J = 6.4$ Hz, 1H), 7.23−7.31 (m, 3H), 7.46−7.49 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 19.5 (overlap), 22.4, 28.3, 74.7, 84.7, 127.3, 128.6, 133.2, 133.6; IR (NaCl) 3074, 2959, 2932, 2870, 1582, 1474, 1435, 1362, 1323, 1265, 1111, 1053, 1026, 891, 745, 691 cm$^{-1}$; HRMS (EI) Calcd for C$_{12}$H$_{18}$OS: 210.1078, Found: 210.1076.
**1-(Phenylthio)ethyl cyclohexyl ether (3ca).** This compound was prepared from cyclohexyl vinyl ether (70.9 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (102.6 mg, 87%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.16−1.41 (m, 5H), 1.48 (d, \(J = 6.0\) Hz, 3H), 1.49−1.57 (m, 1H), 1.67−1.75 (m, 2H), 1.84−1.90 (m, 2H), 3.73−3.80 (m, 1H), 5.01 (q, \(J = 6.0\) Hz, 1H), 7.23−7.31 (m, 3H), 7.48−7.51 (m, 2H); \(^{13}\)C\(^{\{1\}H}\) NMR (100 MHz, CDCl\(_3\), ppm) δ 23.2, 24.0, 24.2, 25.6, 31.1, 33.1, 74.8, 81.5, 127.4, 128.5, 132.9, 134.0; IR (NaCl) 3063, 2932, 2855, 1582, 1477, 1450, 1369, 1312, 1265, 1153, 1099, 1057, 1026, 972, 883, 745, 694, 621 cm\(^{-1}\); Anal. Calcd for C\(_{14}\)H\(_{20}\)OS: C, 71.14; H, 8.53. Found: C, 70.92; H, 8.52.

**1-(Phenylthio)ethyl 2-chloroethyl ether (3da).** This compound was prepared from 2-chloroethyl vinyl ether (50.7 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (97.3 mg, 90%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.52 (d, \(J = 6.4\) Hz, 3H), 3.64 (t, \(J = 5.5\) Hz, 2H), 3.73 (td, \(J = 5.5\) Hz, 10.5 Hz, 1H), 4.11 (td, \(J = 5.5\) Hz, 10.5 Hz, 1H), 4.97 (q, \(J = 6.4\) Hz, 1H), 7.24−7.32 (m, 3H), 7.47−7.50 (m, 2H); \(^{13}\)C\(^{\{1\}H}\) NMR (100 MHz, CDCl\(_3\), ppm) δ 22.2, 42.7, 67.6, 84.8, 127.7, 128.7, 132.4, 133.6; IR (NaCl) 3059, 2978, 2928, 2862, 1582, 1477, 1439, 1373, 1296, 1265, 1200, 1111, 1042, 1003, 968, 926, 814, 748, 694 cm\(^{-1}\); Anal. Calcd for C\(_{10}\)H\(_{13}\)ClO\(_{3}\): C, 55.42; H, 6.05. Found: C, 55.29; H, 5.95.

**1-(Phenylthio)ethyl 2-hydroxyethyl ether (3ea).** This compound was prepared from 2-hydroxyethyl vinyl ether (45.0 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (56.1 mg, 57%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.53 (d, \(J = 6.4\) Hz, 3H), 2.02 (br, 1H), 3.55−3.60 (m, 1H), 3.75 (br, 2H), 3.95−4.00 (m, 1H), 4.97 (q, \(J = 6.4\) Hz, 1H), 7.27−7.33 (m, 3H), 7.46−7.50 (m, 2H); \(^{13}\)C\(^{\{1\}H}\) NMR (100 MHz, CDCl\(_3\), ppm) δ 22.3, 61.6, 68.8, 84.8, 127.7, 128.8, 132.5, 133.7; IR (NaCl) 3402, 3074, 2928, 1585, 1477, 1439, 1377, 1319, 1115, 1080, 937, 887, 829, 748, 694
cm$^{-1}$; HRMS (EI) Calcd for C$_{10}$H$_{14}$O$_2$S: 198.0715, Found: 198.0713.

**1-(Phenylthio)butyl ethyl ether (3fa).** This compound was prepared from ethyl 1-butenyl ether (64.4 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (91.3 mg, 87%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.89 (t, $J = 7.3$ Hz, 3H), 1.22 (t, $J = 7.3$ Hz, 3H), 1.48 (sext, $J = 7.3$ Hz, 2H), 1.66–1.81 (m, 2H), 3.48 (qd, $J = 6.9$ Hz, 9.1 Hz, 1H), 3.95 (qd, $J = 6.9$ Hz, 9.1 Hz, 1H), 4.70 (dd, $J = 6.0$ Hz, 7.3 Hz, 1H), 7.23–7.30 (m, 3H), 7.46–7.49 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 13.6, 14.8, 19.5, 38.0, 63.4, 88.9, 127.3, 128.6, 133.4, 133.6; IR (NaCl) 3059, 2963, 2932, 2870, 1582, 1477, 1439, 1381, 1288, 1261, 1245, 1115, 1080, 1026, 972, 883, 829, 744, 690 cm$^{-1}$; Anal. Calcd for C$_{12}$H$_{18}$OS: C, 68.52; H, 8.63. Found: C, 68.27; H, 8.63.

**Tetrahydro-2-(phenylthio)pyran (3ga).** This compound was prepared from 2,3-dihydropyran (45.6 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (85.5 mg, 88%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.57–1.69 (m, 3H), 1.78–1.89 (m, 2H), 1.99–2.06 (m, 1H), 3.55–3.60 (m, 1H), 4.14–4.19 (m, 1H), 5.20 (dd, $J = 3.6$ Hz, 5.9 Hz, 1H), 7.18–7.29 (m, 3H), 7.45–7.48 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 21.6, 25.4, 31.5, 64.4, 85.2, 126.6, 128.7, 130.7, 135.3; IR (NaCl) 3063, 2940, 2858, 1582, 1477, 1439, 1339, 1323, 1261, 1188, 1103, 1076, 1038, 1007, 868, 810, 741, 691 cm$^{-1}$.

**Tetrahydro-2-(phenylthio)furan (3ha).** This compound was prepared from 2,3-dihydrofuran (37.7 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (75.7 mg, 84%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.79–2.06 (m, 3H), 2.31–2.42 (m, 1H), 3.93–4.05 (m, 2H), 5.63–5.66 (m, 1H), 7.19–7.24 (m, 1H), 7.26–7.31 (m, 2H), 7.49–7.52 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 24.8, 32.6, 67.2, 87.0, 126.7, 128.7, 131.0, 135.6; IR (NaCl) 3063, 2974, 2951, 2870,
1582, 1481, 1296, 1180, 1049, 907, 741, 691 cm$^{-1}$.

I-[(p-Methylphenyl)thio]ethyl butyl ether (3ab). This compound was prepared from n-butyl vinyl ether (64.7 µL, 0.5 mmol) and 4-methylbenzenethiol (62.1 µL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (90.3 mg, 81%);
$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.92 (t, $J$ = 7.3 Hz, 3H), 1.38 (sext, $J$ = 7.3 Hz, 2H), 1.47 (d, $J$ = 6.4 Hz, 3H), 1.52–1.61 (m, 2H), 2.33 (s, 3 H), 3.42 (td, $J$ = 6.4 Hz, 9.2 Hz, 1H), 3.89 (td, $J$ = 6.4 Hz, 9.2 Hz, 1H), 4.82 (q, $J$ = 6.4 Hz, 1H), 7.10 (d, $J$ = 8.1 Hz, 2H), 7.36 (d, $J$ = 8.1 Hz, 2H);
$^{13}$C NMR{$_1^1$H} (100 MHz, CDCl$_3$, ppm) δ 13.9, 19.4, 21.1, 22.6, 31.5, 67.8, 84.8, 129.1, 129.4, 134.2, 137.6; IR (NaCl) 3017, 2959, 2932, 2870, 1738, 1493, 1458, 1396, 1315, 1265, 1241, 1107, 1088, 1049, 968, 907, 810, 756, 648 cm$^{-1}$; Anal. Calcd for C$_{13}$H$_{20}$OS: C, 69.59; H, 8.98. Found: C, 69.36; H, 8.80.

I-[(p-Methoxylphenyl)thio]ethyl butyl ether (3ac). This compound was prepared from n-butyl vinyl ether (64.7 µL, 0.5 mmol) and 4-methoxylbenzenethiol (61.5 µL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a pale yellow oil (69.8 mg, 58%);
$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.93 (t, $J$ = 7.3 Hz, 3H), 1.39 (sext, $J$ = 7.3 Hz, 2H), 1.43 (d, $J$ = 6.4 Hz, 3H), 1.54–1.61 (m, 2H), 3.41 (td, $J$ = 6.9 Hz, 9.2 Hz, 1H), 3.80 (s, 3 H), 3.90 (td, $J$ = 6.9 Hz, 9.2 Hz, 1H), 4.74 (q, $J$ = 6.4 Hz, 1H), 6.82–6.86 (m, 2H), 7.38–7.42 (m, 2H); $^{13}$C{$_1^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 13.9, 19.4, 22.5, 31.5, 55.2, 68.0, 84.9, 114.2, 122.8, 136.4, 159.7; IR (NaCl) 2959, 2932, 2870, 1593, 1493, 1462, 1366, 1285, 1246, 1173, 1107, 1034, 907, 829, 648, 610 cm$^{-1}$; Anal. Calcd for C$_{13}$H$_{20}$O$_2$S: C, 64.96; H, 8.39. Found: C, 64.87; H, 8.45.

I-[(p-Fluorophenyl)thio]ethyl butyl ether (3ad). This compound was prepared from n-butyl vinyl ether (64.7 µL, 0.5 mmol) and 4-fluorobenzenethiol (53.3 µL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (95.7 mg, 83%);
$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.93 (t, $J$ = 7.3 Hz, 3H), 1.38 (sext, $J$ = 7.3 Hz, 2H), 1.45 (d,
Chapter 3. Pd-Catalyzed Hydrothiolation of Heteroatom-Substituted Alkenes

$J = 6.4 \text{ Hz}, 3\text{H}$, 1.54–1.63 (m, 2H), 3.42 (td, $J = 6.4 \text{ Hz}, 9.1 \text{ Hz}, 1\text{H}$), 3.88 (td, $J = 6.4 \text{ Hz}, 9.1 \text{ Hz}, 1\text{H}$), 4.80 (q, $J = 6.4 \text{ Hz}, 1\text{H}$), 6.96–7.02 (m, 3H), 7.42–7.46 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl$_3$, ppm) δ 13.8, 19.4, 22.4, 31.5, 67.9, 84.6, 115.7 (d, $J_{C-F} = 22.0 \text{ Hz}$), 127.6 (d, $J_{C-F} = 3.8 \text{ Hz}$), 136.2 (d, $J_{C-F} = 8.6 \text{ Hz}$), 162.7 (d, $J_{C-F} = 247.3 \text{ Hz}$);

$^{19}\text{F}$ NMR (376 MHz, CDCl$_3$, ppm) δ -113.9; IR (NaCl) 2959, 2932, 2870, 1894, 1740, 1589, 1489, 1462, 1396, 1369, 1265, 1227, 1157, 1107, 1088, 1034, 972, 907, 829, 760 cm$^{-1}$; Anal. Calcd for C$_{12}$H$_{17}$FOS: C, 63.12; H, 7.50. Found: C, 62.98; H, 7.56.

1-(p-Chlorophenyl)thio)ethyl butyl ether (3ae). This compound was prepared from $n$-butyl vinyl ether (64.7 μL, 0.5 mmol) and 4-chlorobenzenethiol (72.3 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (118.6 mg, 97%); $^1\text{H}$ NMR (400 MHz, CDCl$_3$, ppm) δ 0.92 (t, $J = 7.3 \text{ Hz}, 3\text{H}$), 1.38 (sext, $J = 7.3 \text{ Hz}, 2\text{H}$), 1.47 (d, $J = 6.4 \text{ Hz}, 3\text{H}$), 1.53–1.64 (m, 2H), 3.42 (td, $J = 6.9 \text{ Hz}, 9.0 \text{ Hz}, 1\text{H}$), 3.85 (td, $J = 6.9 \text{ Hz}, 9.0 \text{ Hz}, 1\text{H}$), 4.85 (q, $J = 6.4 \text{ Hz}, 1\text{H}$), 7.25 (d, $J = 8.2 \text{ Hz}, 2\text{H}$), 7.39 (d, $J = 8.2 \text{ Hz}, 2\text{H}$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl$_3$, ppm) δ 13.8, 19.4, 22.4, 31.4, 67.7, 84.5, 128.7, 131.5, 133.6, 134.9; IR (NaCl) 2959, 2932, 2870, 1570, 1474, 1389, 1373, 1315, 1269, 1111, 1092, 1015, 972, 907, 822, 741, 625 cm$^{-1}$; Anal. Calcd for C$_{12}$H$_{17}$ClOS: C, 58.88; H, 7.00. Found: C, 58.65; H, 6.88.

