Selective Allylations of Selenothioic Acid *S*-Alkyl Esters with Allylic Bromides

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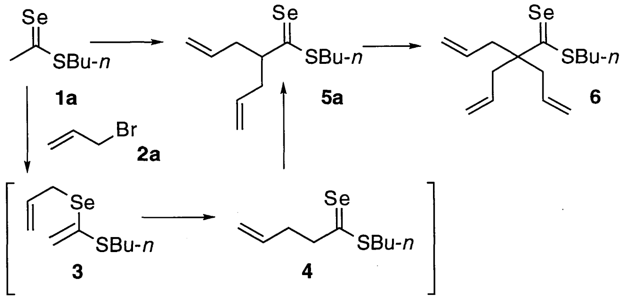
Allylations of selenothioic acid *S*-alkyl esters with allylic bromides in the presence of Et_3N in THF took place selectively at the α-position of selenocarbonyl group to give allylated products with high regio- and stereo-selectivity.

A number of new synthetic methods using organoselenium compounds have been developed over the last twenty years.[1] However, synthetic reactions using compounds having a carbon-selenium double bond are rare,[2] mainly due to their instability and cumbersome preparative procedures. Very recently, we have demonstrated selenoesters substituted with alkylthio or alkylseleno groups (RC(Se)SR', RC(Se)SeR') are relatively stable but highly reactive[3] similarly to seleno-aldehydes and -ketones. We report here the allylation of selenothioic acid *S*-alkyl esters with allylic bromides proceeds smoothly to lead to allylated products in a regio- and stereoselective manner.

Selenothioacetic acid *S*-butyl ester (**1a**) was treated with 3-bromo-1-propene (**2a**) (2 equiv) and triethylamine (2 equiv) in THF at 0 °C for 2 h (Scheme 1). Diallylation of **1a** took place selectively at the α-position of selenocarbonyl group to afford 1,6-heptadienyl ester **5a** in 58% isolated yield.[4]

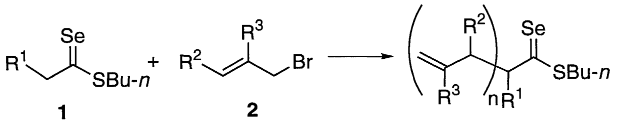


Scheme 1.

Scheme 1 outlines the plausible pathway of the allylation reaction of **1a** leading to ester **5a**. In the first step, the reaction of ester **1a** with allyl bromide may take place at selenium atom of **1a** to give allyl vinyl selenide **3** similarly to the reaction of thioamides with allylic bromides.[5] Then, the seleno-Claisen rearrangement[6] of **3** may occur to lead to ester **4**. In analogy to that, **4** may be converted to **5a**. The mixture obtained from the reaction of ester **1a** and bromide **2a** at –78 °C involved esters **1a**, **4**, and **5a** in a ratio of 38 : 32 : 30. This result has suggested that allylation of monoallylated ester **4** is competitive with that of ester **1a** even at low temperatures. The reaction of **1a** with **2a** (3 equiv) under reflux in THF for 48 h allowed for the introduction of three allyl groups to ester **1a** to afford ester **6** in 90% yield. In this reaction the construction of quaternary carbon center, among the most important processes in organic synthesis,[9] was realized in a single operation by the repetition of allylation of ester **1a** at the α-position of selenocarbonyl group.

The reaction of a variety of esters **1** with allylic bromides **2** was also carried out (Table 1).

