Cadmium Acetate Mediated Conversion of Selenothioic Acid *S*-Alkyl Esters to Selenophenes and Ketene Selenothioacetals

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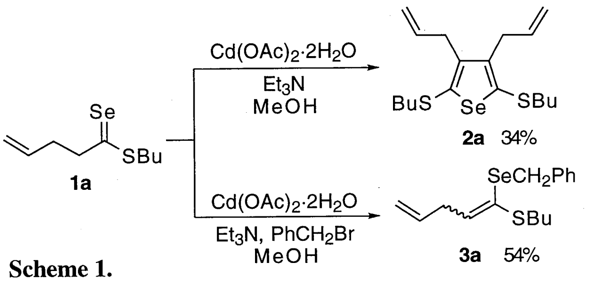
Selenothioic acid *S*-alkyl esters were treated with Et$_3$N and Cd(OAc)$_2$·2H$_2$O to give symmetrically substituted selenophenes, whereas the similar reaction in the presence of alkyl halides afforded ketene selenothioacetals in moderate yields.

The synthesis and characterization of esters bearing selenocarbonyl group have been extensively studied in recent years.[1] We have reported the synthetic methods of selenothioic acid *S*-alkyl esters (RC(Se)SR').[2-4] The esters were found to be highly reactive toward electron deficient alkynes[5] and allylic bromides.[6] As an extension of the synthetic utility of the esters, the esters were allowed to react with a variety of metal salts. We now report Cd(OAc)$_2$·2H$_2$O mediated conversion of the esters to selenophenes and ketene selenothioacetals.

The treatment of selenothiopent-4-enoic acid *S*-butyl ester (**1a**) with Cd(OAc)$_2$·2H$_2$O and Et$_3$N in MeOH at -78–65 °C for 3 h gave symmetrically substituted selenophene **2a** in 34% yield (Scheme 1).[7] On the other hand, the reaction of **1a** with Cd(OAc)$_2$·2H$_2$O in the presence of PhCH$_2$Br afforded ketene selenothioacetal **3a** in 54% yield with an *E* to *Z* ratio of 41 : 59.

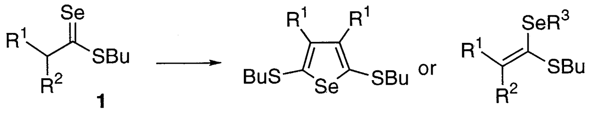


Scheme 1.

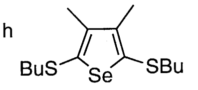
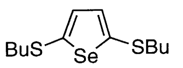
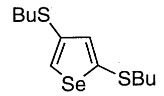
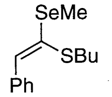
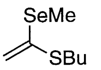
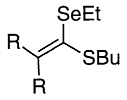
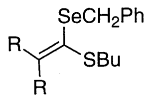
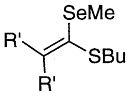
The results of the reaction of a variety of esters **1** are summarized in Table 1. Selenophene **2b** was successfully obtained from monosubstituted ester **1b** (entry 1), whereas the similar reaction of ester **1c** gave the corresponding selenophene only in 4% yield probably because of the steric congestion between two phenyl groups at the 3 and 4-positions of the selenophene ring. In the reaction of unsubstituted ester **1d** with Cd(OAc)$_2$·2H$_2$O, **1d** was consumed within 1 h at room temperature but it gave inseparable mixture. In contrast, the use of NiCl$_2$ as a metal salt improved the yield of selenophene **2c** (entry 2). Interestingly, the reaction of ester **1d** with ZnI$_2$ selectively gave unsymmetrically substituted selenophene **2d** (entry 3).

The synthesis of ketene selenothioacetals was attained by the reaction of esters **1c**–**1f** with alkyl halides in the presence of Cd(OAc)$_2$·2H$_2$O and Et$_3$N in MeOH (entries 4–8). As an alkyl halide, primary and benzylic halides gave products **3b**–**3f**.[8] As for ester **1c**, thermodynamically stable *E*-isomer[4] was predominantly obtained (entry 4). The proton abstraction from α–position of disubstituted esters **1e**, **1f** required higher reaction temperature (entries 6–8).