1-(Phenylmethylthio)ethyl butyl ether (3af). This compound was prepared from $n$-butyl vinyl ether (64.7 μL, 0.5 mmol) and phenylmethylthiol (58.6 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a colorless oil (39.2 mg, 35%); $^1\text{H}$ NMR (400 MHz, CDCl$_3$, ppm) δ 0.93 (t, $J = 7.3 \text{ Hz}, 3\text{H}$), 1.39 (sext, $J = 7.3 \text{ Hz}, 2\text{H}$), 1.52 (d, $J = 6.3 \text{ Hz}, 3\text{H}$), 1.51–1.59 (m, 2H), 3.41 (td, $J = 6.3 \text{ Hz}, 9.1 \text{ Hz}, 1\text{H}$), 3.61 (td, $J = 6.4 \text{ Hz}, 9.1 \text{ Hz}, 1\text{H}$), 3.45 (d, $J = 13.1 \text{ Hz}, 1\text{H}$), 3.79 (d, $J = 13.1 \text{ Hz}, 1\text{H}$), 4.64 (q, $J = 6.3 \text{ Hz}, 1\text{H}$), 7.19–7.34 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl$_3$, ppm) δ 13.9, 19.5, 22.1, 31.7, 32.6, 66.4, 80.6, 126.8, 128.4, 128.9, 138.8; IR (NaCl) 3028, 2959, 2932, 2866, 1597, 1489, 1454, 1369, 1265, 1231, 1103, 1030, 972, 907, 764, 702, 629 cm$^{-1}$. 
1-(Cyclohexylthio)ethyl butyl ether (3ag). This compound was prepared from \( n \)-butyl vinyl ether (64.7 μL, 0.5 mmol) and cyclohexylthiol (61.2 μL, 0.5 mmol) following the general procedure of hydrothiolation of vinyl ethers. Isolated as a pale yellow oil (42.7 mg, 39%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 0.93 (t, \( J = 7.3 \) Hz, 3H), 1.21–1.43 (m, 8H), 1.51–1.63 (m, 5H), 1.72–1.75 (m, 2H), 1.93–2.02 (m, 2H), 2.81–2.89 (m, 1H), 3.44 (td, \( J = 6.4 \) Hz, 9.2 Hz, 1H), 3.63 (td, \( J = 6.4 \) Hz, 9.2 Hz, 1H), 4.78 (q, \( J = 6.4 \) Hz, 1H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) δ 13.9, 19.4, 22.6, 25.7, 31.7, 34.5, 35.0, 41.4, 66.1, 80.6; IR (NaCl) 2928, 2855, 1447, 1369, 1312, 1265, 1204, 1103, 1034, 999, 973, 907, 887, 772, 741, 637 cm\(^{-1}\); HRMS (EI) Calcd for C\(_{12}\)H\(_{24}\)OS: 216.1548, Found: 216.1549.

1-[(1-Phenylthio)ethyl]-2-pyrrolidinone (5aa). This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 μL, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of \( N \)-vinyl lactam. Isolated as a pale yellow oil (104.4 mg, 94%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.48 (d, \( J = 6.9 \) Hz, 3H), 1.76–1.83 (m, 1H), 1.86–1.96 (m, 1H), 2.04–2.12 (m, 1H), 2.22–2.30 (m, 1H), 3.28–3.34 (m, 1H), 3.52–3.58 (m, 1H), 5.89 (q, \( J = 6.9 \) Hz, 1H), 7.20–7.30 (m, 3H), 7.39–7.41 (m, 2H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) δ 17.5, 18.7, 31.0, 41.1, 54.2, 127.3, 128.6, 132.0, 132.8, 174.3; IR (NaCl) 3495, 3071, 2986, 2881, 1686, 1585, 1481, 1458, 1416, 1350, 1269, 1200, 1092, 1065, 1018, 953, 926, 837, 748, 694 cm\(^{-1}\); HRMS (EI) Calcd for C\(_{12}\)H\(_{15}\)NOS: 221.0874, Found: 221.0875.

1-[(1-Phenylthio)pentyl]-2-pyrrolidinone (5ba). This compound was prepared from 1-(1-pentenyl)-2-pyrrolidinone (76.6 mg, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of \( N \)-vinyl lactam. Isolated as a yellow oil (96.3 mg, 73%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 0.90 (t, \( J = 6.9 \) Hz, 3H), 1.25–1.42 (m, 4H), 1.68–1.97 (m, 4H), 2.04–2.12 (m, 1H), 2.24–2.32 (m, 1H), 3.20–3.26 (m, 1H), 3.52–3.58 (m, 1H), 5.73 (dd, \( J = 5.7 \) Hz, 9.4 Hz, 1H), 7.19–7.29 (m, 3H), 7.38–7.40 (m, 2H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) δ 13.8, 17.7, 22.0, 28.5, 31.1, 32.2, 41.3, 58.8, 127.2, 128.7, 132.0,
132.9, 174.8; IR (NaCl) 3441, 3049, 2931, 2861, 1685, 1583, 1486, 1458, 1412, 1348, 1281, 1265, 1186, 1091, 1025, 928, 745, 692 cm\(^{-1}\); HRMS (FAB) Calcd for C\(_{15}\)H\(_{22}\)NOS [M+H]\(^{+}\): 264.1422, Found: 264.1425.

**1-[3-phenyl-(1-Phenylthio)propyl]-2-pyrrolidinone (5ca).** This compound was prepared from 1-(3-Phenyl-1-propenyl)-2-pyrrolidinone (112 mg, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a yellow oil (107.0 mg, 69%); \(^1^H\) NMR (400 MHz, CDCl\(_3\), ppm) δ 1.66−1.84 (m, 2H), 2.00−2.26 (m, 4H), 2.59−2.66 (m, 1H), 2.74−2.81 (m, 1H), 3.14−3.20 (m, 1H), 3.50−3.56 (m, 1H), 5.80 (dd, \(J = 6.0\) Hz, 9.2 Hz, 1H), 7.17−7.30 (m, 8H), 7.38−7.40 (d, \(J = 6.9\) Hz, 2H); \(^{13}\)C\({}^1\)H\) NMR (100 MHz, CDCl\(_3\), ppm) δ 17.6, 31.0, 33.0, 34.3, 41.4, 58.9, 126.1, 127.4, 128.2, 128.4, 128.8, 132.2, 132.6, 140.5, 174.9; IR (NaCl) 3500, 3061, 3024, 2942, 1685, 1585, 1501, 1489, 1411, 1359, 1283, 1265, 1082, 1027, 908, 838, 745, 693 cm\(^{-1}\); HRMS (FAB) Calcd for C\(_{19}\)H\(_{23}\)NOS [M+H]\(^{+}\): 312.1422, Found: 312.1417.

**1-[3,3-dimethyl-(1-Phenylthio)butyl]-2-pyrrolidinone (5da).** This compound was prepared from 1-(3,3-dimethyl-1-butenyl)-2-pyrrolidinone (83.6 mg, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a yellow oil (98.3 mg, 71%); \(^1^H\) NMR (400 MHz, CDCl\(_3\), ppm) δ 0.97 (s, 9H), 1.57 (dd, \(J = 3.2\) Hz, 14.7 Hz, 1H), 1.61−1.70 (m, 1H), 1.74−1.87 (m, 2H), 1.90−1.99 (m, 1H), 2.09−2.20 (m, 1H), 3.26−3.32 (m, 1H), 3.50−3.56 (m, 1H), 5.94 (dd, \(J = 3.2\) Hz, 9.6 Hz, 1H), 7.20−7.28 (m, 3H), 7.40−7.42 (m, 2H); \(^{13}\)C\({}^1\)H\) NMR (100 MHz, CDCl\(_3\), ppm) δ 17.7, 29.3, 31.3, 31.3, 41.2, 44.7, 56.3, 127.5, 128.6, 132.3, 132.6, 174.4; IR (NaCl) 3492, 3057, 2953, 2878, 1691, 1582, 1476, 1411, 1362, 1283, 1266, 1153, 1020, 933, 895, 843, 744, 692 cm\(^{-1}\); Anal. Calcd for C\(_{16}\)H\(_{23}\)NOS: C, 69.27; H, 8.36; N, 5.05. Found: C, 69.00; H, 8.38; N, 5.13.

**1-[2-Phenyl-(1-phenylthio)ethyl]-2-pyrrolidinone (5ea).** This compound was prepared from
1-styryl-2-pyrrolidinone (93.5 mg, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a yellow oil (70.9 mg, 48%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.65–1.81 (m, 2H), 1.95–2.12 (m, 2H), 2.99–3.05 (m, 1H), 3.16–3.29 (m, 2H), 3.53–3.59 (m, 1H), 6.05 (dd, \(J = 6.9\) Hz, \(J = 9.2\) Hz, 1H), 7.21–7.31 (m, 8H), 7.39–7.41 (m, 2H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.7, 30.9, 38.9, 41.7, 59.4, 126.9, 127.5, 128.4, 128.7, 128.8, 132.2, 132.6, 136.4; IR (NaCl) 3491, 3068, 3024, 2969, 1690, 1646, 1583, 1482, 1456, 1438, 1410, 1265, 1157, 1078, 1025, 993, 929, 926, 746, 697 cm\(^{-1}\); HRMS (FAB) Calcd for C\(_{18}\)H\(_{20}\)NOS [M+H]\(^+\): 298.1266, Found: 298.1261.

1-(1-Phenylthio)ethyl-2-caprolactam (5fa). This compound was prepared from 1-vinyl-2-caprolactam (69.6 mg, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a yellow oil (108.0 mg, 87%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.38–1.66 (m, 6H), 1.42 (d, \(J = 6.9\) Hz, 3H), 2.32–2.43 (m, 2H), 3.27–3.33 (m, 1H), 3.41–3.47 (m, 1H), 6.05 (q, \(J = 6.9\) Hz, 1H), 7.15–7.19 (m, 1H), 7.23–7.27 (m, 2H), 7.33–7.35 (m, 2H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 19.0, 23.1, 28.9, 29.7, 37.3, 42.5, 55.7, 126.4, 128.6, 130.0, 133.9, 175.5; IR (NaCl) 3512, 3050, 2929, 2854, 1640, 1477, 1438, 1412, 1366, 1310, 1183, 1147, 1094, 1059, 923, 888, 846, 743, 691 cm\(^{-1}\); Anal. Calcd for C\(_{14}\)H\(_{19}\)NOS: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.17; H, 7.87; N, 5.68.

1-{{[1-(p-Methylphenyl)thio]ethyl}-2-pyrrolidinone (5ab). This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 μL, 0.5 mmol) and 4-methylbenzenethiol (62.1 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a pale yellow oil (100.6 mg, 85%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.47 (d, \(J = 6.8\) Hz, 3H), 1.75–1.98 (m, 2H), 2.05–2.13 (m, 1H), 2.22–2.30 (m, 1H), 2.30 (s, 3H), 3.28–3.34 (m, 1H), 3.56–3.62 (m, 1H), 5.82 (q, \(J = 6.8\) Hz, 1H), 7.08 (d, \(J = 7.7\) Hz, 2H), 7.28–7.31 (m, 2H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.6, 18.7, 21.0, 31.1, 41.1, 54.7, 129.0, 129.5, 132.7, 137.7, 174.3; IR (NaCl) 3499, 2974, 2951, 1928, 2885, 1693, 1493, 1458, 1412, 1350, 1265, 1200, 1099, 1088,
1061, 957, 810, 691 cm⁻¹; HRMS (FAB) Calcd for C₁₃H₁₈NOS [M+H]⁺: 236.1109, Found: 236.1123.

1-[(1-(p-Methoxylphenyl)thio)ethyl]-2-pyrrolidinone (5ac). This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 µL, 0.5 mmol) and 4-methoxybenzenethiol (61.5 µL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a pale yellow oil (109.2 mg, 87%); ¹H NMR (400 MHz, CDCl₃, ppm) δ 1.45 (d, J = 6.9 Hz, 3H), 1.77–1.98 (m, 2H), 2.04–2.12 (m, 1H), 2.21–2.29 (m, 1H), 3.28–3.34 (m, 1H), 3.57–3.63 (m, 1H), 3.77 (s, 3H), 5.74 (q, J = 6.9 Hz, 1H), 6.79–6.83 (m, 2H), 7.33–7.37 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 17.5, 18.5, 31.0, 41.0, 55.0, 55.3, 114.2, 123.0, 135.3, 159.6, 174.2; IR (NaCl) 3483, 2974, 2889, 2835, 1686, 1593, 1493, 1458, 1416, 1354, 1285, 1246, 1200, 1177, 1103, 1057, 1030, 957, 930, 829, 745, 683 cm⁻¹; Anal. Calcd for C₁₃H₁₇NO₂S: C, 62.12; H, 6.82; N, 5.57. Found: C, 61.83; H, 7.00; N, 5.58.

1-[(1-(p-Fluorophenyl)thio)ethyl]-2-pyrrolidinone (5ad). This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 µL, 0.5 mmol) and 4-fluorobenzenethiol (53.3 µL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a pale yellow oil (97.1 mg, 81%); ¹H NMR (400 MHz, CDCl₃, ppm) δ 1.48 (d, J = 6.9 Hz, 3H), 1.76–2.00 (m, 2H), 2.05–2.13 (m, 1H), 2.23–2.32 (m, 1H), 3.29–3.35 (m, 1H), 3.54–3.60 (m, 1H), 5.82 (q, J = 6.9 Hz, 1H), 6.94–7.00 (m, 2H), 7.31–7.41 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 17.5, 18.6, 30.9, 41.0, 55.0, 114.2, 123.0, 135.3, 159.6, 174.2; IR (NaCl) 3483, 2974, 2889, 2835, 1686, 1593, 1493, 1458, 1416, 1354, 1285, 1246, 1200, 1177, 1103, 1057, 1030, 957, 930, 829, 745, 683 cm⁻¹; Anal. Calcd for C₁₂H₁₄FNOS: C, 62.12; H, 6.82; N, 5.85. Found: C, 60.03; H, 5.97; N, 5.84.

1-[(1-(p-Chlorophenyl)thio)ethyl]-2-pyrrolidinone (5ae). This compound was prepared from
1-vinyl-2-pyrrolidinone (53.2 μL, 0.5 mmol) and 4-chlorobenzenethiol (72.3 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a pale yellow oil (109.4 mg, 86%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.49 (d, \(J = 6.9\) Hz, 1H), 1.75–1.86 (m, 1H), 1.89–2.00 (m, 1H), 2.09–2.18 (m, 1H), 2.25–2.33 (m, 1H), 3.29–3.35 (m, 1H), 3.50–3.56 (m, 1H), 5.88 (q, \(J = 6.9\) Hz, 1H), 7.22–7.25 (m, 2H), 7.31–7.34 (m, 2H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.5, 18.7, 30.1, 41.0, 54.3, 128.8, 131.4, 133.2, 133.4, 174.3; IR (NaCl) 3479, 3078, 2978, 2882, 1686, 1574, 1477, 1458, 1412, 1354, 1266, 1204, 1096, 1011, 957, 822, 744, 687, 644 cm\(^{-1}\); Anal. Caled for C\(_{12}\)H\(_{14}\)ClNOS: C, 56.35; H, 5.52; N, 5.48. Found: C, 56.13; H, 5.43; N, 5.50.