Table 1. Allylation reaction of selenothioic acid *S*-butyl esters[a]

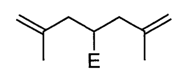
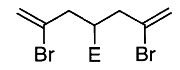
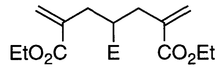
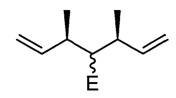
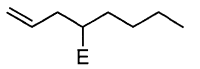
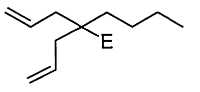
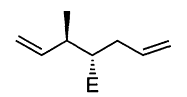
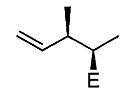


1 **2**

1a R^1 = H,
1b R^1 = *n*-Bu
1c R^1 = CH_2=CHCHCH_3
1d R^1 = CH_3

2a R^2 = R^3 = H
2b R^2 = H, R^3 = CH_3
2c R^2 = H, R^3 = Br
2d R^2 = H, R^3 = CO_2Et
2e R^2 = CH_3, R^3 = H

n = 1 ~ 3

Entry	Ester, Allylic bromide	Temp / °C Time / h	Product[b]	Yield[c]/ %
1	**1a, 2b**	0 °C 4 h	 E **5b**	59% (72%)[d]
2	**1a, 2c**	0 °C 4 h	 Br E Br **5c**	59%
3	**1a, 2d**	25 °C 23 h	 EtO_2C E CO_2Et **5d**	68%
4	**1a, 2e**	66 °C 22 h	 E **5e** (*meso*/*dl* = 82 : 18)	57%
5	**1b, 2a**	0 °C 3.5 h	 E **7**	99%
6	**1b, 2a**	66 °C 48 h	 E **8**	48%
7	**1c, 2a**	66 °C 24 h	 E **9**	51%
8	**1d, 2e**	0 °C 30 min	 E **10**	48%

[a] See Ref. 4 for typical experimental procedures. [b] E represents C(Se)SBu-*n*. [c] Isolated yields. [d] The reaction was carried out at 66 °C for 14 h.

Diallylation of ester **1a** with allylic bromides **2b**-**2e** also proceeded smoothly to give the products **5b**-**5e**, compounds which possess a 1,6-dienyl group,[10] in good to high yields (entries 1-4). Functional groups such as Br and ethoxycarbonyl group did not affect the reaction, although a longer reaction time was necessary in the reaction with **2d**. The process from **1a** to **5** is analogous to the reaction between diethyl malonate and allylic bromides leading to 1,6-diene-4-dicarboxylates.[11] However, the regiochemistry of the reaction of **1a** with **2e** is in sharp contrast to that of the reaction of diethyl malonate, in which less substituted allylic carbon atom of **5e** was selectively attached to the α-carbon atom of the ester.[11]

As for the reaction of α-substituted ester **1b** with 2 equiv of **2a**, monoallylation was attained below 0 °C (entry 5), whereas the reaction of **1b** under reflux in THF afforded selectively diallylated product **8** (entry 6). The reaction of ester **1c** with **2a** proceeded in a highly stereoselective manner to afford unsymmetrically substituted 1,6-dienyl ester **9** as a single stereoisomer (entry 7). The high regio- and stereoselectivity of the reaction was also observed for the reaction of ester **1d** with bromide **2e** (entry 8). The methyl substituted olefinic carbon of **2e** was selectively attached to the α-position of the starting ester, and only *erythro* isomer of **10** was obtained. Diallylation of **1a** with **2e** was achieved with high regioselectivity, and two *meso* forms of **5e** were produced in preference to the *dl* form of **5e** (entry 4).

In summary, we have demonstrated the highly efficient allylations of esters **1** with allylic bromides. The present reaction offers many synthetic advantages in terms of operational simplicity and high regio- and diastereoselectivity. Further synthetic applications of selenothioic acid *S*-alkyl esters on the basis of the unique reactivity of selenocarbonyl group are in progress.

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4 A typical experimental procedure is as follows: THF (5 mL), selenothioic acid *S*-butyl ester **1a** (0.196 g, 1.0 mmol), and 3-bromo-1-propene (**2a**) (0.17 mL, 2.0 mmol) were placed in a 20-mL flask. To this solution was added Et_3N (0.28 mL, 2.0 mmol). The flask was then cooled with stirring at 0 °C for 2 h. The mixture was poured onto water and extracted with ether (25 mL X 2). The organic layer was dried over magnesium sulfate and concentrated. The residue was purified by silica gel column chromatography using hexane as an eluent. The major fraction, being blue violet, afforded 159 mg of the product, which contained **5a** (58%).

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