

Highly Efficient Generation of Ammonium Eneselenolates, Their Reactions and Electronic Properties

Toshiaki Murai, Shuuya Hayakawa, and Shinzi Kato*

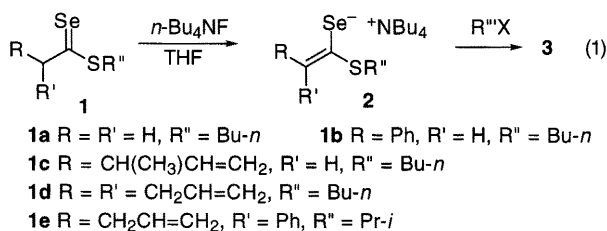
Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-1193

(Received January 12, 2000; CL-000038)

The ammonium eneselenolates generated from selenothioic acid *S*-esters and ammonium fluoride were reacted with carbon electrophiles to furnish ketene selenothioacetals with high stereoselectivities. The spectroscopic properties of the ammonium eneselenolates have suggested that the electrons on the selenium atom efficiently delocalize on the carbon-carbon double bond.

Conjugate anions such as allylic anions and enolates are one of the most important chemical species in organic chemistry.¹ The introduction of a heavier atom to conjugate anions is of great interest. For example, sulfur analogues of enolates have been extensively studied.² In contrast, only a limited examples of metal enolates involving a selenium atom, i.e., eneselenolates have been known to be formed from vinyl metallic species and a selenium atom.³ Very recently, we have disclosed that selenium counterpart of lithium enolates, i.e., lithium eneselenolates were generated by the treatment of selenothioic acid *S*-esters with LDA⁴ similarly to the ordinary esters and thioesters. We report herein highly efficient generation, reaction and electronic properties of ammonium eneselenolates.

The purple selenothioacetic acid *S*-butyl ester **1a** turned light brown almost instantly by adding a THF solution of tetrabutylammonium fluoride (eq 1).⁵ The aqueous workup of the reaction mixture gave a complex mixture, but a similar treatment of the ester **1a** with ammonium fluoride in the presence of a variety of carbon electrophiles gave the products **3**, which cannot be easily obtained by other methods.⁶ The results are summarized in Table 1.⁷



The use of methyl iodide and ethyl bromide afforded ketene selenothioacetals **3a** and **3b** within 1 min in 85 and 81% yields, respectively (entries 1 and 2).⁸ In the reaction of epibromohydrin the substitution reaction selectively took place at the bromine-substituted carbon atom to give the product **3c** (entry 3). The use of allylic halides gave the γ,δ -unsaturated selenothioic acid *S*-esters **1c**, **1f**, and **1g** in good yields (entries 4–6). In these reactions the carbon atoms having substituents such as methyl, ethoxycarbonyl, and phenyl groups were selectively introduced to the α -carbon atom to the selenocarbonyl group.

The deprotonation with ammonium fluoride was also appli-

Table 1. Reactions of selenothioic acid *S*-esters with *n*-Bu₄NF and carbon electrophiles^a

Entry	Ester	Carbon electrophile	Product	Yield/% ^b
1	1a	Mel		3a R' = Me 85%
2	1a	EtBr		3b Et 81%
3	1a			3c 47%
				3d 73%
4	1a		1c R' = Me 73%	
5	1a		1f R' = CO ₂ Et 61%	
6	1a		1g R' = Ph 66%	
	1b	Mel		3e 87% (<i>E</i> : <i>Z</i> = 54 : 46) ^c
7				82% (<i>E</i> : <i>Z</i> = 12 : 88) ^{c,d}
8				
9	1c	Mel		3f 68% (<i>E</i> : <i>Z</i> = 32 : 68) ^{c,e}
10	1c			3g 49% (<i>E</i> : <i>Z</i> = 5 : 95) ^{c,f}
11	1d	Mel		3h 62%
12	1e	Mel		3i 82% (<i>E</i> : <i>Z</i> = 5 : 95) ^c