1-\{1-(phenylmethylthio)ethyl\}-2-pyrrolidinone (5af). This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 μL, 0.5 mmol) and phenylmethylthiol (58.6 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a yellow oil (85.3 mg, 72%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.35 (d, \(J = 7.3\) Hz, 1H), 1.42–1.54 (m, 1H), 1.77–1.88 (m, 1H), 2.06–2.14 (m, 1H), 2.24–2.32 (m, 1H), 3.15–3.21 (m, 1H), 3.34–3.40 (m, 1H), 3.63 (d, \(J = 14.2\) Hz, 1H), 3.73 (d, \(J = 14.2\) Hz, 1H), 5.61 (q, \(J = 7.3\) Hz, 1H), 7.19–7.23 (m, 1H), 7.26–7.34 (m, 4H); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.1, 19.1, 31.3, 35.8, 40.8, 52.8, 126.7, 128.2, 128.4, 138.4, 174.5; IR (NaCl) 3503, 3028, 2974, 2928, 2882, 1686, 1597, 1493, 1454, 1416, 1350, 1312, 1269, 1196, 1061, 1026, 957, 918, 849, 768, 710, 640 cm\(^{-1}\); Anal. Caled for C\(_{13}\)H\(_{17}\)NOS: C, 66.34; H, 7.28; N, 5.95. Found: C, 65.95; H, 7.35; N, 6.01.

1-(1-Cyclohexylthio)ethyl-2-pyrrolidinone (5ag). This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 μL, 0.5 mmol) and cyclohexylthiol (61.2 μL, 0.5 mmol) following the general procedure of hydrothiolation of N-vinyl lactam. Isolated as a pale yellow oil (67.1 mg, 59%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.22–1.38 (m, 5H), 1.38 (d, \(J = 6.9\) Hz, 3H), 1.55–1.58 (m, 1H), 1.71–1.80 (m, 3H), 1.98–2.06 (m, 2H), 2.10–2.14 (m, 1H), 2.42 (t, \(J = 8.2\) Hz, 2H), 2.50–2.61 (m, 1H), 3.27–3.33 (m, 1H), 3.61–3.66 (m, 1H), 5.61 (q, \(J = 6.9\) Hz, 1H);
\[^{13}\text{C}^1\text{H}\] NMR (100 MHz, CDCl\textsubscript{3}, ppm) \(\delta\) 17.7, 19.5, 25.6, 25.7, 26.0, 31.5, 33.3, 34.0, 40.9, 42.9, 50.4, 174.2; IR (NaCl) 3510, 2974, 2928, 2851, 1686, 1497, 1447, 1412, 1265, 1196, 1061, 995, 953, 929, 888, 849, 748, 694 cm\(^{-1}\); HRMS (FAB) Calcd for C\(_{12}\)H\(_{22}\)NOS [M+H]\(^{+}\): 228.1422, Found: 228.1420.

### 3-6 References


7. For hydrothiolation to alkenes by using transition metal catalyst as protic catalyst, see: Weiwer, M.; Coulombel, L.; Duñach, E. Chem. Commun. 2006, 332.


10. Hydrothiolation product 3 ga is probably one stereoisomer with the thiol group in axial position due to stereoelectronic effect.

12. An alternative reaction mechanism, which proceeds via Palladium intermediate C’, is possible as shown below. Although the author tries to get some information about the reaction intermediates, the clear evidence could not be obtained. Palladium intermediate C immediately converts to C’ due to stabilization by intramolecular coordination of the ether oxygen atom. The author thinks this stabilization prevents to take place β-elimination of C. The subsequent protonation of palladium intermediate C’ with thiol provides the Markovnikov hydrothiolation product selectively.


Chapter 4

Palladium-Catalyzed Markovnikov-Selective Hydroselenation of N-Vinyl Lactams with Selenols Affording N,Se-Acetals

4-1 Introduction

A number of organoselenium compounds serve as synthetic intermediates, bioactive compounds, and functional materials. Among them, Se,Se-, O,Se- and N,Se-acetals are excellent synthetic intermediates as protecting groups for carbonyl and iminyl moieties, and especially, Se,Se-acetals have been used as practical umpolung species. Selenium-containing acetals are usually prepared by the nucleophilic addition of selenols to carbonyl and iminyl groups. The regioselective addition of selenols to enol ethers and enamines is a promising alternative method to synthesize acetal derivatives. This chapter describes a novel Markovnikov-selective hydroselenation of N-vinyl lactams with selenols as an alternative approach toward N,Se-acetals (Eq. 4-1).

\[
\begin{align*}
\text{N} & \text{O} & \text{N} & \text{R}^1 \\
\text{1} & \text{+} & \text{R}^2\text{SeH} & \text{2} \\
\text{self-promoted or Pd-catalyzed} & \text{hydroselenation} & \text{N} & \text{O} & \text{SeR}^2 & \text{R}^1 \\
\text{3} & \text{(4-1)}
\end{align*}
\]

To date, numerous regioselective addition reactions of heteroatom-containing compounds such as boron, silicon, phosphorus, and sulfur to C–C unsaturated bonds have been developed, e.g., ionic, radical and transition-metal-catalyzed additions. Although the addition of
selenols to alkynes has been established in acid- or base-assisted ionic reactions, radical reactions, and transition-metal-catalyzed reactions, the corresponding addition to alkenes has considerable limitations.\textsuperscript{4,5,6,7} In general, the radical addition of selenols to alkenes gives \textit{anti}-Markovnikov adducts regioselectively, and limited examples of Markovnikov-selective hydroselenations are known.\textsuperscript{5} Although Markovnikov adducts may be synthesized by transition-metal-catalyzed reactions, catalyst poisoning by selenols often hinders catalytic reactions.\textsuperscript{7,8} Moreover, most known Markovnikov-selective hydroselenation reactions require additives, such as Brønsted acids, to promote the addition. In chapter 3, similar limitation in transition-metal-catalyzed hydrothiolations is described to be overcome by using alkenes bearing alkoxy or amino group directly bonded to carbon–carbon double bond.\textsuperscript{9}

In this chapter, the author describes that selenols promote the hydroselenation of terminal \(N\)-vinyl lactams. This self-promoted hydroselenation requires no additives; therefore, this method exhibits high atom economy. Furthermore, the hydroselenation of internal \(N\)-vinyl lactams proceeds with excellent regioselectivity (Markovnikov-selective) in the presence of palladium catalysts such as \(\text{Pd(OAc)}_2\).

### 4-2 Markovnikov-Selective Hydroselenation of \(N\)-Vinyl Lactams

First, the addition of benzeneselenol to \(N\)-vinylpyrrolidone, as a manageable terminal \(N\)-vinyl lactam, was investigated without the addition of any additives (Table 4-1). When \(N\)-vinylpyrrolidone (1a) was reacted with benzeneselenol (2a) at 45 \(^\circ\)C for 20 h in THF, the Markovnikov-type adduct was obtained regioselectively in 93\% yield (entry 1). When \(\text{CH}_3\text{CN}\)
Chapter 4. Pd-Catalyzed Hydroselenation of N-Vinyl Lactams

and toluene were used as solvents, the yield of the desired hydroselenation product decreased (entries 2 and 3). Next, the influences of reaction time and temperature were examined (entries 4–7). The results clearly indicated that the optimal reaction conditions were 45 °C for 20 h in THF.

**Table 4-1. Optimization of Hydroselenation of Terminal N-VinylPyrrolidone**

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>time, h</th>
<th>temp., °C</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>20</td>
<td>45</td>
<td>93</td>
</tr>
<tr>
<td>2</td>
<td>CH₃CN</td>
<td>20</td>
<td>45</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>toluene</td>
<td>20</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>THF</td>
<td>6</td>
<td>45</td>
<td>73</td>
</tr>
<tr>
<td>5</td>
<td>THF</td>
<td>3</td>
<td>45</td>
<td>53</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>20</td>
<td>reflux</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>20</td>
<td>r.t.</td>
<td>67</td>
</tr>
</tbody>
</table>

*a* Reaction conditions: N-vinylpyrrolidone (1a, 0.5 mmol), benzeneselenol (2a, 0.5 mmol), and solvent (0.3 mL). *b* Determined by ¹H NMR analysis.

Next, the hydroselenation of internal N-vinyl lactams was conducted under similar reaction conditions (in the absence of additives); however, the corresponding hydroselenation product could not be obtained. Therefore, the Pd-catalyzed hydroselenation of internal N-vinyl lactams was examined (Scheme 4-1). When the Pd(OAc)₂ was used as the catalyst, the desired Markovnikov hydroselenation proceeded very efficiently. When a low-valent palladium catalyst Pd(PPh₃)₄ was employed, the hydroselenation product was obtained in only 12% yield. This result indicated that Pd(0) was not effective for the hydroselenation of internal N-vinyl lactams.
Thus, the hydroselenation was examined in the presence of Pd(II) catalysts, such as PdCl₂(PhCN)₂, PdCl₂(cod), and PdCl₂(PPh₃)₂. The tested Pd(II) complexes catalyzed the hydroselenation of internal N-vinyl lactam 1b to produce Markovnikov-adduct 3ba in moderate to good yields.

![Scheme 4-1](image)

**Scheme 4-1.** Optimization of Hydroselenation of Internal N-Vinyl Lactam

Next, the scope of viable N-vinyl lactams was examined under the optimized reaction conditions (Table 4-2). When terminal N-vinyl lactams 1a and 1c were used for the hydroselenation in the absence of a catalyst, the corresponding hydroselenation products 3aa and 3ca were obtained in 93% and 57% yields, respectively (entries 1 and 3). In the case of N-vinyl caprolactam 1c, the yield was dramatically improved by the addition of 5 mol% of Pd(OAc)₂ (entry 4). In the case of internal N-vinyl lactams 1b, 1d, 1e, and 1f, the desired hydroselenation was ineffective in the absence of a catalyst (entries 5, 7, 9, 11). However, the Pd(OAc)₂-catalyzed hydroselenation proceeded successfully and the corresponding hydroselenation products were obtained in good to excellent yields (entries 6, 8, 10, 12). These results indicated that a Pd(II) catalyst was essential for the efficient hydroselenation of internal N-vinyl lactams.
Table 4-2. Hydroselenation of Several N-Vinyl Lactams

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>yield, %&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>—</td>
<td>3aa</td>
<td>(93)</td>
</tr>
<tr>
<td>2</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>3aa</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>3ca</td>
<td>(57)</td>
</tr>
<tr>
<td>4</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>3ca</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>—</td>
<td>3ba</td>
<td>(13)</td>
</tr>
<tr>
<td>6</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>3ba</td>
<td>82</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>3da</td>
<td>(28)</td>
</tr>
<tr>
<td>8</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>3da</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>—</td>
<td>3ea</td>
<td>(7)</td>
</tr>
<tr>
<td>10</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>3ea</td>
<td>85</td>
</tr>
<tr>
<td>11</td>
<td>—</td>
<td>3fa</td>
<td>ND</td>
</tr>
<tr>
<td>12</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>3fa</td>
<td>50</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: N-vinyl lactam (1, 0.5 mmol), benzeneselenol (2a, 0.5 mmol), solvent (0.3 mL). <sup>b</sup> The yields in parentheses are determined by <sup>1</sup>H NMR analysis.

The hydroselenation of N-vinyl lactams using several selenols was performed; the results are summarized in Table 4-3. Recently, a convenient method was developed to prepare areneselenols by the reduction of the corresponding diaryl diselenides with diphenylphosphine oxide. In general, selenols are air-sensitive and foul-smelling, and therefore, in situ generation and direct use are desired. By using this method, the hydroselenation of N-vinylpyrrolidone...
with various areneselenols in the absence of a Pd catalyst was successfully accomplished, as shown in Table 4-3. Diaryl diselenides bearing either electron-donating group such as \( p \)-methoxy or -withdrawing groups such as \( m \)-methoxy, chloro, fluoro, and trifluoromethyl moieties, afforded the corresponding hydroselenation products \( 3ab, 3ac, 3ad, 3ae, 3af, 3ag, \) and \( 3ah \), respectively (entries 2–8). In the case of di(1-naphthyl) diselenide, the desired hydroselenation product \( 3ai \) was obtained in a moderate yield (entry 9). When dibenzyl diselenide as an aliphatic diselenide was used for the hydroselenation, the corresponding hydroselenation product \( 3aj \) was obtained in 16% yield (entry 10).

