Lewis Acid Mediated Reactions of Allyl Chalcogenides with Ethyl Glyoxylate

Kazunori Hirabayashi, Hideki Sato, Yu Kuriyama, Jun-ichi Matsuo, Soichi Sato,
Toshio Shimizu,* and Nobumasa Kamigata
Department of Chemistry, Graduate School of Science and Engineering, Tokyo Metropolitan University,
1-1 Minami-ohsawa, Hachioji, Tokyo 192-0397

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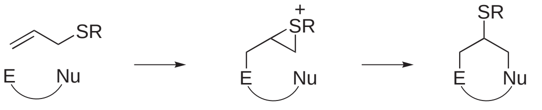
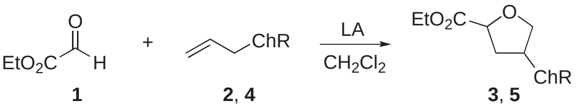
Allyl mesityl sulfide reacted with ethyl glyoxylate in the presence of tin(IV) chloride to give a tetrahydrofuran derivative. The presence of a bulky substituent on the sulfur atom was crucial to the present reaction. The reaction of allyl mesityl selenide also gave a cycloaddition product, whereas allylation occurred when allyl mesityl telluride was used.

Episulfonium ions are synthetically useful and mechanistically interesting functional groups.[1] The nucleophilic addition to episulfonium ions occurs to form carbon–carbon or carbon–heteroatom bonds. Episulfonium ions are often generated in situ and used without isolation because they are relatively unstable. Usually, episulfonium ions are prepared from sulfides that possess an sp^2 or sp carbon or a leaving group at the β-position.[2] It was also reported that the reaction of allylic sulfides, which possessed an sp^2 carbon at the β-position, with bromine proceeded through the episulfonium ion as an intermediate.[3] Thus, the reaction of allylic sulfides with substrates having both electrophilic and nucleophilic functional groups would afford cycloaddition products (eq 1).



(1)

In the reactions of carbonyl compounds with weak nucleophiles, Lewis acid catalysts are usually used to enhance the electrophilicity of carbonyl compounds.[4] Various Lewis acids catalyzed reactions, such as allylation or cycloaddition, of allylic reagents with carbonyl compounds have been reported.[5] However, to the best of our knowledge, no Lewis acid catalyzed reactions of allylic sulfides with carbonyl compounds have been reported so far. Similarly, the reactions of allylic selenides and tellurides with carbonyl compounds are unknown. Reported here are the first Lewis acid catalyzed [3 + 2] cycloaddition reactions of allyl sulfides and selenides with carbonyl compounds (eq 2) and the allylation reactions of allyl telluride.



(2)

1 **2**, **4** **3**, **5**

2a, **3a** : Ch = S, R = Me
2b, **3b** : Ch = S, R = Ph
2c, **3c** : Ch = S, R = Mes
4a, **5a** : Ch = Se, R = Mes
4b, **5b** : Ch = Se, R = Ph

The cycloaddition reactions of allyl sulfides **2** with ethyl glyoxylate (**1**) were surveyed (Table 1). The reaction of allyl methyl sulfide (**2a**) with **1** proceeded in the presence of $SnCl_4$ at room temperature to give tetrahydrofuran derivative **3a** in very low yield (Entry 1). When the reaction time was extended, the yield was slightly increased (Entry 2). When the substituents on the sulfur atom were changed from methyl group to phenyl or mesityl (Mes) group, the product yields were increased as well (Entries 3 and 4). The results showed that the [3 + 2] cycloaddition reactions required a bulky group on the sulfur atom of allyl sulfides. Lewis acids can interact with sulfide groups or carbonyl groups; however, such bulky groups as mesityl group hinder the interaction with sulfide groups. Hence, Lewis acids could activate carbonyl groups and the reaction of **2c** proceeded smoothly to give **3c** in good yield. The stereochemistry of the product was determined by X-ray analysis of a carboxylic acid derivative obtained by hydrolysis of **3c**.[6] These cycloaddition reactions gave cis adducts as major products (cis/trans = 9/1). When $BF_3 \cdot OEt_2$ was used, the yield was low even though the reaction time was long, and the major product was a trans adduct (cis/trans = 3/7) (Entry 5). This is because the coordination of Lewis acids to ethyl glyoxylate were different between $SnCl_4$ and $BF_3 \cdot OEt_2$.[7] In contrast, no reactions occurred when other Lewis acids ($TiCl_4$, $Ti(O^iPr)_4$, $AlCl_3$, or $ZnCl_2$) were used.

Table 1. Lewis acid catalyzed [3 + 2] cycloaddition reactions of **1** with **2**[a]

Entry	**2**	LA	Time/h	Yield/%	cis/trans[b]
1	**2a**	$SnCl_4$	1	18 (**3a**)	9/1
2	**2a**	$SnCl_4$	18	30 (**3a**)	9/1
3	**2b**	$SnCl_4$	0.5	43 (**3b**)	9/1
4	**2c**	$SnCl_4$	0.5	78 (**3c**)	9/1
5	**2c**	$BF_3 \cdot OEt_2$	96	36 (**3c**)	3/7

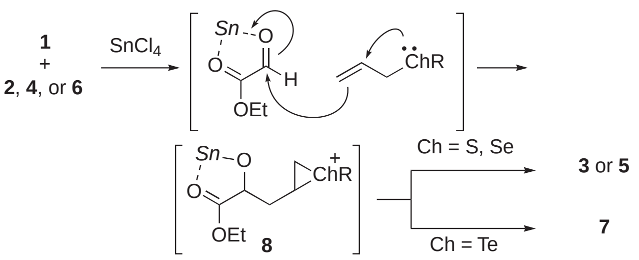
[a] All reactions were carried out with **1** (1.0 mmol), **2** (1.0 mmol), and Lewis acid (LA) (1.0 mmol) in CH_2Cl_2 (2 mL) at rt. [b] The ratio was determined by ^{1}H NMR.

