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One-Pot Synthesis of Selenothioic Acid *S*-Alkyl Esters by the Reaction of Lithium Alkyneselenolates with Thiols

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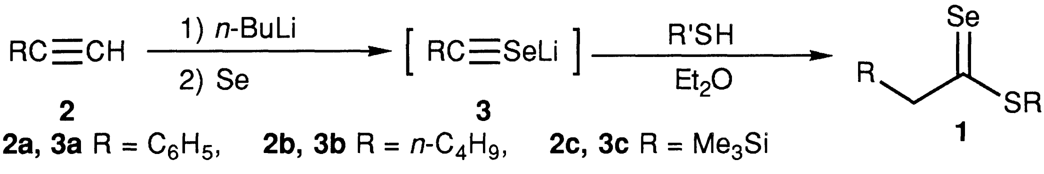
The reaction of lithium alkyneselenolates generated from lithium alkynides and selenium powder with a variety of thiols afforded selenothioic acid *S*-alkyl esters in moderate to high yields. The product yields were highly dependent on the substituents of the starting acetylenes. The formation of unstable *S*-aryl ester was confirmed by the enolization followed by alkylation.

Synthesis and synthetic applications of dithioic acid esters (RCS_2R'') have been widely developed for over 30 years.$^{1)}$ In contrast, no attention had been paid to the chemistry of selenothioic acid *S*-organyl esters **1** (also called selenonthiolesters) because of the lack of efficient synthetic methods as well as the misleading understanding of their instability.$^{2)}$ We have recently succeeded in the isolation of the esters **1** prepared by acid-catalyzed reaction of selenocarboxylic acid *Se*-alkynyl esters with thiols as a blue-violet liquid and proved their synthetic potentials.$^{3)}$ However, the more straightforward and efficient preparative methods of the esters **1** were necessary in the course of our studies on the properties of chalcogen isologues of carboxylic acid esters.$^{4)}$ Herein we report the one-pot synthesis of *S*-alkyl esters **1** by the treatment of terminal acetylenes, *n*-BuLi, Se, and thiols.$^{5)}$



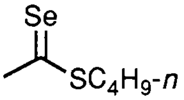
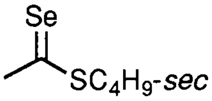
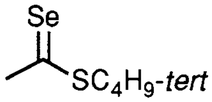
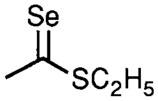
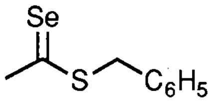
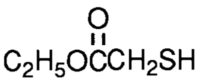
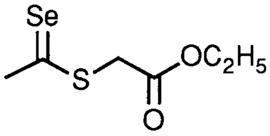
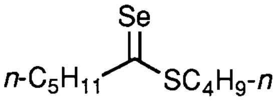
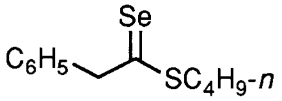
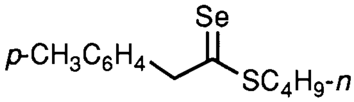
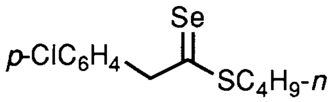
(1)

2a, 3a R = C_6H_5, **2b, 3b** R = *n*-C_4H_9, **2c, 3c** R = Me_3Si

Initially, phenylacetylene (**2a**), 1-hexyne (**2b**), and trimethylsilylacetylene (**2c**) were chosen as a precursor of lithium alkyneselenolate **3**. Butanethiol was added to the Et_2O solution involving lithium alkyneselenolate **3a** generated from the acetylene **2a**, *n*-BuLi and selenium powder at 0 °C. The desired ester **1** was not detected. Instead, the diselenafulvene **4** (R = C_6H_5) shown in Scheme 1 was mainly obtained. In contrast, during the reaction using the acetylene **2c** the reaction mixture clearly changed to light purple, that was indicative of the formation of the desired product **1**, and it gave 66% yield of the ester **1** (R = H, R' = C_4H_9-*n*).$^{6,7)}$

A variety of esters **1** were synthesized in a similar way using the acetylene **2c** and thiols as listed in Table 1. Noteworthy is that the secondary and even tertiary thiols could be used and gave the esters **1** in 54 and 42% yields, respectively (entries 2, 3). The reaction with ethanethiol gave the product only in low yields. This was overcome by slowly adding Et_2O solution of **3c** to the thiol (entry 4). The treatment of **3c** in Et_2O with α-toluenethiol afforded the ester in high yields (entry 5), although it gradually decomposed to form a yellow solid

Table 1. Synthesis of Selenothioic Acid *S*-Alkyl Esters [a)]