The Pd-catalyzed hydroselenation of \( N \)-vinylpyrrolidone \( 1a \) using diphenyl diselenides and diphenylphosphine oxide was carried out (Scheme 4-2). When di(1-naphthyl) diselenide \( 4i \) and dibenzyl diselenide \( 4j \) were employed, the yields of the desired hydroselenation products, \( 3ai \) and \( 3aj \), were dramatically improved. The results clearly indicated that the palladium diacetate efficiently catalyzed hydroselenation even in the presence of diselenides and diphenylphosphine oxide, serving as a convenient tool to synthesize \( N,Se \)-acetal derivatives.

\[
\text{Scheme 4-2. Pd-Catalyzed Hydroselenation of Terminal } N\text{-VinylPyrrolidone Using Diselenides}
\]
Table 4-3. Self-Promoted Hydroselenation of N-Vinylpyrrolidone Using Several Diselenides

<table>
<thead>
<tr>
<th>entry</th>
<th>RSH, 4</th>
<th>product</th>
<th>3</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4a</td>
<td>3aa</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4b</td>
<td>3ab</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4c</td>
<td>3ac</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4d</td>
<td>3ad</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>4e</td>
<td>3ae</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4f</td>
<td>3af</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>4g</td>
<td>3ag</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4h</td>
<td>3ah</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>4i</td>
<td>3ai</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>4j</td>
<td>3aj</td>
<td>16</td>
<td></td>
</tr>
</tbody>
</table>

\( \text{Reaction conditions: } N\text{-vinylpyrrolidone (1a, 0.25 mmol), diselenide (4, 0.25 mmol), } \text{Ph}_3\text{P(O)H (0.3 mmol), THF (0.15 mL), 45 °C, 20 h.} \)
Finally, the hydroselenation of $N$-vinyl lactam was evaluated in the large scale reaction using 0.39 g of the $N$-vinyl pyrrolidone. The reaction was completed in 48 h at 45 °C and 92% of the isolated yield of the hydroselenation product was obtained selectively (Scheme 4-3). These $N,Se$-acetal derivatives can be transformed into the corresponding aldehydes under the radical reaction.\(^2f\)

![Scheme 4-3. Hydroselenation of $N$-Vinyl Pyrrolidone with Benzeneselenol in the Large Scale](image)

A plausible reaction pathway for the present hydroselenation of $N$-vinyl lactams is shown in Scheme 4-4. In the absence of the Pd-catalyst, firstly, the terminal $N$-vinyl lactam is easily protonated by selenol. Then, the generated cation of terminal $N$-vinyl lactam is stabilized by electron donation from nitrogen atom. Finally, selenol attacks the cation of terminal $N$-vinyl lactam to give the Markovnikov-type hydroselenation product regioselectively. In the case of the Pd-catalyzed hydroselenation, the Pd(OAc)$_2$ catalyst initially reacts with selenol to form Pd selenide complex A. Then, $N$-vinyl lactam coordinates to Pd selenide complex A, providing Pd selenide-alkene complex B, where heteroatoms might coordinate to palladium, thereby stabilizing complex B. Subsequent selenopalladation takes place regioselectively to generate palladium intermediate C. Protonation of palladium intermediate C with the selenol provides the Markovnikov hydroselenation product regioselectively, with regeneration of Pd selenide complex A.
**Terminal N-Vinyl Lactam (in the Absence of Palladium Catalyst)**

![Scheme for terminal N-vinyl lactam hydroselenation](image)

**Internal N-Vinyl Lactam (in the Presence of Palladium Catalyst)**

![Scheme for internal N-vinyl lactam hydroselenation](image)

**Scheme 4-4. A Possible Reaction Pathway for the Hydroselenation of N-Vinyl Lactams**

### 4-3 Conclusion

In conclusion, the highly selective hydroselenation of N-vinyl lactams to produce N,Se-acetal derivatives was developed. The hydroselenation of terminal N-vinyl lactams proceeded smoothly to give Markovnikov-type adducts selectively. Palladium(II) diacetate catalyzed the hydroselenation of internal N-vinyl lactams, despite the inefficiency of the self-promoted hydroselenation. Furthermore, Markovnikov-selective hydroselenation was demonstrated using a series of areneselenols, which were generated in situ from the corresponding diselenides and diphenylphosphine oxide.
4-4 Experimental Section

General Comment

Unless otherwise stated, all starting materials and catalysts were purchased from commercial sources and used without further purification. The following substrates were prepared by using dehydrative condensation of pyrrolidinone and the corresponding aldehydes with p-TsOH: \((E)-1-(1\text{-pentenyl})-2\text{-pyrrolidinone},\) \((E)-1-(3\text{-phenyl-1-propenyl})-2\text{-pyrrolidinone},\) \((E)-1-(3,3\text{-dimethyl-1-butenyl})-2\text{-pyrrolidinone},\) \((E)-1\text{-styryl-2-pyrrolidinone}.\)\(^{11}\) The all diorganyl diselenides were synthesized according to the literature.\(^{12}\) THF as solvent was used after distillation from CaH\(_2\). \(^{1}H\) NMR spectra (400 MHz), \(^{13}C\) NMR spectra (100 MHz) were taken in CDCl\(_3\) with Me\(_4\)Si as an internal standard. \(^{19}F\) NMR spectra (373 MHz) were taken in CDCl\(_3\) with CFCl\(_3\) as an external standard. \(^{77}Se\) NMR spectra (75 MHz) were taken in CDCl\(_3\) with Me\(_2\)Se as an external standard. Chemical shifts in \(^1H\) NMR were measured relative to CDCl\(_3\) and converted to \(\delta\) (Me\(_4\)Si) values by using \(\delta\) (CDCl\(_3\)) 7.26 ppm. Chemical shifts in \(^{13}C\) NMR were measured relative to CDCl\(_3\) and converted to \(\delta\) (Me\(_4\)Si) values by using \(\delta\) (CDCl\(_3\)) 77.00 ppm. IR spectra were reported in wavenumbers (cm\(^{-1}\)). ESI and EI mass spectra were obtained by employing double focusing mass spectrometers in the Nara Institute of Science and Technology (NAIST).

General Procedure for Self-Promoted Hydroselenation of N-Vinyl Lactams.

In a two-necked 10 mL flask with a magnetic stirring bar under N\(_2\) atmosphere were placed freshly distilled THF (0.3 mL), N-vinyl lactam (0.5 mmol) and selenol (0.5 mmol). The reaction was conducted at 45 °C for 20 h, and then the resulting solution was concentrated in vacuo. The product was purified by preparative TLC (silica gel, eluent: hexane; AcOEt = 2:1) to
afford the hydroselenation product.

**General Procedure for Pd-Catalyzed Hydroselenation of N-Vinyl Lactams.**

In a two-necked 10 mL flask with a magnetic stirring bar under N\(_2\) atmosphere were placed Pd(OAc)\(_2\) (5.6 mg, 0.025 mmol), freshly distilled THF (0.3 mL), N-vinyl lactam (0.5 mmol), and selenol (0.5 mmol), in that order. The reaction was conducted at 45 °C for 20 h, and then the resulting solution was filtered through Celite with ethyl acetate as an eluent. Concentration in vacuo, and purification by preparative TLC (silica gel, eluent: hexane; AcOEt = 2:1) provided the hydroselenation product.

**General Procedure for Pd-Catalyzed Hydroselenation of N-Vinyl Lactam by Using Selenols Generated from Diselenides and Diphenylphosphine Oxide.**

In a two-necked 10 mL flask with a magnetic stirring bar under N\(_2\) atmosphere were placed diphenylphosphine oxide (60.7 mg, 0.3 mmol), freshly distilled THF (0.15 mL), diselenide (0.25 mmol), and N-vinyl lactam (0.25 mmol). The reaction was conducted at 45 °C for 20 h, and then the resulting solution was filtered through Celite with ethyl acetate as an eluent. Concentration in vacuo, and purification by preparative TLC (silica gel, eluent: hexane; AcOEt = 2:1) provided the hydroselenation product.

**1-[(1-Phenylseleno)ethyl]-2-pyrrolidinone (3aa).** This compound was prepared from 1-vinyl-2-pyrrolidinone (53.2 μL, 0.5 mmol) and benzeneselenol (53.1 μL, 0.5 mmol) following the general procedure of Pd-catalyzed hydroselenation of N-vinyl lactam. Isolated as a pale yellow oil (128.9 mg, 96%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.57 (d, \(J = 6.9\) Hz, 3H), 1.69–1.80 (m, 1H), 1.85–1.94 (m, 1H), 1.96–2.05 (m, 1H), 2.18–2.27 (m, 1H), 3.29–3.35 (m, 1H), 3.48–3.54 (m, 1H), 6.04 (q, \(J = 6.9\) Hz, 1H), 7.22–7.30 (m, 3H), 7.54–7.56 (m, 2H); \(^{13}\)C\({^1\)H} NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.3, 19.8, 30.8, 42.0, 49.4, 127.9, 128.6 (overlap), - 61 -
Chapter 4. Pd-Catalyzed Hydroselenation of N-Vinyl Lactams

135.3, 173.9; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 409.7; IR (NaCl) 3510, 3055, 2976, 2879, 1696, 1576, 1477, 1410, 1352, 1283, 1184, 1021, 999, 952, 845, 740, 692 cm$^{-1}$; HRMS (EI) Calcd for C$_{12}$H$_{15}$NOSe [M]+: 269.0319, Found: 269.0324.

1-[(1-Phenylseleno)pentyl]-2-pyrrolidinone (3ba). This compound was prepared from 1-(1-pentenyl)-2-pyrrolidinone (76.6 mg, 0.5 mmol) and benzenethiol (51.1 μL, 0.5 mmol) following the general procedure of Pd-catalyzed hydroselenation of N-vinyl lactam. Isolated as a yellow oil (127.6 mg, 82%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 0.88 (t, $J = 6.9$ Hz, 3H), 1.24–1.37 (m, 4H), 1.58–1.75 (m, 1H), 1.76–2.02 (m, 4H), 2.18–2.26 (m, 1H), 3.20–3.26 (m, 1H), 3.46–3.52 (m, 1H), 5.91 (dd, $J = 6.3$ Hz, 9.1 Hz, 1H), 7.21–7.27 (m, 3H), 7.53–7.55 (m, 2H); $^{13}$C{^1}$H}$ NMR (100 MHz, CDCl$_3$, ppm) δ 13.7, 17.4, 21.8, 29.0, 30.8, 33.2, 42.1, 54.5, 127.8, 128.6 (overlap), 135.3, 174.5; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 391.4; IR (NaCl) 3472, 3061, 2956, 2930, 2871, 1685, 1577, 1476, 1410, 1363, 1265, 1160, 1112, 1072, 1022, 923, 843, 741, 692 cm$^{-1}$; HRMS (ESI) Calcd for C$_{15}$H$_{21}$NONaSe [M+Na]$^+$: 334.0686, Found: 334.0681.

1-(1-Phenylseleno)ethyl-2-caprolactam (3ca). This compound was prepared from 1-vinyl-2-caprolactam (69.6 mg, 0.5 mmol) and benzeneselenol (53.1 μL, 0.5 mmol) following the general procedure of Pd-catalyzed hydroselenation of N-vinyl lactam. Isolated as a pale yellow oil (140.7 mg, 95%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.42–1.71 (m, 6H), 1.52 (d, $J = 6.9$ Hz, 3H), 2.26–2.41 (m, 2H), 3.26–3.28 (m, 1H), 3.42–3.48 (m, 1H), 6.62 (q, $J = 6.9$ Hz, 1H), 7.22–7.26 (m, 3H), 7.49–7.53 (m, 2H); $^{13}$C{^1}$H}$ NMR (100 MHz, CDCl$_3$, ppm) δ 20.0, 23.1, 28.9, 29.7, 37.2, 43.9, 52.4, 127.4, 128.8, 128.9, 134.1, 175.3; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 408.3; IR (NaCl) 3515, 3049, 2928, 2855, 1642, 1476, 1437, 1410, 1363, 1308, 1259, 1226, 1193, 1144, 1082, 1022, 976, 928, 885, 846, 739, 691 cm$^{-1}$; HRMS (ESI) Calcd for C$_{14}$H$_{19}$NONaSe [M+Na]$^+$: 320.0530, Found: 320.0534.

1-[3-Phenyl-(1-phenylseleno)propyl]-2-pyrrolidinone (3da). This compound was prepared from
1-(3-Phenyl-1-propenyl)-2-pyrrolidinone (112 mg, 0.5 mmol) and benzeneselenol (53.1 μL, 0.5 mmol) following the general procedure of Pd-catalyzed hydroselenation of N-vinyl lactam. Isolated as a yellow oil (143.3 mg, 80%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.60–1.83 (m, 2H), 1.93–2.04 (m, 1H), 2.13–2.23 (m, 3H), 2.56–2.63 (m, 1H), 2.68–2.76 (m, 1H), 3.14–3.20 (m, 1H), 3.44–3.50 (m, 1H), 5.97 (dd, \(J = 6.3\) Hz, 8.6 Hz, 1H), 7.15–7.29 (m, 8H), 7.54–7.55 (m, 2H); \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl\(_3\), ppm) δ 17.4, 31.0, 33.7, 35.3, 42.4, 54.5, 126.1, 127.7, 128.0, 128.3, 128.4, 135.5, 140.4, 174.7; \(^{77}\)Se NMR (75 MHz, CDCl\(_3\), ppm) δ 394.7; IR (NaCl) 3500, 3062, 3018, 2938, 2878, 1684, 1602, 1496, 1490, 1476, 1437, 1409, 1361, 1283, 1265, 1222, 1071, 1022, 996, 907, 843, 741, 700 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{19}\)H\(_{21}\)NONaSe \([M+Na]^+\): 382.0686, Found: 382.0684.

1-[3,3-Dimethyl-(1-Phenylseleno)butyl]-2-pyrrolidinone (3ea). This compound was prepared from 1-(3,3-dimethyl-1-butene)-2-pyrrolidinone (83.6 mg, 0.5 mmol) and benzeneselenol (53.1 μL, 0.5 mmol) following the general procedure of Pd-catalyzed hydroselenation of N-vinyl lactam. Isolated as a yellow oil (138.2 mg, 85%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 0.93 (s, 9H), 1.54–1.65 (m, 2H), 1.77–1.94 (m, 3H), 2.08–2.16 (m, 1H), 3.29–3.35 (m, 1H), 3.45–3.51 (m, 1H), 6.19 (dd, \(J = 2.7\) Hz, 10.9 Hz, 1H), 7.22–7.30 (m, 3H), 7.54–7.56 (m, 2H); \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl\(_3\), ppm) δ 17.5, 29.2, 31.1, 31.8, 42.2, 45.4, 52.1, 128.0, 128.2, 128.7, 135.7, 174.3; \(^{77}\)Se NMR (75 MHz, CDCl\(_3\), ppm) δ 405.3; IR (NaCl) 3512, 3062, 3018, 2938, 2878, 1684, 1602, 1496, 1490, 1476, 1437, 1409, 1361, 1283, 1265, 1222, 1071, 1022, 996, 907, 843, 739, 691 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{16}\)H\(_{23}\)NONaSe \([M+Na]^+\): 348.0843, Found: 348.0848.

