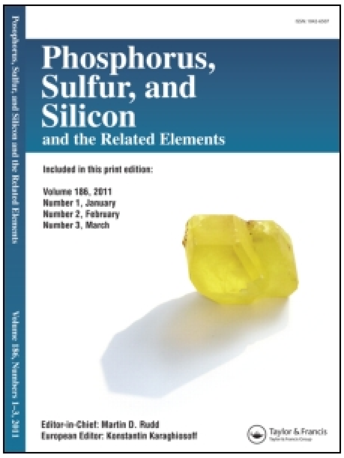

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Reactions of Lithium Eneselenolates of Selenoamides with Carbonyl Compounds

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Reactions of Lithium Eneselenolates of Selenoamides with Carbonyl Compounds

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The reaction of lithium eneselenolates and dieneselenolates derived form selenoamides with a variety of carbonyl compounds has been described. In the reaction with α,β-unsaturated esters and ketones Michael addition reaction took place very rapidly, whereas the reaction with α,β-unsaturated aldehydes gave selectively 1,2-adducts. As for the reaction of lithium dieneselenolates allyl group and aldehydes were selectively introduced to the position α to the selenocarbonyl group.

Keywords: selenoamides; Michael addition; aldol-type condensation; lithium eneselenolates; lithium dieneselenolates; β-hydroxy seleno amides; δ-oxo selenoamides

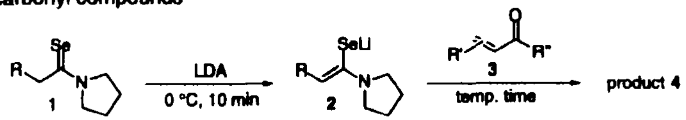
INTRODUCTION

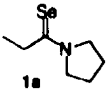
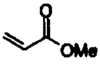
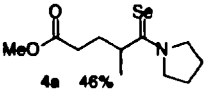
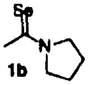
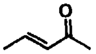
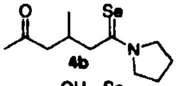
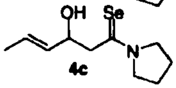
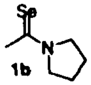
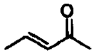
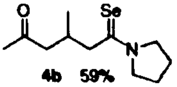
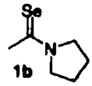
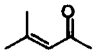
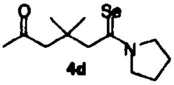
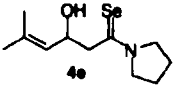
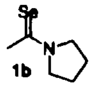
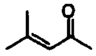
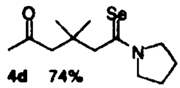
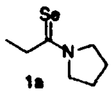
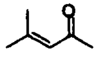
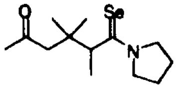
It is of great importance to develop new carbon-carbon bond-forming reactions with high efficiency and selectivity in organic synthetic chemistry. For example, Michael addition reaction and aldol condensation reaction are very useful transformations and their examples have been reported in great depth.[1,2]

During the course of our studies on the synthesis and reactions of selenocarbonyl compounds[3] we envisioned the availability of lithium eneselenolates and dieneselenolates as reactive nucleophiles toward carbonyl compounds since a wide variety of selenolate ions have been used as highly reactive soft nucleophiles to provide synthetic reactions under mild reaction conditions[4] We report herein Michael addition reaction of lithium eneselenolates to α,β-unsaturated esters and ketones[3a] and aldol-type condensation reaction of lithium ene selenolates and dieneselenolates.

The reaction of lithium eneselenolates **2** generated from propaneselenoamide **1a** or selenoacetamide **1b** and LDA with α,β-unsaturated esters and ketones was carried out. The results are summarized in Table 1. Selenoamide **1a** was treated with LDA at 0 °C for 10 min. Then, to the reaction mixture were added 5 equiv of methyl acrylate **3a** and water successively at -78 °C. The purification of the product by column chromatography on silica gel gave 1,4-adduct **4a** in 46% yield (entry 1). The Michael addition of **2b** to **3a** was complete within 1 sec. The prolonged reaction time between **2b** and **3a** reduced the yields of **4a**.

Table 1. Michael addition of selenoamides 1 to α,β-unsaturated carbonyl compounds[a]



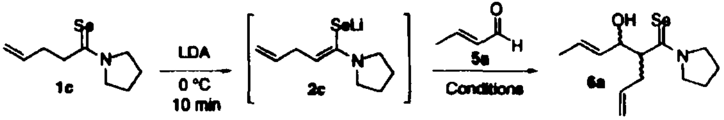
entry	selenoamide	temp. time	α,β-unsaturated carbonyl compound	product yield[b]
1[c]	 1a	-78 °C 1 sec	 3a	 4a 46%
2	 1b	0 °C 1 sec	 3b	 4b  4c 4b+ 4c[d] (50 : 50)[e]
3	 1b	40 °C 1 sec	 3b	 4b 59%
4	 1b	0 °C 1 sec	 3c	 4d  4e 4d + 4e 46%[f] (40 : 60)[e]
5	 1b	40 °C 1 min	 3c	 4d 74%
6	 1a	0 °C 1 sec	 3c	 4f 69%

[a] The selenoamide 1 (1 mmol) was treated with LDA (1.2 mmol) in THF (5 mL) at 0 °C for 10 min, then to the reaction mixture were added the carbonyl compound (1 mmol) and water (1 mL) successively. [b] Isolated yield. [c] To the reaction mixture was added 5 equiv of 3a. [d] The yield of the products was not determined. [e] The ratio of 1,2-and 1,4-adducts is shown in parenthesis. [f] The starting material 1b was recovered in 45% yield.