Table 1. Cd(OAc)$_2$·2H$_2$O Mediated conversion of selenothioic acid *S*-butyl esters to selenophenes and ketene selenothioacetals[a]

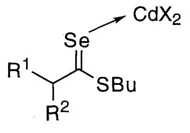


1b R^1 = CH$_3$ R^2 = H, **1c** R^1 = Ph, R^2 = H, **1d** R^1 = R^2 = H, **1e** R^1 = R^2 = CH$_2$=CHCH$_2$, **1f** R^1 = R^2 = CH$_2$=C(CH$_3$)CH$_2$

Entry	Ester Alkyl halide	Temp. /°C Time /h	Product[b]		Yield[c]/ %
1	**1b**	65 °C, 3 h		**2b**	44%
2[d]	**1d**	-78 °C, 2.5 h rt, 2 h		**2c**	49%
3[e]	**1d**	rt, 3 h		**2d**	32%
4	**1c** MeI	65 °C, 3 h		**3b**	85% (65 : 35)[f]
5	**1d** MeI	rt, 3 h		**3c**	38%
6	**1e** EtI	65 °C, 3 h		**3d**	51%
7	**1e** PhCH$_2$Br	65 °C, 3 h		**3e**	35%
8	**1f** MeI	65 °C, 3 h		**3f**	37%

[a] See Ref. 7 for typical experimental procedures. [b] R and R' represent CH$_2$=CHCH$_2$ and CH$_2$=C(CH$_3$)CH$_2$, respectively. [c] Isolated yields. [d] NiCl$_2$ was used. [e] ZnI$_2$ was used. [f] The ratio of *E*- and *Z*- isomers.

In the initial step of the present reaction selenium atom of esters **1** may coordinate to metal salts to form intermediates **4**. Then, proton abstraction from **4** with Et_3N may lead to metal eneselenolates **5**.[9] Alkylation of **5** may give ketene selenothioacetals **3a–3f**. When the reaction of ester **1e** was carried out in the absence of alkyl halides, diselenide **6** was formed as a major product.



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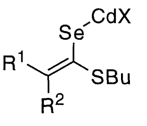

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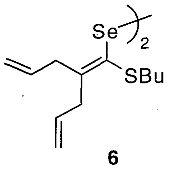

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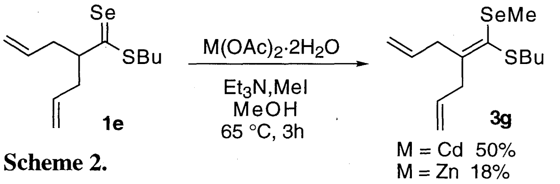
Finally, the reactivity of ester **1e** toward Zn and Cd salts was compared (Scheme 2). The reaction of **1e** with $Cd(OAc)_2{\cdot}2H_2O$ gave the product **3g** in 50% yield. In the similar reaction with $Zn(OAc)_2{\cdot}2H_2O$, the starting ester **1e** was also recovered in 39% yield along with 18% yield of **3g**.[10] These results clearly prove the high affinity of selenocarbonyl compounds toward cadmium salts rather than ordinary Lewis acids possessing high affinity to carbonyl compounds.[11]



Scheme 2.

In summary, we have demonstrated the high reactivity of esters **1** in the presence of $Cd(OAc)_2{\cdot}2H_2O$. The present reaction provides new synthetic ways to selenophenes[12] and ketene selenothioacetals.[13] Further synthetic applications of selenothioic acid *S*-alkyl esters on the basis of the unique reactivity of selenocarbonyl group are in progress.

References and Notes

1 For reviews: S. Kato, T. Murai, and M. Ishida, *Org. Prep. Proceds. Int.*, **18**, 369 (1986). F. S. Jr. Guziec, in "The Chemistry of Organic Selenium and Tellurium Compounds," ed by S. Patai; Z. Rappoport, John Wiley & Sons, New York (1987), Vol. 2, p 215; F. S. Jr. Guziec, in "Organoselenium Chemistry," ed by D. Liotta, Wiley-Interscience, New York (1987), p 277; A. Ogawa and N. Sonoda, in "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, Oxford (1991), Vol. 6, p 461; A. Ishii and J. Nakayama, in Comprehensive Organic Functional Group Transformations," ed by A. R. Katritzky, O. Meth-Cohn, and C. W. Rees, Pergamon, Oxford (1995), Vol. 5, p 505.