1-[2-Phenyl-(1-phenylseleno)ethyl]-2-pyrrolidinone (3fa). This compound was prepared from 1-styryl-2-pyrrolidinone (93.5 mg, 0.5 mmol) and benzeneselenol (53.1 μL, 0.5 mmol) following the general procedure of Pd-catalyzed hydroselenation of N-vinyl lactam. Isolated as a yellow oil (86.1 mg, 50%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.59–1.81 (m, 2H), 1.86–1.94 (m, 1H), 2.02–2.10 (m, 1H), 3.10–3.16 (m, 1H), 3.20–3.30 (m, 2H), 3.47–3.53 (m, 1H), 6.22 (dd, \(J = 6.8\) Hz, 10.9 Hz, 1H), 7.15–7.29 (m, 8H), 7.54–7.55 (m, 2H).
1-\{1-(p-Methoxyphenyl)seleno\}ethyl-2-pyrrolidinone (3ab). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(4-methoxyphenyl) diselenide (93.0 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (58.8 mg, 79%); 1H NMR (400 MHz, CDCl₃, ppm) δ 1.55 (d, J = 7.3 Hz, 3H), 1.74–1.85 (m, 1H), 1.88–2.07 (m, 2H), 2.20–2.28 (m, 1H), 3.30–3.36 (m, 1H), 3.51–3.57 (m, 1H), 3.78 (s, 3H), 5.95 (q, J = 7.3 Hz, 1H), 6.77–6.81 (m, 2H), 7.46–7.49 (m, 2H); 13C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 17.5, 19.8, 31.1, 42.1, 49.7, 55.2, 114.4, 118.2, 137.7, 159.9, 174.1; 77Se NMR (75 MHz, CDCl₃, ppm) δ 394.6; IR (NaCl) 3466, 3058, 2980, 2848, 1685, 1590, 1570, 1461, 1440, 1377, 1286, 1244, 1181, 1130, 1095, 1022, 998, 803, 753, 730, 698 cm⁻¹; HRMS (ESI) Calcd for C₁₃H₁₇NO₂NaSe [M+Na]^+: 322.0322, Found: 322.0323.

1-\{1-(m-Methoxyphenyl)seleno\}ethyl-2-pyrrolidinone (3ac). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(3-methoxyphenyl) diselenide (93.1 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (63.6 mg, 85%); 1H NMR (400 MHz, CDCl₃, ppm) δ 1.59 (d, J = 7.3 Hz, 3H), 1.72–1.83 (m, 1H), 1.87–1.98 (m, 1H), 2.02–2.11 (m, 1H), 2.22–2.31 (m, 1H), 3.31–3.37 (m, 1H), 3.49–3.55 (m, 1H), 3.79 (s, 3H), 6.08 (q, J = 7.3 Hz, 1H), 6.80–6.82 (m, 1H), 7.11–7.18 (m, 3H); 13C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 17.5, 20.0, 31.1, 42.2, 49.5, 55.3, 114.1, 119.9, 127.0, 129.1, 129.5, 159.5, 174.1; 77Se NMR (75 MHz, CDCl₃, ppm) δ 414.0; IR
(NaCl) 3490, 3062, 2963, 2828, 1685, 1586, 1573, 1476, 1412, 1353, 1312, 1283, 1245, 1228, 1184, 1095, 1037, 991, 953, 840, 780, 689 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{13}\)H\(_{17}\)NO\(_2\)NaSe [M+Na]\(^+\): 322.0322, Found: 322.0326.

1-[(1-(p-Chlorophenyl)seleno)ethyl]-2-pyrrolidinone (3ad). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(4-chlorophenyl) diselenide (96.6 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of \(N\)-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (53.0 mg, 70%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.58 (d, \(J = 6.8\) Hz, 3H), 1.72–1.86 (m, 1H), 1.90–2.00 (m, 1H), 2.03–2.12 (m, 1H), 2.23–2.32 (m, 1H), 3.32–3.38 (m, 1H), 3.47–3.53 (m, 1H), 6.05 (q, \(J = 6.9\) Hz, 1H), 7.21–7.23 (m, 2H), 7.47–7.49 (m, 2H); \(^{13}\)C\(_{\{^1\}H}\) NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.5, 19.9, 31.0, 42.1, 49.9, 126.3, 129.0, 134.3, 136.6, 174.2; \(^{77}\)Se NMR (75 MHz, CDCl\(_3\), ppm) \(\delta\) 406.0; IR (NaCl) 3485, 3055, 2976, 2880, 1693, 1472, 1410, 1352, 1267, 1185, 1089, 1053, 1011, 953, 816, 730, 743 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{12}\)H\(_{14}\)NONaClSe [M+Na]\(^+\): 325.9827, Found: 325.9823.

1-[(1-(p-Fluorophenyl)seleno)ethyl]-2-pyrrolidinone (3ae). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(4-fluorophenyl) diselenide (87.0 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of \(N\)-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (53.0 mg, 70%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 1.57 (d, \(J = 6.8\) Hz, 3H), 1.72–2.10 (m, 3H), 2.22–2.30 (m, 1H), 3.31–3.37 (m, 1H), 3.49–3.55 (m, 1H), 6.01 (q, \(J = 6.8\) Hz, 1H), 6.92–6.98 (m, 2H), 7.51–7.55 (m, 2H); \(^{13}\)C\(_{\{^1\}H}\) NMR (100 MHz, CDCl\(_3\), ppm) \(\delta\) 17.5, 19.9, 31.0, 42.1, 49.9, 126.3, 129.0, 134.3, 136.6, 174.2; \(^{19}\)F NMR (373 MHz, CDCl\(_3\), ppm) \(\delta\) -112.8; \(^{77}\)Se NMR (75 MHz, CDCl\(_3\), ppm) \(\delta\) 406.0; IR (NaCl) 3485, 3055, 2976, 2880, 1693, 1472, 1410, 1352, 1267, 1185, 1089, 1053, 1011, 953, 816, 730, 743 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{12}\)H\(_{14}\)NOFNaSe [M+Na]\(^+\): 325.9827, Found: 325.9823.
I-\{(1-(m-Fluorophenyl)seleno)ethyl\}-2-pyrrolidinone (3af). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(3-fluorophenyl) diselenide (87.1 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselelenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (50.8 mg, 71%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.59 (d, $J$ = 6.8 Hz, 3H), 1.78–1.89 (m, 1H), 1.91–2.02 (m, 1H), 2.06–2.15 (m, 1H), 2.24–2.33 (m, 1H), 3.30–3.39 (m, 1H), 3.50–3.56 (m, 1H), 6.07 (q, $J$ = 6.8 Hz, 1H), 6.96–7.01 (m, 1H), 7.20–7.35 (m, 3H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 17.5, 20.0, 31.1, 42.2, 50.1, 115.1 (d, $J_{C-F}$ = 21.0 Hz), 121.9 (d, $J_{C-F}$ = 21.0 Hz), 129.7 (d, $J_{C-F}$ = 6.7 Hz), 130.1 (d, $J_{C-F}$ = 7.6 Hz), 130.9 (d, $J_{C-F}$ = 2.9 Hz), 162.2 (d, $J_{C-F}$ = 250 Hz), 174.2; $^{19}$F NMR (373 MHz, CDCl$_3$, ppm) δ -111.9; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 418.2; IR (NaCl) 3491, 3068, 2977, 2881, 1693, 1591, 1471, 1411, 1352, 1284, 1263, 1210, 1185, 1053, 1000, 954, 858, 782, 743, 682 cm$^{-1}$; HRMS (ESI) Calcd for C$_{12}$H$_{14}$NOFNaSe $[M+Na]^+$: 310.0122, Found: 310.0125.

I-\{(1-(p-Trifluoromethylphenyl)seleno)ethyl\}-2-pyrrolidinone (3ag). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(4-trifluoromethylphenyl) diselenide (112.0 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselelenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (82.2 mg, 98%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.62 (d, $J$ = 7.3 Hz, 3H), 1.74–1.85 (m, 1H), 1.91–2.02 (m, 1H), 2.05–2.13 (m, 1H), 2.26–2.34 (m, 1H), 3.34–3.40 (m, 1H), 3.46–3.52 (m, 1H), 6.17 (q, $J$ = 7.3 Hz, 1H), 7.48–7.50 (m, 2H), 7.64–7.66 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 17.5, 20.1, 31.1, 42.3, 49.8, 124.0 (q, $J_{C-F}$ = 272.6 Hz), 125.6 (q, $J_{C-F}$ = 3.8 Hz), 129.7 (d, $J_{C-F}$ = 33.4 Hz), 133.6, 134.3, 174.3; $^{19}$F NMR (373 MHz, CDCl$_3$, ppm) δ -62.6; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 416.1; IR (NaCl) 3491, 3068, 2929, 2882, 1672, 1601, 1490, 1459, 1399, 1324, 1269, 1163, 1110, 1078, 1057,
1014, 954, 831, 775, 744 cm$^{-1}$; HRMS (ESI) Calcd for C$_{13}$H$_{14}$NOF$_3$NaSe [M+Na]$^+$: 360.0090, Found: 360.0091.

1-{$\text{[1-(m-Trifluoromethylphenyl)seleno]ethyl}$}-2-pyrrolidinone (3ah). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.5 mmol) and bis(3-trifluoromethylphenyl) diselenide (112.0 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (66.5 mg, 79%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.60 (d, $J$ = 7.3 Hz, 3H), 1.76–1.87 (m, 1H), 1.92–2.09 (m, 2H), 2.22–2.31 (m, 1H), 3.33–3.39 (m, 1H), 3.51–3.57 (m, 1H), 6.09 (q, $J$ = 7.3 Hz, 1H), 7.37–7.41 (m, 1H), 7.53–7.55 (m, 1H), 7.76–7.81 (m, 2H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 17.3, 19.9, 30.9, 42.0, 50.4, 123.6 (q, $J_{C-F} = 271.8$ Hz), 124.7 (q, $J_{C-F} = 3.8$ Hz), 129.2, 131.0 (q, $J_{C-F} = 33.4$ Hz), 131.8 (q, $J_{C-F} = 2.9$ Hz), 138.9, 174.1; $^{19}$F NMR (373 MHz, CDCl$_3$, ppm) δ -62.6; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 417.0; IR (NaCl) 3490, 3062, 2988, 2889, 1694, 1495, 1458, 1414, 1322, 1271, 1165, 1126, 1098, 1069, 993, 895, 798, 695 cm$^{-1}$; HRMS (ESI) Calcd for C$_{13}$H$_{14}$NOF$_3$NaSe [M+Na]$^+$: 360.0090, Found: 360.0091.

1-{$\text{[1-(1-Naphthyl)seleno]ethyl}$}-2-pyrrolidinone (3ai). This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(1-naphthyl) diselenide (103.1 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (23.8 mg, 30%); $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.49–1.64 (m, 1H), 1.61 (d, $J$ = 6.8 Hz, 3H), 1.75–1.86 (m, 2H), 2.07–2.16 (m, 1H), 3.25–3.31 (m, 1H), 3.43–3.49 (m, 1H), 6.03 (q, $J$ = 6.8 Hz, 1H), 7.35–7.39 (m, 1H), 7.47–7.59 (m, 2H), 7.80–7.90 (m, 3H), 8.49–8.51 (m, 1H); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, ppm) δ 17.3, 20.2, 30.8, 42.4, 50.4, 125.6, 126.1, 126.7, 127.9, 128.0, 128.6, 129.5, 133.8, 135.2, 135.9, 173.9; $^{77}$Se NMR (75 MHz, CDCl$_3$, ppm) δ 339.8; IR (NaCl) 3473, 3051, 2964, 2881, 1681, 1587, 1557, 1500, 1456, 1411, 1374, 1313, 1269,
1182, 1099, 1020, 957, 798, 771 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{16}\)H\(_{17}\)NONaSe [M+Na]\(^+\): 342.0373, Found: 342.0380.

**1-\{(Phenylmethylseleno)ethyl\}-2-pyrrolidinone (3aj).** This compound was prepared from 1-vinyl-2-pyrrolidinone (26.6 μL, 0.25 mmol) and bis(phenylmethyl) diselenide (85.0 mg, 0.25 mmol) and diphenylphosphine oxide (60.7 mg, 0.3 mmol) following the general procedure of hydroselenation of N-vinyl lactam by using selenols generated from diselenides. Isolated as a pale yellow oil (11.1 mg, 16%); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 1.47 (d, \(J = 7.3\) Hz, 3H), 1.56–1.69 (m, 1H), 1.85–1.95 (m, 1H), 2.16–2.24 (m, 1H), 2.29–2.37 (m, 1H), 3.22–3.28 (m, 1H), 3.38–3.44 (m, 1H), 3.75 (d, \(J = 12.7\) Hz, 1H), 3.87 (d, \(J = 12.7\) Hz, 1H), 5.92 (q, \(J = 7.3\) Hz, 1H), 7.17–7.21 (m, 1H), 7.25–7.34 (m, 4H); \(^{13}\)C{\(^1\)H} NMR (100 MHz, CDCl\(_3\), ppm) δ 17.3, 20.3, 28.0, 31.5, 42.0, 47.0, 125.5, 126.6, 128.4, 128.7, 174.4; \(^{77}\)Se NMR (75 MHz, CDCl\(_3\), ppm) δ 352.9; IR (NaCl) 3478, 3024, 2975, 2926, 1685, 1494, 1452, 1412, 1350, 1313, 1268, 1178, 1096, 1054, 1029, 956, 759, 730 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{13}\)H\(_{17}\)NONaSe [M+Na]\(^+\): 306.0373, Found: 306.0375.

### 4-5 References


Chapter 5

Gold-Catalyzed *anti*-Markovnikov Selective Hydrothiolation of Inactivated Alkenes

5-1 Introduction

Transition-metal-catalyzed addition reactions of heteroatoms are very attractive methods for selective synthesis of heteroatom-functionalized molecules.\(^1\) Organosulfur compounds as the heteroatom-functionalized molecules have demonstrated many utilities in applications such as synthetic intermediates, bioactive compounds, and functional materials.\(^2\) Although the transition-metal-catalyzed reactions have been generally thought incompatible with the organosulfur compounds due to the feature of catalyst poison of organosulfur compounds,\(^3\) a lot of transition-metal-catalyzed additions of organosulfur compounds to alkynes and allenes were reported in the last decade.\(^4,5\) However, transition-metal-catalyzed reactions of alkenes with organosulfur compounds have some difficulty to occur due to lower coordination ability of alkenes compared with that of alkynes. Indeed, very limited examples of the transition-metal-catalyzed addition of organosulfur compounds to alkenes have been reported in hitherto.\(^6\) Chapter 3 describes Pd-catalyzed hydrothiolation of directly functionalized alkenes, such as vinyl ethers and vinyl lactams;\(^7\) however, the transition-metal-catalyzed hydrothiolation of inactivated alkenes remains unsolved challenge.