This results are in a marked contrast to the Michael addition of ordinary amide enolates, which generally required more than 10 min.[1a] In the reaction of lithium eneselenolate **2b** with 3-pentene-2-one **3b** not only 1,4- but also 1,2-adducts were formed in a ratio of 50 : 50 (entry 2). Then, the temperature of the reaction was raised to 40 °C to give the 1,4-adduct **4b** with high selectivity (entry 3). A similar result was observed for the reaction of **1b** with mesityl oxide **3c**. The reaction at 0 °C gave the mixture of the 1,4-adduct **4d** and 1,2-adduct **4e**, and the starting material **1b** was recovered in 45% yield, whereas the reaction at 40 °C gave **4d** selectively. On the contrary the selenoamide **1a** gave only 1,4-adduct **4f** even at 0 °C.

Secondly, the reaction with α,β-unsaturated aldehydes was examined. The results of the reaction of lithium eneselenolate **2c** generated from 4-penteneselenoamide **1c** with crotonaldehyde **5a** are summarized in Table 2.

Table 2. Reaction of selenoamide **1c** with crotonaldehyde [a]

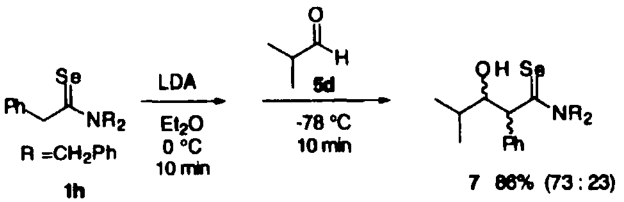


entry	Reaction conditions				yield [%][c]	diastereomer ratio (*syn/anti*)[e]
	temp. / °C	time[b]	solvent	additive / equiv.		
1	-78	1 sec	THF	-	70	55/45
2	-78	1 sec	THF	TMEDA(2.4) 0 °C, 30 min[d]	-	69/31[f]
3	-78	1 sec	Et_2O	TMEDA(2.4) 0 °C, 4 h[d]	-	<50/>50[f]

[a] The selenoamide **1c** (1 mmol) was treated with LDA (1.2 mmol) in a solvent (5 mL) at 0 °C for 10 min, then to the reaction mixture were added the additive and **5a** (1.2 mmol) and water (1 mL) succesaively. [b] Reaction time after the addition of **5a**. [c] Isolated yield. [d] Reaction time and temp. after the addition of the additives. [e] The ratio of the diastereomer was determined by ^1H NMR spectra. [f] The ratio of the diastereomer was determined by ^1H NMR spectra of the crude products.

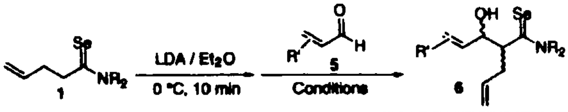
The reaction of lithium eneselenolate **2c** with crotonaldehyde **5a** proceeded smoothly to give selectively 1,2-adduct **6a** as a stereo isomeric mixture in 70% yield (entry 1). No product derived from 1,4-addition of **1c** to **5a** was observed. To improve the diastereoselectivity TMEDA was used as an additive (entries 2 and 3). However, no dramatic effect was not observed in these reactions. Then, the effect of the substituents attached to the nitrogen atom in selenoamides toward the stereoselectivity was examined. The results are shown in Table 3. The starting selenoamides were prepared from (trimethylsilyl)acetylene, selenium, allyl bromide, and amines by the reported procedure[4]. Among selenoamides **1d** – **1g** selenoamides **1d** and **1g** showed better diastereoselectivity to the aldol-type reaction with crotonaldehyde **5a** (entries 1 – 4). Likewise, high diastereoselectivity was observed for the reaction of selenoamides **1d** and **1g** with aldehydes **5b** and **5c** (entries 5 and 9).

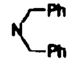
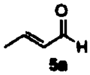
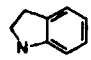
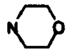
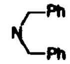
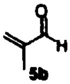
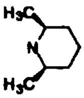
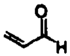
The effect of *N*,*N*-dibenzylamino group to control the stereoselectivity was further illustrated by the reaction of selenoamide **1h** with isobutyraldehyde **5d** (eq 1). One of two diastereomers was predominantly obtained in 86% yield.



