Lewis Acid Catalyzed Selenoamidation of Olefins: 
Chemoselective Synthesis of Allylic Amide

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ABSTRACT

Haloamidation of olefins can give the corresponding 1,2-trans-haloamide adducts. However, some of these adducts will be transformed into oxazolines simultaneously in the reaction mixture. On the other hand, selenoamidation of olefins, under the same conditions as that of the haloamidation, should give the trans-phenylselenoamide adduct without undergoing cyclization simultaneously. Oxidation, followed by syn-elimination of the trans-phenylselenoamide adduct could give a mild and efficient route to allylic amides.

\begin{center}
\begin{tikzpicture}
\node (olefin) at (0,0) {Olefin};
\node (halo) at (2,0) {trans-bromoacetamide adduct};
\node (cyclic) at (4,0) {Oxazoline};
\node (olefin2) at (0,-2) {Olefin};
\node (coselenyl) at (2,-2) {trans phenylselenoamide adduct};
\node (allylic) at (4,-2) {Allylic amide};
\node (halo2) at (2,-2) {trans phenylselenoamide adduct};
\node (cyclic2) at (4,-2) {Allylic amide};
\node (r) at (0,-3) {R = H, Alkyl};
\draw[->] (olefin) -- (halo);
\draw[->] (halo) -- (cyclic);
\draw[->] (olefin2) -- (coselenyl);
\draw[->] (coselenyl) -- (allylic);
\end{tikzpicture}
\end{center}

INTRODUCTION

Cohalogenation is a general term for reactions that involve a halogen and another group being added across a double bond of the olefins. Haloamidation is one of the cohalogenation reactions because it involves a halogen and an amide group being added across the double bond. Olefins

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undergo haloamidation reaction to give the corresponding 1,2-trans-haloamide adducts. However, some of the adducts formed can undergo cyclization simultaneously to form the oxazolines. This was observed in the previous work\textsuperscript{3} published for several olefinic substrates. The corresponding haloamide adducts were unable to be isolated and purified after the reaction was completed. Therefore, to prevent simultaneous cyclization of these adducts such that we can use them to form the allylic amides or use for other reactions, selenium compounds were used to substitute the use of Br\textsuperscript{+}-donating compounds. This reaction is known as the selenoamidation reaction, whereby the phenylseleno and the amide groups are added across the double bond. The adduct synthesized was found to be stable\textsuperscript{4}. In these experiments, \textit{N}-(phenylseleno) phthalimide (NPSP) was used for the selenoamidation reaction.

**MATERIALS and METHODS**

In general, nuclear magnetic resonance (NMR) spectra were measured with a Bruker Avance 300 (AV300) NMR spectrometer at 300.13MHz (\textsuperscript{1}H) in CDCl\textsubscript{3} solutions. All chemical shifts were recorded in ppm relative to CDCl\textsubscript{3} (\(\delta = 7.26\)ppm). All reactions were monitored by analytical thin layer chromatography (TLC) on Merck aluminium-precoated plates of silica gel 60 F254 or Merck glass plates of silica gel 60 F254 with detection by UV light and/or immersing in aqueous potassium manganate and subsequent heating. Merck silica gel 60 of particle size 0.040 – 0.063 mm (230 – 400 mesh) was used for flash column chromatography. Chemicals were commercially available and solvents were freshly distilled under N\textsubscript{2}. Stock solution of 1.0M Lewis acid catalyst was prepared.

**EXPERIMENTAL PROCEDURE**

To a vigorously stirred suspension of \textit{N}-(phenylseleno) phthalimide (0.20g, 0.66mmol) in dry acetonitrile (3ml) under N\textsubscript{2} in the dark at room temperature was added the Lewis acid catalyst of different catalyst loading as shown in table 1. The mixture was allowed to stir for 5 minutes. Cyclohexene (1.2ml, 45.3mmol) and water (22\(\mu\)l, 11.9mmol) was added into the mixture under N\textsubscript{2} at room temperature and stirred accordingly to the respective amount of reaction time as shown in table 1. The mixture was then quenched with saturated aqueous NaHCO\textsubscript{3} (10ml) and extracted with

\textsuperscript{3}Yeung \textit{et al.} (2006)
\textsuperscript{4}Nicolaou \textit{et al.} (1985)
CH₂Cl₂ (3 x 20ml). The combined organic extracts were dried (Na₂SO₄) and filtered. Concentration of the filtrate, followed by flash column chromatography (n-hexane: Et₂O 1:1) gave the trans-phenylseleno acetamide adduct as yellow solids. The yields are recorded in table 2. ¹H NMR δ 3.8 (1H, m). 7.3 – 7.6 (5H, m), 3.01 (1H, dt).