Thus, the author has focused attention on gold catalyst as transition metal catalyst to overcome the limitation of alkenes. Gold catalyst is very attractive for the unique affinity to the
unsaturated compounds. Recently, many gold-catalyzed reactions have been investigated and become one of the most useful reactions for catalytic transformations. This chapter deals with a gold-catalyzed addition reaction of thiols to inactivated alkenes, which proceeds with excellent regioselectivity to afford the corresponding anti-Markovnikov adducts in good yield (Eq. 5-1).

\[
\begin{align*}
\text{R}^1\text{C} &= \text{R}^2\text{SH} \\
&\quad \text{PPh}_3\text{AuNTf}_2 (2 \text{ mol%}) \\
\hline
1 & \quad 2 & \rightarrow \quad \text{R}^1\text{C} = \text{R}^2\text{S}^2 \\
\end{align*}
\]

(5-1)

5-2 Gold-Catalyzed Hydrothiolation of Inactivated Alkenes

The examination of the catalyst for the anti-Markovnikov selective hydrothiolation of inactivated alkenes was conducted (Table 5-1). When the reaction of 1-decene (1a) and benzenethiol (2a) in the presence of 2 mol% of PPh\textsubscript{3}AuNTf\textsubscript{2}, as the high reactive gold catalyst, was conducted at 45 °C for 17 h, the anti-Markovnikov-type adduct was obtained in 65% yield without formation of a Markovnikov-type adduct (entry 1). When the amount of PPh\textsubscript{3}AuNTf\textsubscript{2} decreased to 1 mol%, the anti-Markovnikov hydrothiolation proceeded efficiently (entry 2). In the presence of 5 mol% or absence of the PPh\textsubscript{3}AuNTf\textsubscript{2} catalyst, the desired hydrothiolation product was formed inefficiently (entries 3 and 4). Next, hydrothiolation of 1-decene using other gold catalyst was performed. (Me\textsubscript{2}S)AuCl as the gold catalyst also promoted the desired hydrothiolation, and afforded the product in good yield (entry 5). PPh\textsubscript{3}AuCl and AuCl\textsubscript{3} were ineffective for the reaction, and the product yield was unsatisfactory (entries 6 and 7). The author then used Bi(OTf)\textsubscript{3} as the Lewis acid catalyst, expecting good results, as both Bi and Au are located in period 6 of the periodic table and may have identical reactivities. Contrary to expectation, Bi(OTf)\textsubscript{3} did not catalyze hydrothiolation at all, and the desired product was not obtained (entry 8). Furthermore, when Pd and Ru catalysts were used, the hydrothiolation did not
proceed at all (entries 9–12). Moreover, when 2 mol% of CuCl$_2$ was used as an oxidant with PPh$_3$AuNTf$_2$ (to clarify whether higher valent Au species exhibits catalytic activity toward the hydrothiolation of alkene), the hydrothiolation product was not obtained (entry 13).

**Table 5-1. Examination of Catalyst for Hydrothiolation of 1-Decene**

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>yield, %$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PPh$_3$AuNTf$_2$ (2 mol%)</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>PPh$_3$AuNTf$_2$ (1 mol%)</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>PPh$_3$AuNTf$_2$ (5 mol%)</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>none</td>
<td>trace</td>
</tr>
<tr>
<td>5</td>
<td>(Me$_2$S)AuCl (1 mol%)</td>
<td>66</td>
</tr>
<tr>
<td>6</td>
<td>PPh$_3$AuCl (1 mol%)</td>
<td>trace</td>
</tr>
<tr>
<td>7</td>
<td>AuCl$_3$ (1 mol%)</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>Bi(OTf)$_3$ (1 mol%)</td>
<td>ND</td>
</tr>
<tr>
<td>9</td>
<td>Pd(OAc)$_2$ (5 mol%)</td>
<td>ND</td>
</tr>
<tr>
<td>10</td>
<td>PdCl$_2$(PhCN)$_2$ (5 mol%)</td>
<td>ND</td>
</tr>
<tr>
<td>11</td>
<td>Ru(NH$_3$)$_3$Cl$_3$ (5 mol%)</td>
<td>ND</td>
</tr>
<tr>
<td>12</td>
<td>RuHCl(CO)(PPh)$_3$ (5 mol%)</td>
<td>ND</td>
</tr>
<tr>
<td>13</td>
<td>PPh$_3$AuNTf$_2$ (2 mol%) + CuCl$_2$ (2 mol%)</td>
<td>ND</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 1-decene (1a, 0.5 mmol), benzenethiol (2a, 0.5 mmol), THF (0.3 mmol). $^b$ Determined by $^1$H NMR analysis.

Next, the optimization of reaction conditions of gold-catalyzed hydrothiolation was conducted by using PPh$_3$AuNTf$_2$ as the gold catalyst (Table 5-2). Firstly, examinations of solvents and reaction temperature for hydrothiolation were performed. When the solvents, such as toluene and CH$_3$CN, were used for gold-catalyzed hydrothiolation, the yields of the desired
adducts decreased substantially (entries 4 and 6). The high reaction temperature was incompatible with the gold-catalyzed hydrothiolation (entries 3 and 5). This was probably because PPh_3AuNTf_2 decomposed at high reaction temperature. Next, the author examined the amounts of THF for the gold-catalyzed hydrothiolation. As the result, the combination of PPh_3AuNTf_2 (2 mol%) and THF (0.15 mL) exhibited good yield (entry 8). In addition, the yield of hydrothiolation product was improved by prolonging the reaction time (entry 10). Furthermore, when excess amounts of PhSH were added additionally after 4 h, the desired product was obtained in excellent yield (entry 11).

Table 5-2. Optimization of Hydrothiolation of 1-Decene a

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>time, h</th>
<th>temp., °C</th>
<th>yield, % b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF (0.3 mL)</td>
<td>17</td>
<td>45</td>
<td>65</td>
</tr>
<tr>
<td>2 c</td>
<td>THF (0.3 mL)</td>
<td>17</td>
<td>45</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>THF (0.3 mL)</td>
<td>17</td>
<td>70</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>Toluene (0.3 mL)</td>
<td>17</td>
<td>45</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Toluene (0.3 mL)</td>
<td>17</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>CH_3CN (0.3 mL)</td>
<td>17</td>
<td>45</td>
<td>2</td>
</tr>
<tr>
<td>7 c</td>
<td>THF (0.15 mL)</td>
<td>17</td>
<td>45</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>THF (0.15 mL)</td>
<td>17</td>
<td>45</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>THF (0.6 mL)</td>
<td>17</td>
<td>45</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>THF (0.15 mL)</td>
<td>20</td>
<td>45</td>
<td>87</td>
</tr>
<tr>
<td>11 d</td>
<td>THF (0.15 mL)</td>
<td>20</td>
<td>45</td>
<td>99</td>
</tr>
</tbody>
</table>

a Reaction conditions: 1-decene (1a, 0.5 mmol), benzenethiol (2a, 0.5 mmol), PPh_3AuNTf_2 (2 mol%). b Determined by ^1H NMR analysis. c 1 mol% of PPh_3AuNTf_2 was used. d Excess amounts of benzenethiol (2a, 0.33 mmol) were added additionally after 4 h.
Next the scope and limitations of the gold-catalyzed hydrothiolation of inactivated alkenes were examined, the results are summarized in Table 5-3. The reaction of allylbenzene 1b and 4-phenyl-1-butene 1c afforded the corresponding *anti*-Markovnikov hydrothiolation products in excellent yields, respectively (entries 2 and 3). When the reaction of phenylallyl ether was employed, the desired hydrothiolation product was also obtained in good yield (entry 4). This gold-catalyzed hydrothiolation tolerated using alkenes bearing functional groups, such as nitrile, hydroxyl, and chloro group, to afford the corresponding adducts 3ea, 3fa, and 3ga in moderate yields, respectively (entries 5–7). In the case of 1,6-heptadiene 1h, the bishydrothiolation product 3ha was obtained in 47% yield accompanied by 20% of monohydrothiolation product (entry 8). The reaction of internal alkene, norbornene 1i, took place efficiently to afford the hydrothiolation product 3ia (entry 9).
Table 5-3. Gold-Catalyzed Hydrothiolation of Several Inactivated Alkenes

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>3</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R&lt;sub&gt;1&lt;/sub&gt;</td>
<td>R&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3aa</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>Ph&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Ph&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3ba</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>Ph&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Ph&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3ca</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>PhO&lt;sub&gt;1&lt;/sub&gt;</td>
<td>PhO&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3da</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>NC&lt;sub&gt;1&lt;/sub&gt;</td>
<td>NC&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3ea</td>
<td>45</td>
</tr>
<tr>
<td>6</td>
<td>HO&lt;sub&gt;1&lt;/sub&gt;</td>
<td>HO&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3fa</td>
<td>51</td>
</tr>
<tr>
<td>7</td>
<td>Cl&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Cl&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3ga</td>
<td>53</td>
</tr>
<tr>
<td>8</td>
<td>PhS&lt;sub&gt;1&lt;/sub&gt;</td>
<td>PhS&lt;sub&gt;2&lt;/sub&gt; - SPh</td>
<td>3ha</td>
<td>47</td>
</tr>
<tr>
<td>9</td>
<td>3ha'</td>
<td>3ia</td>
<td>3ia</td>
<td>69</td>
</tr>
</tbody>
</table>

* Reaction conditions: alkene (1, 0.5 mmol), benzenethiol (2a, 0.5 mmol), PPh<sub>3</sub>AuNTf<sub>2</sub> (2 mol%), THF (0.15 mL), 45 °C, 20 h.*
Furthermore, gold-catalyzed hydrothiolation of inactive alkenes using several thiols were performed. The results of the reaction of 1-decene 1a with several thiols 2 were summarized in Table 4. Benzenethiol bearing either electron-donating or -withdrawing group, such as methyl, fluoro, and chloro group, is suitable for this hydrothiolation to give the anti-Markovnikov adducts in excellent to good yields (entries 2–4). The reaction of pentafluorobenzenethiol proceeded to obtain anti-Markovnikov adduct moderate yield (entry 5). In the cases of aliphatic thiols, phenylmethanethiol 2f, cyclohexanethiol 2g, and decanethiol 2h, the desired gold-catalyzed hydrothiolation products were obtained, respectively (entries 6–8).

To obtain insight into the present gold-catalyzed hydrothiolation reaction, the author examined the hydrothiolation of a vinylcyclopropane derivative (Scheme 1). The hydrothiolation of 1-cyclopropyl-1-phenylethene 1j afforded anti-Markovnikov adduct 3ja without ring opening of the cyclopropyl ring. It was known that the rate constant for ring opening of the cyclopropylcarbinyl radical is very large \( k = 1.3 \times 10^8 \text{ s}^{-1} \).\(^ {11} \) Therefore, this result indicated that the present gold-catalyzed hydrothiolation did not proceed via radical reaction mechanism.

Scheme 5-1. Examination of Reaction Mechanism for Gold-Catalyzed Hydrothiolation
Table 5-4. Gold-Catalyzed Hydrothiolation Using Several Thiols

<table>
<thead>
<tr>
<th>entry</th>
<th>RSH, 2</th>
<th>product</th>
<th>3</th>
<th>yield, % b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>3aa</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>3ab</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2c</td>
<td>3ac</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2d</td>
<td>3ad</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2e</td>
<td>3ae</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2f</td>
<td>3af</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2g</td>
<td>3ag</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2h</td>
<td>3ah</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

a Reaction conditions: 1-decene (1a, 0.5 mmol), thiol (2, 0.5 mmol), PPh₃AuNTf₂ (2 mol%), THF (0.15 mL), 45 °C, 20 h.
To obtain insights into the reaction mechanism, the catalytic hydrothiolation of 1-decene 1a with benzenethiol 2a was monitored by $^{31}$P NMR analysis. The $^{31}$P NMR spectrum during the hydrothiolation immediately showed peaks at 35.3 ppm, attributed to the formation of gold-sulfide complex A. To determine the structure of A, a stoichiometric reaction of PPh$_3$AuNTf$_2$ with PhSH was performed (Scheme 5-2). After the reaction, the $^{31}$P NMR spectrum showed a signal at 35.3 ppm. Complex A was recrystallized, and X-ray analysis unambiguously established that it was a tetranuclear gold complex, [(PPh$_3$)$_4$Au$_4$(SPh)$_2$](NTf$_2$)$_2$. The NMR data of [(PPh$_3$)$_4$Au$_4$(SPh)$_2$](NTf$_2$)$_2$ were identical to those for a very similar tetranuclear gold complex reported in the literature.$^{12}$ Next, the author conducted the hydrothiolation using the synthesized [(PPh$_3$)$_4$Au$_4$(SPh)$_2$](NTf$_2$)$_2$. Interestingly, the desired hydrothiolation proceeded efficiently, indicating that tetranuclear gold complex A is a key intermediate in the hydrothiolation of inactivated alkenes.

**Stoichiometric Reaction**

\[
PPh_3AuNTf_2 + PhSH \xrightarrow{d_{r}-THF, r.t., 10 \text{ min}} [(PPh_3)_4Au_4(SPh)_2](NTf_2)_2
\]

$^{31}$P NMR

- Before: 28.5 ppm
- After: 35.3 ppm

**Catalytic Reaction**

\[
PPh_3AuNTf_2 + PhSH \xrightarrow{THF, 10 \text{ min}} 1\text{-decene (0.5 mmol)} \xrightarrow{\text{PhSH (0.83 mmol)}} {^{\cdot}\text{Oct}} \xrightarrow{77\%} SPh
\]

**Scheme 5-2. Effects of Gold Catalyst on Hydrothiolation**
Chapter 5. Gold-Catalyzed Hydrothiolation of Inacticated Alkenes

Figure 5-1. ORTEP drawing of gold-sulfide complex A (50% thermal ellipsoids). For clarity, all hydrogen atoms and counter anion have been omitted, and only the ipso-carbons of the phenyl ring of triphenylphosphine are shown.