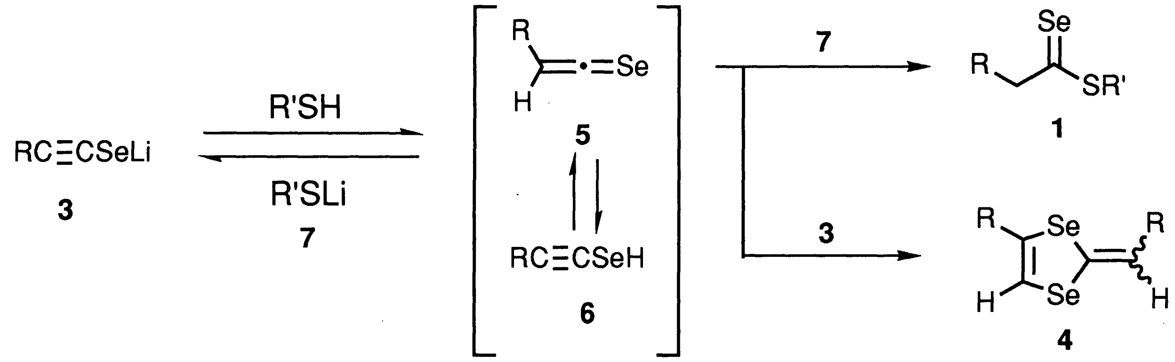
Entry	Acetylene	Thiol	Time/h	Product **1**	Yield/%
1	$Me_3SiC\equiv CH$ **2c**	*n*-C_4H_9SH	1.5		66
2	**2c**	*sec*-C_4H_9SH	2		54
3	**2c**	*tert*-C_4H_9SH	4		42
4	**2c**	C_2H_5SH	1		5 (51)[b)]
5	**2c**	$C_6H_5CH_2SH$	1		83
6	**2c**	 $C_2H_5O\overset{\overset{O}{\parallel}}{C}CH_2SH$	0.5		20
7	*n*-$C_4H_9C\equiv CH$ **2b**	*n*-C_4H_9SH	1.5		16 (58)[c)]
8	$C_6H_5C\equiv CH$ **2a**	*n*-C_4H_9SH	1.5		0 (29)[d)]
9	*p*-$CH_3C_6H_4C\equiv CH$	*n*-C_4H_9SH	1		19[c)]
10	*p*-Cl-$C_6H_4C\equiv CH$	*n*-C_4H_9SH	1		13[c)]

a) The reaction of lithium alkyneselenolate **3** generated from acetylene (1 or 2 mmol), *n*-BuLi, and Se (1 or 2 mmol) with thiol (1 or 2 mmol) was carried out with Et_2O (10 or 20 mL) as a solvent at 0 - 20 °C unless otherwise noted. b) Slow addition of Et_2O solution of **3c** to thiol at 0 °C. c) In THF. d) Slow addition of THF solution of **3a** to thiol at -78 °C.

because of the low thermal stability compared with other esters. The *S*-ethoxycarbonylmethyl ester could be prepared from the reaction with ethyl thioglycolate but in poor yields (entry 6).

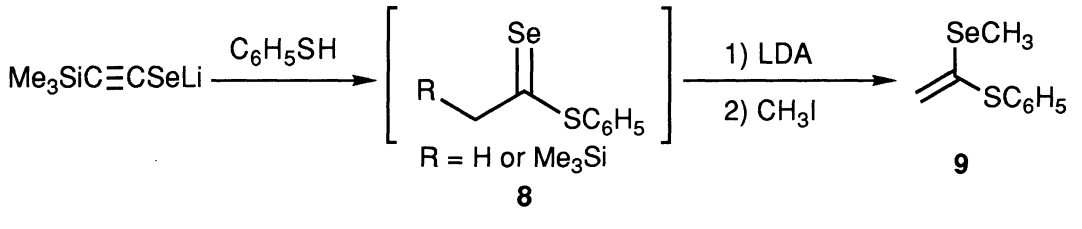
The reaction using the acetylenes **2a** and **2b** were examined again so as to yield esters having substituents at α-carbon in reasonable yields. After several unsuccessful attempts, the use of THF as a solvent gave 58% yield of the ester (entry 7). The slow addition of THF solution of lithium alkyneselenolate **3a** at -78 °C improved the product yields (entry 8), although the reaction using aromatic acetylenes could give the esters at most in 20% yields (entries 9, 10).

As shown in Scheme 1, the present reaction may proceed via selenoketene intermediate **5** generated by protonation of lithium alkyneselenolate **3** with thiol. At this stage the selenoketene **5** and alkyneselenol **6** appears to be in equilibrium.[8)] In solution the lithium alkyneselenolate **3** would also equilibrate with lithium thiolate **7**. When the nucleophilicity of **3** is higher than that of **7**, the attack of **3** to **5** would take place predominantly to give mainly diselenafulvene **4**.[9)] This would be the cases of the reaction of aromatic acetylenes. On the other hand, the product **1** may be formed by the attack of **7** to **5**. When alcohols were employed instead of thiols, **4** was the major product. This results may suggest that a stronger nucleophile is necessary to suppress the reaction of **5** with **3**. Moreover, the yields of esters from the acetylene **2c** are relatively compatible with the nucleophilicity of the thiols used.[10)]



Scheme 1.

Finally, benzenethiol was employed as a thiol. Similarly to the reaction with other thiols, the solution gradually changed to deep purple. However, when the mixture was concentrated, it quickly turned yellow and failed to give *S*-phenyl ester **8**.[11)] The formation of **8** was confirmed by the Se-alkylation as follows; the deep purple solution was treated with LDA at -78 °C and then with CH_3I to give 48% yield of ketene selenothioacetal **9** (eq. 2).



(2)

In summary, we have demonstrated that the treatment of lithium alkyneselenolate **2** with thiols provides one-pot synthetic method of selenothioic acid *S*-alkyl esters. The properties and synthetic applications of the esters will be reported in due course.

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Center, the Institute for Molecular Science, for assistance in obtaining 400 MHz ^{1}H and 100 MHz ^{13}C NMR spectra.

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7) When the ester **1** was purified, Me_3Si group in the starting acetylene **2c** was removed. It presumably occurred during the column purification since the distillation of the crude product gave the ester **1** (R = Me_3Si) together with the ester **1** (R = H). Alternatively, it may be possible that the elimination of Me_3Si group takes place in the presence of excess thiol after α-trimethylsilyl ester was initially formed.
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