^aSelenothioic acid *S*-esters **1** (1 mmol) were treated with a THF solution of *n*-Bu₄NF (1.5 mmol, 1.5 mL) and a carbon electrophile (1 mmol) at 0 °C for 30 min. ^bIsolated yields. ^cThe ratio of *E* and *Z* isomers of **3** determined by ¹H NMR is shown in parentheses. ^dThe ester **1b** was stirred with *n*-Bu₄NF for 30 min, and then methyl iodide was added to the reaction mixture. ^eThe ester **1c** was stirred with *n*-Bu₄NF for 2 h, and then methyl iodide was added to the reaction mixture. ^fThe ester **1c** was stirred with *n*-Bu₄NF for 2 h, and then benzoyl chloride was added to the reaction mixture at -78 °C. ^gR represents CH₂CH=CH₂.

cable to α -monosubstituted and disubstituted selenothioic acid esters **1b–1e**. The subsequent treatment of **2b–2e** with alkyl halides gave ketene selenothioacetals **3d–3h** (entries 7–12). Noteworthy is the ratio of *E* and *Z* isomers of the ketene selenothioacetal **3d**. The generation of ammonium eneselenolate **2b** was complete within one minute, but the quick addition of methyl iodide gave both isomers of **3d** in a nearly equal ratio (entry 7). The stereoselective formation of **3d** was attained by mixing the ester **1b** with ammonium fluoride for 30 min, followed by the addition of MeI (entry 8). Benzoylation of **2c** gave the product **3f** exclusively as a *Z*-isomer (entry 10). Even α -disubstituted esters **1d** and **1e** were converted to ketene selenothioacetals **3g** and **3h** with high stereoselectivity (entry 12).

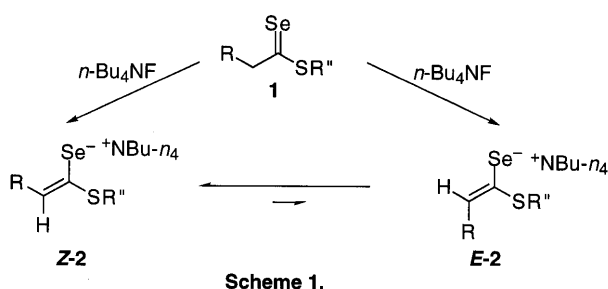
The ammonium salts **2** were stable enough to monitor NMR spectra. The results are shown in Table 2.

Table 2. Spectroscopic data of esters **1**, ammonium eneselenolates **2**, and ketene selenothioacetals **3**

compound	¹ H NMR ^a	¹³ C NMR ^a		⁷⁷ Se NMR ^a	
	H-C-C-Se	C-Se	C-C-Se	C-Se	¹ J _{C-Se}
1b	4.50	241.0	64.1	1570.7	224.3
2b	6.82	147.6	119.7	253.5	187.5
Z-3d	7.13	129.9	134.5	202.2	125.6
1c	2.91	242.1	64.4	1518.4	223.9
2c	5.12	136.4	109.1	282.8	175.7
Z-3e	5.88	127.3	142.1	231.4	122.6

^aNMR spectra were recorded in THF-*d*₈.

NMR spectra of ammonium eneselenolates **2b** and **2c** have clearly indicated that they were formed as the single stereoisomer of **2b** and **2c** despite the fact that the stereoselectivity of alkylation of **2b** depended on the reaction time as shown in Table 1. The stereochemistry of **2b** and **2c** was assigned as *Z*-geometries on the basis of their phase sensitive NOESY spectra. Thus the generation of the ammonium eneselenolates may take place with no stereoselectivity, but the isomerization of *E*-**2** to *Z*-**2** may smoothly proceed through the rotation of the carbon-carbon double bond in **2** (Scheme 1).⁹



The selenium atom of ketene selenothioacetals **Z-3d** and **Z-3e** was observed at 202.2 and 231.4 ppm, respectively, in ⁷⁷Se NMR spectra. It should be noted that those of ammonium salts **2b** and **2c** was shifted lower field by about 50 ppm. The selenium atom having negative charge is generally observed in the field higher than 0 ppm.¹⁰ In contrast, the selenium of ammonium salts **2b** and **2c** is strongly deshielded even if it has an anionic character. This may be explained by noting that the electrons on the selenium atom efficiently delocalize on the carbon-carbon double bond. Further evidence for the delocalization of the electrons in ammonium eneselenolates **2** is the coupling

constants between the carbon atom and the selenium atom of the ammonium salts **2b** (¹J = 187.5) and **2c** (¹J = 175.7). They are close to the normal value of the carbon-selenium double bond (ca. 200 Hz),¹¹ and this is in good agreement with a partial double bond character of the carbon-selenium bond in **2**. Thus, this properties may allow for the easy isomerization of two isomers of **2**.