Although the mechanistic details of the present gold-catalyzed hydrothiolation remain to be elucidated, a plausible reaction pathway for hydrothiolation of inactivated alkene 1 with arenethiol 2 is shown in Scheme 5-3. The PPh₃AuNTf₂ catalyst reacts with thiols to form PPh₃AuSPh. Next, PPh₃AuSPh forms tetranuclear gold complex A by reaction with PPh₃AuNTf₂ again. Then, Inactivated alkenes 1 was activated by coordination of gold complex A. Next, subsequent insertion of Au–S bond to double bond of inactivated alkenes took place to give
gold-alkene complex C through the four-membered ring transition structure B. Finally, subsequent protonation of gold-alkene intermediate C with thiol provides the *anti*-Markovnikov hydrothiolation product selectively, with regeneration of gold complex A. The plausible mechanism and regioselectivity of this reaction were identical with recent mechanistic investigation about gold-catalyzed hydrothiolatation of unsaturated bonds.

![Scheme 5-3](image)

**Scheme 5-3.** A Plausible Reaction Pathway of Gold-Catalyzed Hydrothiolation of Inactivated Alkenes

### 5-3 Conclusion

In summary, the author has developed a novel gold-catalyzed *anti*-Markovnikov-selective hydrothiolation of inactivated alkenes. Although
transition-metal-catalyzed reaction of organosulfur compounds to inactivated alkenes has been considered a problematic method for introduction of organosulfur group into organic molecules, the author revealed that high cationic gold catalyst enables selective hydrothiolation of inactivated alkenes. The author believes that this gold-catalyzed hydrothiolation will open up a transition-metal-catalyzed addition toward inactivated alkenes.

5-4 Experimental Section

General Comment

Unless otherwise stated, all starting materials and catalysts were purchased from commercial sources and used without further purification. THF as solvent was used after distillation from CaH₂. ¹H NMR spectra (400 MHz), ¹³C NMR spectra (100 MHz) were taken in CDCl₃ with Me₄Si as an internal standard. ¹⁹F NMR spectra (373 MHz) were taken in CDCl₃ with CFCl₃ as an external standard. Chemical shifts in ¹H NMR were measured relative to CDCl₃ and converted to δ (Me₄Si) values by using δ (CDCl₃) 7.26 ppm. Chemical shifts in ¹³C NMR were measured relative to CDCl₃ and converted to δ (Me₄Si) values by using δ (CDCl₃) 77.00 ppm. IR spectra were reported in wave numbers (cm⁻¹). ESI and EI mass spectra were obtained by employing double focusing mass spectrometers.

General Procedure for Gold-Catalyzed Hydrothiolation of Inactivated Alkenes.

In a two-necked 10 mL flask with a magnetic stirring bar under N₂ atmosphere were placed PPh₃AuNTf₂ (7.4 mg, 0.01 mmol), freshly distilled THF (0.15 mL), alkene (0.5 mmol) and thiol (0.5 mmol). The reaction was conducted at 45 °C for 20 h, and the thiol (0.33 mmol) was added additionally 4 h later. After the reaction, the resulting mixture was filtered through
silica gel and the crude solution was concentrated in vacuo. The product was purified by recycle GPC (eluent: CHCl₃) to afford the hydrothiolation product.

1-(Phenylthio)decane (3aa) [CAS: 13910-18-4]. Colorless oil; ¹H NMR (400 MHz, CDCl₃, ppm) δ 0.88 (t, J = 6.8 Hz, 3H), 1.18–1.46 (m, 14H), 1.63 (quint, J = 7.8 Hz, 2H), 2.90 (t, J = 7.8 Hz, 2H), 7.11–7.16 (m, 1H), 7.22–7.32 (m, 4H); ¹³C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 14.1, 22.6, 28.8, 29.1 (overlap), 29.3, 29.5 (overlap), 31.9, 33.5, 125.5, 128.7 (overlap), 137.1; IR (NaCl) 3062, 2925, 2852, 1585, 1480, 1465, 1439, 1375, 1299, 1268, 1092, 1064, 1025, 736, 690 cm⁻¹; MS (EI) [M]+ m/z = 250.

1-(Phenylthio)-3-phenylpropane (3ba) [CAS: 30134-12-4]. Colorless oil; ¹H NMR (400 MHz, CDCl₃, ppm) δ 1.96 (quint, J = 7.3 Hz, 2H), 2.75 (t, J = 7.3 Hz, 2H), 2.91 (t, J = 7.3 Hz, 2H), 7.13–7.20 (m, 4H), 7.23–7.31 (m, 6H); ¹³C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 30.6, 32.8, 34.6, 125.8, 125.9, 128.4, 128.5, 128.8, 129.1, 136.5, 141.2; IR (NaCl) 3060, 3024, 2933, 2855, 1603, 1583, 1559, 1496, 1480, 1453, 1438, 1420, 1351, 1280, 1251, 1183, 1155, 1093, 1070, 1025, 1002, 968, 738, 691 cm⁻¹; MS (EI) [M]+ m/z = 228.

1-(Phenylthio)-4-phenylbutane (3ca) [CAS: 64740-40-5]. Colorless oil; ¹H NMR (400 MHz, CDCl₃, ppm) δ 1.65–1.80 (m, 4H), 2.62 (t, J = 7.3 Hz, 2H), 2.93 (t, J = 7.3 Hz, 2H), 7.13–7.19 (m, 4H), 7.23–7.36 (m, 6H); ¹³C{¹H} NMR (100 MHz, CDCl₃, ppm) δ 28.6, 30.4, 33.5, 35.3, 125.7, 125.8, 128.3, 128.3, 128.8, 129.0, 136.8, 142.0; IR (NaCl) 3068, 3024, 2932, 2855, 1609, 1581, 1573, 1480, 1452, 1438, 1299, 1259, 1234, 1179, 1158, 1072, 1025, 907, 738, 691 cm⁻¹; MS (EI) [M]+ m/z = 242.

1-(Phenylthio)propyl phenyl ether (3da) [CAS: 59950-10-6]. Colorless oil; ¹H NMR (400 MHz, CDCl₃, ppm) δ 2.09 (tt, J = 6.0, 6.9 Hz, 2H), 3.11 (t, J = 6.9 Hz, 2H), 4.05 (t, J = 6.0 Hz, 2H),
6.86−6.95 (m, 3H), 7.13−7.18 (m, 1H), 7.24−7.29 (m, 4H), 7.33−7.35 (m, 2H); $^{13}$C{\textsuperscript{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ 28.9, 30.1, 65.8, 114.4, 120.7, 125.9, 128.9, 129.1, 129.4, 136.2, 158.7; IR (NaCl) 3062, 3043, 2927, 2871, 1599, 1585, 1502, 1479, 1439, 1386, 1302, 1286, 1244, 1172, 1152, 1078, 1042, 993, 929, 882, 815, 739, 691 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 244.

6-(Phenylthio)hexanenitrile (3ea) [CAS: 99965-76-1]: Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.54−1.71 (m, 6H), 2.32 (t, $J$ = 6.9 Hz, 2H), 2.92 (t, $J$ = 6.9 Hz, 2H), 7.16−7.20 (m, 1H), 7.25−7.34 (m, 4H); $^{13}$C{\textsuperscript{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ 17.0, 24.9, 27.6, 28.2, 33.2, 119.5, 126.0, 128.9, 129.2, 136.2; IR (NaCl) 3074, 3055, 2934, 2860, 2245, 1583, 1573, 1480, 1438, 1425, 1278, 1091, 1076, 1025, 741, 691 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 205.

6-(Phenylthio)-1-hexanol (3fa) [CAS: 99965-82-9]: Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.33−1.50 (m, 5H), 1.56 (quint, $J$ = 6.9 Hz, 2H), 1.66 (quint, $J$ = 7.3 Hz, 2H), 2.92 (t, $J$ = 7.3 Hz, 2H), 3.63 (t, $J$ = 6.8 Hz, 2H), 7.14−7.18 (m, 1H), 7.25−7.33 (m, 4H); $^{13}$C{\textsuperscript{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ 25.3, 28.5, 29.0, 32.6, 33.5, 62.8, 125.7, 128.8, 128.9, 136.8; IR (NaCl) 3236, 3068, 3043, 2928, 2855, 1586, 1482, 1461, 1438, 1119, 1072, 1054, 1020, 965, 962, 892, 732, 690 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 210.

1-Chloro-6-(phenylthio)hexane (3ga) [CAS: 64740-56-3]. Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.41−1.48 (m, 4H), 1.62−1.69 (m, 2H), 1.72−1.79 (m, 2H), 2.92 (t, $J$ = 7.8 Hz, 2H), 3.52 (t, $J$ = 6.9 Hz, 2H), 7.14−7.18 (m, 1H), 7.25−7.33 (m, 4H); $^{13}$C{\textsuperscript{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ 26.4, 28.0, 28.9, 32.4, 33.4, 33.6, 44.9, 125.7, 128.8, 128.9, 136.7; IR (NaCl) 3073, 3049, 2933, 2856, 1584, 1573, 1514, 1480, 1438, 1309, 1271, 1234, 1179, 1158, 1091, 1067, 1025, 738, 691 650 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 228.

1,7-Bis(phenylthio)heptane (3ha). Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 1.25−1.45 (m, 6H), 1.59−1.69 (m, 4H), 2.87−2.92 (m, 4H), 7.12−7.17 (m, 2H), 7.24−7.32 (m, 8H); $^{13}$C{\textsuperscript{1}H} NMR (100 MHz, CDCl$_3$, ppm) δ 28.6 (overlap), 29.0, 33.5, 125.6, 128.8 (overlap), 136.9; IR
Chapter 5. Gold-Catalyzed Hydrothiolation of Inactivated Alkenes

(\text{NaCl})\ 3057,\ 2929,\ 2854,\ 1583,\ 1480,\ 1464,\ 1438,\ 1424,\ 1309,\ 1279,\ 1217,\ 1148,\ 1089,\ 1070,\ 1025,\ 998,\ 909,\ 739,\ 691\ \text{cm}^{-1};\ \text{HRMS (FAB) Calcd for C}_{19}H_{25}S_{2} [M+H]^+: 317.1398, \text{Found: } 317.1396.

\textit{7-}(\text{Phenylthio})-1-heptene (3ha') [\text{CAS: 99404-72-5}]. Colorless oil; $^1\text{H NMR (400 MHz, CDCl}_3$, ppm) δ 1.38–1.46 (m, 4H), 1.66 (quint, $J = 7.3$ Hz, 2H), 2.02–2.07 (m, 2H), 2.91 (t, $J = 7.3$ Hz, 2H), 4.92–5.01 (m, 2H), 5.74–5.84 (m, 1H), 7.14–7.18 (m, 1H), 7.25–7.33 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl$_3$, ppm) δ 28.3, 28.4, 29.0, 33.5, 33.6, 114.4, 125.6, 128.8, 128.9, 136.9, 138.7; IR (NaCl) 3074, 3060, 2975, 2928, 2855, 1640, 1584, 1480, 1458, 1438, 1299, 1278, 1093, 1025, 993, 910, 737, 691 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 206.

\textit{(exo)}-2-(\text{Phenylthio})-bicyclo[2.2.1]heptane (3ia) [\text{CAS: 41327-09-7}]. Colorless oil; $^1\text{H NMR (400 MHz, CDCl}_3$, ppm) δ 1.15–1.27 (m, 3H), 1.39–1.45 (m, 1H), 1.48–1.65 (m, 2H), 1.67–1.71 (m, 1H), 1.77–1.83 (m, 1H), 2.27–2.31 (m, 2H), 3.17–3.20 (m, 1H), 7.12–7.16 (m, 1H), 7.24–7.32 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl$_3$, ppm) δ 28.7, 28.9, 35.6, 36.4, 38.5, 42.3, 48.1, 125.5, 128.7, 128.9, 137.7; IR (NaCl) 3057, 2954, 2868, 1585, 1572, 1480, 1451, 1438, 1313, 1300, 1289, 1269, 1252, 1237, 1198, 1138, 1091, 1070, 1046, 1025, 954, 946, 924, 875, 838, 762, 737, 690 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 204.

2-Cyclopropyl-2-phenyl-1-(phenylthio)ethane (3ja). Colorless oil; $^1\text{H NMR (400 MHz, CDCl}_3$, ppm) δ 0.42–0.45 (m, 2H), 0.53–0.57 (m, 2H), 1.39–1.46 (m, 4H), 7.12–7.31 (m, 8H), 7.58–7.60 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl$_3$, ppm) δ 2.8, 3.0, 21.6, 23.6, 55.1, 126.5, 127.6, 127.8, 128.1, 128.2, 132.8, 136.2, 145.7; IR (NaCl) 3056, 3005, 2981, 2930, 1951, 1887, 1804, 1581, 1491, 1472, 1438, 1377, 1223, 1171, 1067, 1047, 1025, 916, 906, 825, 749, 693 cm$^{-1}$; HRMS (FAB) Calcd for C$_{17}$H$_{10}$S [M+H]$^+$: 255.1207, Found: 255.1214.

1-\{(4-Methylphenyl)thio\}decane (3ab) [\text{CAS: 66605-96-7}]. Colorless oil; $^1\text{H NMR (400 MHz, CDCl}_3$, ppm) δ 0.88 (t, $J = 6.8$ Hz, 3H), 1.15–1.45 (m, 14H), 1.61 (quint, $J = 7.7$ Hz, 2H), 2.30 (s,
Chapter 5. Gold-Catalyzed Hydrothiolation of Inactivated Alkenes

3H), 2.86 (t, \( J = 7.7 \) Hz, 2H), 7.06−7.09 (m, 2H), 7.22−7.24 (m, 2H); \(^{13}\)C\(^{1}H\) NMR (100 MHz, CDCl\(_{3}\), ppm) \( \delta 14.1, 20.9, 22.6, 28.8, 29.1, 29.2, 29.3, 29.5, 31.9, 34.3, 129.5, 129.7, 133.1, 135.7; IR (NaCl) 3018, 2925, 2853, 1492, 1456, 1437, 1372, 1299, 1213, 1093, 1017, 800, 721 cm\(^{-1}\); MS (EI) [M]\(^{+}\) m/z = 264.