RESULTS

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst used</th>
<th>Mol%</th>
<th>Reaction time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>0%</td>
<td>23hrs</td>
<td>Trace amounts</td>
</tr>
<tr>
<td>2</td>
<td>SnCl₄</td>
<td>10</td>
<td>23hrs</td>
<td>16.7mg, 10.2%</td>
</tr>
<tr>
<td>3</td>
<td>SnCl₄</td>
<td>40</td>
<td>18hrs</td>
<td>90.2mg, 55.2%</td>
</tr>
<tr>
<td>4</td>
<td>BF₃ · Et₂O</td>
<td>5</td>
<td>23hrs</td>
<td>36.1mg, 22.1%</td>
</tr>
<tr>
<td>5</td>
<td>BF₃ · Et₂O</td>
<td>10</td>
<td>23hrs</td>
<td>90.0mg, 55.1%</td>
</tr>
<tr>
<td>6</td>
<td>BF₃ · Et₂O</td>
<td>20</td>
<td>12hrs</td>
<td>41.5mg, 25.4%</td>
</tr>
<tr>
<td>7</td>
<td>BF₃ · Et₂O</td>
<td>20</td>
<td>23hrs</td>
<td>0.12g, 73.8%</td>
</tr>
<tr>
<td>8</td>
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<td>20</td>
<td>48hrs</td>
<td>0.15g, 89.1%</td>
</tr>
<tr>
<td>9</td>
<td>BF₃ · Et₂O</td>
<td>40</td>
<td>23hrs</td>
<td>0.12g, 75.0%</td>
</tr>
</tbody>
</table>

Table 1: Selenoamidation of cyclohexene at room temperature

From the various selenoamidation reactions of the cyclohexene substrate shown in table 1, the optimum condition was found to be the usage of 20mol% BF₃ · Et₂O catalyst loading and letting the reaction run for 48hours at room temperature. The presence of a Lewis acid catalyst is also crucial for the production of the trans-phenylseleno acetamide adduct with relatively high yields.

DISCUSSION

Cyclization of some trans-bromo acetamide adducts occur due to the possible geometry of the substituents of the six-membered ring. For the cyclohexane ring, ring flip occurs at room temperature. A substituent in the equatorial position is more stable due to the reduction in the steric repulsion. However, when there is a methyl group attached to the carbon which is also bonded to the acetamide group, there is a higher chance of cyclization to occur due to the positioning of the substituents. The oxygen in the acetamide in the axial position is likely to attack the carbon bonded to the bromine atom due to its favourable position. Moreover, the Br⁻ is a good leaving group and as
a result of the simultaneous cyclization, the equilibrium is shifted from the left to the right. On the other hand, the phenylseleno substituent is not a good leaving group. Therefore, cyclization is probably not feasible.

**CONCLUSION**

In conclusion, selenoamidation is a good reaction in such that allylic amide can be synthesized relatively easily without the formation of the undesired compounds. Lewis acid catalyst can catalyze the reaction under mild conditions and in relatively good yield. This is favourable as it is practically convenient and less cumbersome when performing experiments under room temperature and using mild conditions, as compared to the previous works published\(^5\), where the authors used harsh reaction conditions. The chemicals are also readily available too. Therefore, the selenoamidation of olefins is a good method for the conversion of olefins into their trans-phenylseleno acetamide adducts and it could be an alternative method for olefinic substrates with different substituents at the double bond. It can find its way in wider and useful applications in an indirect manner.

**REFERENCES**


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\(^5\) Akio et al. (1981)