(1)

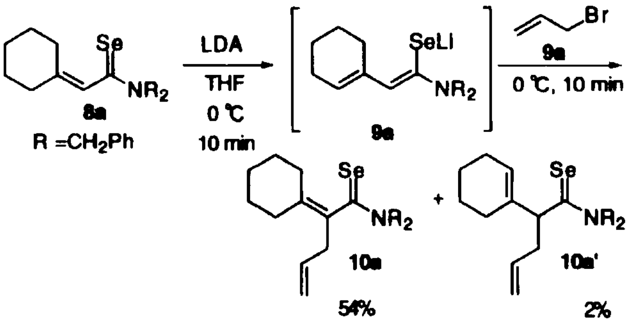
Table 3. Reaction of 4-pentenoselenoamides with α,β-unsaturated aldehydes. [a]



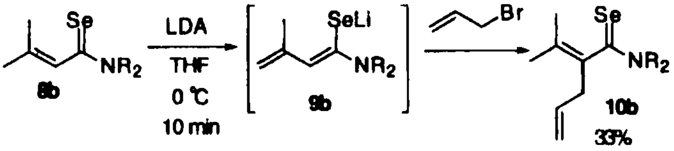
entry	Reaction conditions				yield [%][b]	diastereomer ratio (syn/anti)[c]
	temp / °C	time / min	NR_2	aldehyde		
1	-78	1	 1d	 5a	6b 83	75/25
2	-78	1	 1e	5a	6c 48	70/30
3	-78	3	 1f	5a	6d 78	<50/>50[d]
4	-78	10	 1g	5a	6f 75	74/26
5	-78	15 5	 1d	 5b	6g 81 62[e]	93/7 77/23
6	-78	5	$N(CH_2CH{=}CH_2)_2$ 1h	5b	6h 70	74/26
7	-78	10	 1i	5b	6i 18	80/20
8	-78	5	 1c	5b	6j 71	61/39
9	-78	10	 1g	 5c	6k 34	87/13

[a] The selenoamide 1 (1 mmol) was treated with LDA (1.2 mmol) in a solvent (5 mL) at 0 °C for 10 min, then to the reaction mixture was added α,β-unsaturated aldehyde (1.2 mmol) at -78 °C and water. [b] Isolated yield. [c] The ratio of the diastereomer was determined by ^1H NMR. [d] The ratio of the diastereomer was determined by ^{13}C NMR. [e] The reaction was carried out in the presence of TMEDA (2.4 mmol).

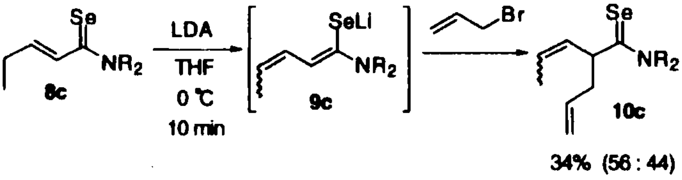
Finally, the reactivity of lithium dieneselenolates generated from α,β-unsaturated selenoamides **8** was studied. To confirm the generation of lithium dieneselenolates **9a** – **9c** from selenoamides **8a** – **8c** and LDA, allyl bromide was added to the reaction mixture to give allylated products **10a** – **10c** although the yields of the products in the latter two cases were moderate. In these reactions allyl group was selectively introduced to the carbon atom α to the selenocarbonyl group. Furthermore, in the reaction in eqs 2 and 3 γ,δ-unsaturated selenoamides such as **10a'** may be initially formed. Then, the isomerization of the olefinic parts took place to result in the formation of α,β-unsaturated selenoamides.



(2)

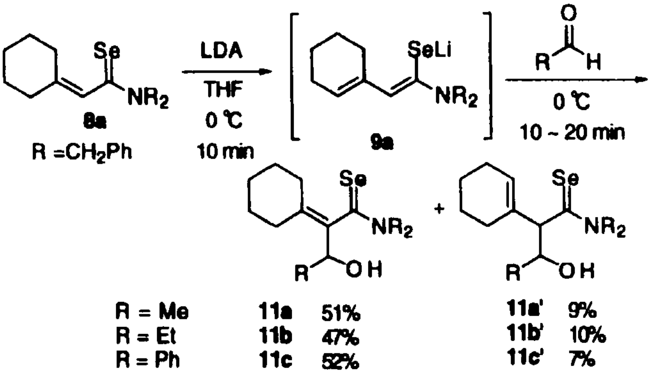


(3)



(4)

Then, lithium dieneselenolate **9a** was reacted with aldehydes (eq 5). Aldol-type condensation reaction of lithium dieneselenolate **9a** with acetaldehyde, propionaldehyde, and benzaldehyde proceeded smoothly to give β-hydroxy selenoamides **11a** – **11c** along with small amounts of β-hydroxy selenoamides **11a'** – **11c'**.



(5)

In summary, the reactivity of lithium eneselenolates and dieneselenoates derived from selenoamides toward carbonyl compounds was demonstrated. Michael addition of lithium ene selenolates to α,β-unsaturated esters and ketones was complete very rapidly. The highly diastereoselective aldol-type condensation reaction was attained by using the selenoamides having *N*,*N*-dibenzylamino group. The reaction of the lithium dieneselenolate with aldehydes selectively gave β-hydroxy selenoamides.

ACKNOWLEDGMENT

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