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3 T. Murai, A. Hayashi, T. Kanda, and S. Kato, *Chem. Lett.*, **1993**, 1469; T. Murai, Y. Ogino, T. Mizutani, T. Kanda, and S. Kato, *J. Org. Chem.*, **60**, 2942 (1995).

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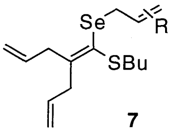
7 A typical experimental procedure is as follows: In a two-necked 20 mL flask, $Cd(OAc)_2{\cdot}2H_2O$ (0.267 g, 1 mmol) was dissolved in MeOH (7 mL). Then, the mixture was cooled to -78 °C, and to this were added selenothiopent-4-enoic acid *S*-butyl ester (**1a**) (0.236 g, 1 mmol) and Et_3N (0.14 mL, 1 mmol). It was stirred at -78 °C for 15 min and at 65 °C for 3 h. The reaction mixture was poured into ice/water. The organic layer was washed with saturated aqueous NH_4Cl solution and dried over sodium sulfate and concentrated. The residue was purified by silica gel column chromatography using hexane-CH_2Cl_2 as eluent. The major fraction, being yellow, afforded 67 mg of the product **2a** as a yellow liquid. **2a**: ^1H NMR (400 MHz, $CDCl_3$); δ 0.90 (t, J = 7.3 Hz, 6H, CH_3), 1.41 (sex, J = 7.3 Hz, 4H, CH_2), 1.62 (qui, J = 7.3 Hz, 4H, CH_2), 2.80 (t, J = 7.3 Hz, 4H, SCH_2); 3.39 (dt, J = 1.7, 7.3 Hz, 4H, CH_2), 4.90 (dd, J = 1.7, 17.1 Hz, 2H, =CH), 5.00 (dd, J = 1.7, 10.3 Hz, 2H, =CH), 5.84 (ddt, J = 5.6, 10.3, 17.1, 2H, =CH); $\{^1H\}^{13}C$ NMR (100 MHz, $CDCl_3$) δ 13.6, 21.8, 31.4, 33.6, 39.1, 115.3, 136.1, 137.4, 144.2. Found: C 55.94, H 7.53%. Calcd for $C_{18}H_{28}S_2Se$: C 55.78, H 7.28%.

8 When allylic bromides such as crotyl bromide and 2,3-dibromoprop-1-ene were employed as an alkylating agent, the mixture of ketene selenothioacetals **7** and esters **8**, which were formed through seleno-Claisen rearrangement[6] of **7**, was obtained.



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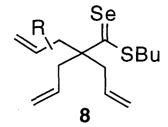

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9 Although the mechanistic detail of the reaction with $NiCl_2$ and ZnI_2 has not yet been disclosed, the former reaction may proceed via 3,3-sigmatropic rearrangement of the diselenide derived from **1d** analogous to **6**. On the contrary, two molecules of **1d** may undergo Claisen condensation via zinc eneselenolate in the presence of ZnI_2.

10 As other metal salts, $Mn(OAc)_3{\cdot}2H_2O$, $FeSO_4{\cdot}7H_2O$, and $Co(OAc)_2$ were stirred with ester **1e**, MeI, and Et_3N in MeOH at 65 °C for 3 h. The crude mixture mainly involved **1e**, and **3g** was not detected.

11 R. F. Childs, D. L. Mulholland, and A. Nixon, *Can. J. Chem.*, **60**, 801 (1982); P. Laszlo and M. Teston, *J. Am. Chem. Soc.*, **112**, 8750 (1990).

12 M. Renson, in "The Chemistry of Organic Selenium and Tellurium Compounds," ed by S. Patai and Z. Rappoport, John Wiley & Sons, New York (1986), Vol. 1, p 399; C. W. Bird, G. W. H. Cheeseman, in "Comprehensive Heterocyclic Chemistry The Structure, Reaction, Synthesis and Use of Heterocyclic Compounds," ed by A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford (1984), Vol. 4, p 935.

13 In contrast to the synthesis and reactions of ketene dithioacetals, the chemistry of ketene selenothioacetals has been studied to lesser extent.[2,4,14]

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