1-\{(4-Fluorophenyl)thio\}decane (3ac) [CAS: 61671-40-7]. Colorless oil; \(^{1}H\) NMR (400 MHz, CDCl\(_{3}\), ppm) \( \delta 0.88\ (t, \( J = 7.3 \) Hz, 3H), 1.22−1.45 (m, 14H), 1.59 (quint, \( J = 7.3 \) Hz, 2H), 2.85 (t, \( J = 7.3 \) Hz, 2H), 6.95−7.01 (m, 2H), 7.30−7.35 (m, 2H); \(^{13}\)C\(^{1}H\) NMR (100 MHz, CDCl\(_{3}\), ppm) \( \delta 14.1, 22.7, 28.7, 29.1, 29.3, 29.5\) (overlap), 31.9, 35.0, 115.9 (d, \( J_{C-F} = 21.9 \) Hz), 131.7 (d, \( J_{C-F} = 3.8 \) Hz), 131.9 (d, \( J_{C-F} = 7.6 \) Hz), 161.6 (d, \( J_{C-F} = 245.1 \) Hz); \(^{19}\)F NMR (373 MHz, CDCl\(_{3}\), ppm) \( \delta -116.1\); IR (NaCl) 2925, 2854, 1589, 1490, 1458, 1437, 1395, 1377, 1288, 1229, 1155, 1092, 1014, 820, 759, 722, 631 cm\(^{-1}\); MS (EI) [M]\(^{+}\) m/z = 268.

1-\{(4-Chlorophenyl)thio\}decane (3ad) [CAS: 59985-48-7]. White solid; mp 27−28 °C; \(^{1}H\) NMR (400 MHz, CDCl\(_{3}\), ppm) \( \delta 0.88\ (t, \( J = 7.3 \) Hz, 3H), 1.17−1.42 (m, 14H), 1.62 (quint, \( J = 7.3 \) Hz, 2H), 2.88 (t, \( J = 7.3 \) Hz, 2H), 7.23 (s, 4H); \(^{13}\)C\(^{1}H\) NMR (100 MHz, CDCl\(_{3}\), ppm) \( \delta 14.1, 22.7, 28.8, 29.0, 29.1, 29.3, 29.5\) (overlap), 31.9, 33.8, 128.9, 130.1, 131.5, 135.6; IR (NaCl) 2924, 2852, 1558, 1476, 1457, 1385, 1223, 1096, 1010, 809, 721 cm\(^{-1}\); MS (EI) [M]\(^{+}\) m/z = 284.

1-\{(2,3,4,5,6-Pentafluorophenyl)thio\}decane (3ae). Pale yellow oil; \(^{1}H\) NMR (400 MHz, CDCl\(_{3}\), ppm) \( \delta 0.88\ (t, \( J = 7.3 \) Hz, 3H), 1.22−1.45 (m, 14H), 1.59 (quint, \( J = 7.3 \) Hz, 2H), 2.87 (t, \( J = 7.3 \) Hz, 2H); \(^{13}\)C\(^{1}H\) NMR (100 MHz, CDCl\(_{3}\), ppm) \( \delta 14.1, 22.7, 28.3, 29.0, 29.3, 29.5\) (overlap), 31.9, 35.0, 109.5 (m), 136.4 (m), 138.9 (m), 142.4 (m), 146.3 (m), 148.7 (m); \(^{19}\)F NMR (373 MHz, CDCl\(_{3}\), ppm) \( \delta -161.2\ (m), -153.3\ (m), -132.6\ (m); IR (NaCl) 2928, 2855, 1638, 1313, 1486, 1469, 1437, 1378, 1292, 1216, 1146, 1091, 1016, 981, 908, 862, 761, 737, 727, 668 cm\(^{-1}\); HRMS (FAB) Calcd for C\(_{16}\)H\(_{22}\)F\(_{5}\)S [M+H]\(^{+}\): 341.1362, Found: 341.1350.

1-(Phenylmethylthio)decane (3af) [CAS: 94801-99-7]. Colorless oil; \(^{1}H\) NMR (400 MHz, CDCl\(_{3}\), ppm) \( \delta 0.88\ (t, \( J = 7.3 \) Hz, 3H), 1.22−1.45 (m, 14H), 1.54 (quint, \( J = 7.3 \) Hz, 2H), 2.87 (t, \( J = 7.3 \) Hz, 2H); \(^{13}\)C\(^{1}H\) NMR (100 MHz, CDCl\(_{3}\), ppm) \( \delta 14.1, 22.7, 28.3, 29.0, 29.3, 29.4, 29.5, 31.9, 35.0, 109.5 (m), 136.4 (m), 138.9 (m), 142.4 (m), 146.3 (m), 148.7 (m); \(^{19}\)F NMR (373 MHz, CDCl\(_{3}\), ppm) \( \delta -161.2\ (m), -153.3\ (m), -132.6\ (m); IR (NaCl) 2928, 2855, 1638, 1313, 1486, 1469, 1437, 1378, 1292, 1216, 1146, 1091, 1016, 981, 908, 862, 761, 737, 727, 668 cm\(^{-1}\); HRMS (FAB) Calcd for C\(_{16}\)H\(_{22}\)F\(_{5}\)S [M+H]\(^{+}\): 341.1362, Found: 341.1350.
CDCl$_3$, ppm) $\delta$ 0.88 (t, $J = 6.9$ Hz, 3H), 1.25–1.35 (m, 14H), 1.55 (quint, $J = 7.8$ Hz, 2H), 2.40 (t, $J = 7.8$ Hz, 2H), 3.70 (s, 2H), 7.21–7.31 (m, 5H); $^{13}$C{$^{1}$H} NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 14.1, 22.7, 28.9, 29.2, 29.3, 29.5 (overlap), 31.4, 31.9 (overlap), 36.3, 126.8, 128.4, 128.8, 138.7; IR (NaCl) 3018, 2924, 2853, 1737, 1602, 1494, 1453, 1437, 1420, 1375, 1216, 1106, 1070, 1028, 913, 759, 699 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 264.

1-(Cyclohexylthio)decane [CAS: 41346-30-9]. Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 0.88 (t, $J = 7.3$ Hz, 3H), 1.21–1.39 (m, 20H), 1.53–1.63 (m, 2H), 1.72–1.79 (m, 2H), 1.93–1.99 (m, 2H), 2.52 (t, $J = 7.3$ Hz, 2H), 2.58–2.67 (m, 1H); $^{13}$C{$^{1}$H} NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 14.1, 22.6, 25.9, 26.1, 29.0, 29.2, 29.3, 29.5 (overlap), 30.0, 30.1, 31.9, 33.7, 43.4; IR (NaCl) 2919, 2852, 2668, 1448, 1377, 1340, 1299, 1262, 1201, 1122, 999, 886, 822, 759, 721 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 256.

1-(Decylthio)dodecane [CAS: 54934-48-4]. White solid; mp 30–31 °C; $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 0.88 (t, $J = 7.3$ Hz, 3H), 1.19–1.39 (m, 32H), 1.57 (quint, $J = 7.7$ Hz, 4H), 2.94 (t, $J = 7.7$ Hz, 4H); $^{13}$C{$^{1}$H} NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 14.1, 22.7, 28.9, 29.3 (overlap), 29.5, 29.6 (overlap), 29.7 (overlap); IR (NaCl) 2957, 2916, 2848, 1471, 1461, 730, 719, 668 cm$^{-1}$; MS (EI) [M]$^+$ m/z = 342.
5-5 References


Chapter 6

Conclusion

In this research work, the development of new highly selective addition reactions of group 16 heteroatom compounds to unsaturated bonds has been investigated.

Chapter 2 described a novel photoinduced perfluoroalkyltelluration to terminal alkynes by using ditelluride and perfluoroalkyl iodide mixed system upon photoirradiation. In the reaction with alkynes, perfluoroalkyltelluration took place regio- and stereoselectively, upon irradiation with a Hg high pressure lamp through a filter (hν >400 nm) to afford 1-(perfluoroalkyl)-2-(aryltelluro)alkenes. Furthermore, the obtained vinyl telluride was easily converted to the corresponding alcohol derivative by nucleophilic addition to aldehyde via lithium-tellurium exchange reaction.

Chapter 3 mentioned a highly selective palladium-catalyzed hydrothiolation of alkenes bonded directly to heteroatoms, such as oxygen and nitrogen. Despite the undeveloped region concerning transition-metal-catalyzed reaction of organosulfur compounds of alkenes, a novel Pd-catalyzed addition of thiols to alkenes bearing a heteroatom, such as vinyl ethers and N-vinyl lactams, is found to proceed under mild conditions to give the corresponding Markovnikov adducts, regioselectively, in good yields. Since the produced O,S- and N,S-acetal units are known as useful synthetic intermediates and bioactive compounds, this hydrothiolation is a useful straightforward methodology for construction these heteroacetal structures.

Chapter 4 described palladium-catalyzed addition of areneselenols to N-vinyl lactams affording the corresponding N,Se-acetals as Markovnikov adducts. In the case of terminal N-vinyl lactams, Markovnikov-selective hydroselenation proceeds efficiently in the absence of any catalyst (or additive), owing to the acidity of the selenols. In contrast, the self-promoted
hydroselenation is inefficient with internal $N$-vinyl lactams. In the presence of palladium diacetate, however, the desired hydroselenation of internal $N$-vinyl lactams proceeds efficiently to afford the corresponding $N,Se$-acetals.

Chapter 5 described gold-catalyzed hydrothiolation of inactivated alkenes with high anti-Markovnikov selectivity. In particular, the addition of organosulfur compounds to inactivated alkenes in the presence of transition metal catalysts remained an unsolved challenge. However, a novel gold-catalyzed hydrothiolation of inactivated alkenes is found to proceed effectively to give the anti-Markovnikov-selective adducts in good yields.

In summary, several novel addition reactions of group 16 heteroatom compounds to unsaturated bonds have been developed. The author believes that this unprecedented research work will make a great contribution for the development of heteroatom chemistry.
List of Publications

1. Highly Selective Perfluoroalkylchalcogenation of Alkynes by the Combination of Iodoperfluoroalkanes and Organic Dichalcogenides upon Photoirradiation
   Tamai, T.; Nomoto, A.; Tsuchii, K.; Minamida, Y.; Mitamura, T.; Sonoda, M.; Ogawa, A.
   (Chapter 2)

2. Regioselective Hydrothiolation of Alkenes Bearing Heteroatoms with Thiols Catalyzed by Palladium Diacetate
   Tamai, T.; Ogawa, A.
   (Chapter 3)

3. Palladium-Catalyzed Markovnikov-Selective Hydroselenation of *N*-vinyl Lactams with Selenols Affording *N*,*Se*-acetals
   (Chapter 4)

4. Gold-Catalyzed anti-Markovnikov Hydrothiolation of Inactivated Alkenes
   *Org. Lett.* Submitted.
   (Chapter 5)
Other Publications

5. Novel Cyclization of o-Alkynylaryl Isocyanides with Highly Selective Introduction of Heteroatom Groups
   Ogawa, A.; Tamai, T.; Mitamura, T.; Nomoto, A.

6. Highly Selective Perfluoroalkylation of Unsaturated Molecules upon Photoirradiation in BTF as an Organic/Fluorous Hybrid Solvent
   Tamai, T.; Sonoda, M.; Ogawa, A

7. An Efficient and Highly Selective Carbonylative Bisthiolation of Internal Alkynes with Organic Disulfides Catalyzed by [Co$_2$(CO)$_8$]
   Higuchi, Y.; Higashimae, S.; Tamai, T.; Nomoto, A.; Sonoda, M.; Ogawa, A.

8. Highly Regioselective Palladium-catalyzed Double Hydroselenation of Terminal Alkynes with Benzeneselenol in the Presence of Acetic Acid
9. A Highly Selective Cobalt-Catalyzed Carbonylative Cyclization of Internal Alkynes with Carbon Monoxide and Organic Thiols

Higuchi, Y.; Higashimae, S.; Tamai, T.; Ogawa, A.


10. Selective Thiolative Lactonization of Internal Alkynes Bearing a Hydroxyl Group with Carbon Monoxide and Organic Disulfide Catalyzed by Transition-Metal Complexes

Higashimae, S.; Tamai, T.; Nomoto, A.; Ogawa, A.

List of Awards

1. 2nd TKU-OPU & 4th TKU-ECUST-OPU-KIST International Symposium “Best in Poster Award”
   (September 26, 2014)

2. President’s Award of Osaka Prefecture University First Semester of 2014
   (October 31, 2014)
Acknowledgement

First of all, I would like to express my sincerest gratitude and thanks to my research supervisor Professor Akiya Ogawa for their kind guidance, helpful suggestions, continuous encouragement, and invaluable assistance throughout the course of this challenging work.

I also would like to express grateful to Professor Tsutomu Nagaoka and Professor Akikazu Matsumoto of Osaka Prefecture University for their helpful remarks and suggestions to this thesis.

I would also like to express my thanks to Visiting Professor Michio Ueshima and Lecturer Akihiro Nomoto of Osaka Prefecture University for their significant advices and stimulating discussions on this work. I would like to acknowledge the continuous encouragement and valuable discussions of Associate Professor Motohiro Sonoda of Osaka Prefecture University and Lecturer Yoshimasa Makita of Osaka Dental University.

I express my acknowledgement to my co-workers of my research group: Mr. Shinya Higashimae, Ms. Megumi Yoshikawa, and Ms. Keiko Fujiwara.

Special thanks are also given to all other members of Ogawa’s research group for their assistances, daily discussions, and profound suggestions to this work.

Furthermore, I acknowledge the Research Fellowship from Japan Society for the Promotion of Science (JSPS) for Young Scientists for financial support.

Finally, I would like to express my deepest appreciation to all my family for their understanding, continuous encouragement, and supports.

January 2016

Taichi Tamai