In summary, we have found the first example of ammonium eneselenolates from selenothioic acid *S*-esters. Alkylations of ammonium eneselenolates provided highly stereoselective synthetic methods for ketene selenothioacetals. Electronic properties of eneselenolates have also been disclosed. Further studies on the application of the present system are in progress.

This work was supported in part by a Grant-in-Aid for Scientific Research on Priority Areas (No. 11120222) and by Grant-in-Aid for Scientific Research (No. 9355032) from the Ministry of Education, Science, Sports and Culture, Japan.

References and Notes

- For reviews: K. Afarinkia, *J. Chem. Soc., Perkin Trans. 1*, **1999**, 2025; A. R. Katritzky, M. Piffel, H. Lang, and E. Anders, *Chem. Rev.*, **99**, 665 (1999).
- P. Metzner and A. Thuillier, "Sulfur Reagents in Organic Synthesis," Academic Press, New York (1994); P. Metzner, "Topics in Current Chemistry," ed by P. C. B. Page, Springer-Verlag, Berlin (1999), Vol. 204, p. 128.
- J. V. Comasseto, L. W. Ling, N. Petragnani, and H. A. Stefani, *Synthesis*, **1997**, 373; K. Shimada, M. Asahida, K. Takahashi, Y. Sato, S. Aoyagi, Y. Takikawa, and C. Kabuto, *Chem. Lett.*, **1998**, 513.
- S. Kato, T. Komuro, T. Kanda, H. Ishihara, and T. Murai, *J. Am. Chem. Soc.*, **115**, 3000 (1993); T. Murai, M. Fujii, and S. Kato, *Chem. Lett.*, **1997**, 545; T. Murai, H. Endo, M. Ozaki, and S. Kato, *J. Org. Chem.*, **64**, 2130 (1999).
- Typical experimental procedure for the synthesis of ketene selenothioacetals: To a solution of THF (5 mL) and selenothioic acid *S*-butyl ester **1** (1 mmol) were added a THF solution of tetrabutylammonium fluoride (1.5 mmol) and alkyl halides (1 mmol) successively at 0 °C. The mixture was then stirred for 30 min at 0 °C, poured into water and extracted with Et₂O three times. The combined organic layers were dried over MgSO₄ and concentrated. The residue was chromatographed through silica gel column with hexane–Et₂O as eluent to give the corresponding ketene selenothioacetals **3**.
- A. Krief, in "Comprehensive Organometallic Chemistry," ed by E. W. Abel, F. G. A. Stone, and G. Wilkinson, Pergamon, Oxford (1995), Vol. 11, p. 515.
- All new compounds gave satisfactory spectral and microanalytical data.
- The high reactivity of the ammonium eneselenolate **2a** toward alkyl halides is in sharp contrast to the reactivity of lithium eneselenolates generated from **1a** and LDA. The methylation of lithium eneselenolates gave **3a** only in low yields.
- Very recently, the isomerization between *Z* and *E*-isomers of lithium enethiolates was observed for the first time: A. L. Schwan and M. D. Refvik, *Synlett*, **1998**, 96.
- The NMR sample was prepared as follows. The reaction mixture of esters **1** (0.5 mmol) and a THF solution of tetrabutylammonium fluoride (0.75 mmol) was concentrated in vacuo at room temperature over 1 h. Then, to the remaining viscous liquid was added THF-*d*₈ (0.8 mL).
- H. Duddack, *Prog. NMR Spectrosc.*, **27**, 1 (1995); T. M. Klapötke and M. Broschag, "Compilation of Reported ⁷⁷Se NMR Chemical Shifts," Wiley, New York, (1996).
- E. R. Cullen, F. S. Guziec, Jr., C. J. Murphy, T. C. Wong, and K. K. Andersen, *J. Am. Chem. Soc.*, **103**, 7055 (1981); J. Peng, M. E. Barr, D. A. Ashburn, J. D. Odom, R. B. Dunlap, and L. A. Silks III, *J. Org. Chem.*, **59**, 4977 (1994).