The reactions of allyl selenides **4a** and **4b** were carried out initially at −80 °C, after which the reaction temperature was gradually raised to room temperature. Cycloaddition products **5a** and **5b** were obtained in good yields (Table 2, Entries 1 and 2). However, the stereoselectivity of **5a** was different from that of **5b**. These results indicated that the substituents on the selenium atom affected not the yield but the stereoselectivity.

Table 2. Lewis acid catalyzed [3 + 2] cycloaddition reactions of **1** with **4**[a]

Entry	**4**	LA	Time/h	Yield/%	cis/trans[b]
1	**4a**	$SnCl_4$	2	84 (**5a**)	3/7
2	**4b**	$SnCl_4$	2	94 (**5b**)	5/5
3[c]	**4a**	$SnCl_4$	3	18 (**5a**)	7/3
4	**4a**	$BF_3 \cdot OEt_2$	17	22 (**5a**)	3/7

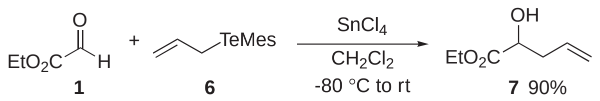
[a] Unless otherwise noted, the reactions were carried out with **1** (1.0 mmol), **4** (1.0 mmol), and LA (1.0 mmol) in CH_2Cl_2 (2 mL) at −80 °C to rt. [b] The ratio was determined by ^{1}H NMR. [c] The reaction was carried out at −80 °C.



Scheme 1. Plausible reaction mechanism.

Then, the stereochemistry of **5a** was determined with the same procedure as that for **3c**.[6] The reaction of **4a** produced a trans adduct as the major product, in contrast to a cis adduct in the case of **2c**. In order to clarify the mechanism of the reaction, the reaction was carried out at low temperature (−80 °C) to give product **5a** in 18% yield, the selectivity of which was reversed (cis/trans = 7/3) (Entry 3). The cis/trans ratio of the product **5a** changed from 7/3 to 3/7 in the presence of $SnCl_4$ at room temperature. In addition, product **5a** was treated with an equivalent amount of **4b** in the presence of $SnCl_4$ at room temperature under similar reaction conditions to afford a mixture of **5a** (47%) and **5b** (45%). Therefore, in the case of **4**, equilibrium exists between **4** and **5**. Other Lewis acids, such as $BF_3 \cdot OEt_2$, $TiCl_4$, $Ti(O\textit{i}\text{-}Pr)_4$, and $AlCl_3$, were also examined, but the reaction occurred only in the case of $BF_3 \cdot OEt_2$ (Entry 4).

On the other hand, allyl mesityl telluride (**6**) reacted with **1** to give allylation product **7** in 90% yield instead of the [3 + 2] cycloaddition product (eq 3).



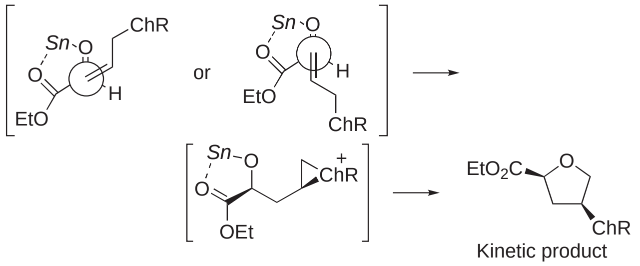
(3)

A plausible reaction mechanism is shown in Scheme 1. First, a Lewis acid coordinated to the two carbonyl groups of **1**, increasing electrophilicity of formyl carbon. Carbon–carbon bond formation between γ-position of the allyl group and formyl carbon was accompanied by nucleophilic addition of the lone pair on chalcogen atom to the β-carbon. Finally, in the cases of **2** and **4**, the tin alkoxide moiety attacked the carbon of epichalcogenonium ions to form a carbon–oxygen bond. There are two sites on the epichalcogenonium ions that can be attacked by the tin alkoxide moiety. Since a five-membered ring is more easily formed than a four-membered one, products **3** and **5** were afforded. In contrast, in the case of **6**, since the epitelluronium ion was very labile, the epitelluronium ion group of **8** decomposed to give homoallyl alcohol **7**.[8]

Nucleophilic addition of the allyl group occurred via synclinal or antiperiplanar transition states, as shown in Scheme 2.[9] Therefore, in the reactions of **2** at room temperature, the major products were cis adducts as kinetic products. Cis adducts were also afforded in the reactions of **4** at −80 °C, based on a similar reason. In contrast, in the reactions of **4** at room temperature, the nucleophilic addition of a seleno group of product **5** to the α-position of furan occurred. Hence, trans adducts as thermodynamic products were produced for the equilibrium between **4** and **5** (eq 5).

$$1 + 2 \rightarrow 8 \rightarrow 3 \qquad (4)$$

$$1 + 4 \rightleftharpoons 8 \rightleftharpoons 5 \qquad (5)$$



Scheme 2. Plausible reaction pathways for cis adduct.

In summary, it was found that Lewis acid mediated reactions of allyl sulfides and selenides proceeded to afford cycloaddition products. These reactions required introduction of a bulky substituent on the chalcogen atoms. In addition, allylation proceeded when allyl mesityl telluride was used. Therefore, allyl chalcogenides can be used in Lewis acid mediated reactions.

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