Tetrahedron Letters, Vol.32, No.50, pp 7427-7430, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

A Useful Method for the Synthesis of Selenoaldehydes with Electron-withdrawing Substituents

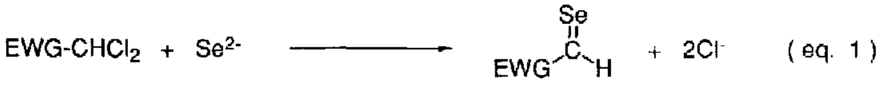
Masahito Segi,* Masakazu Kato, and Tadashi Nakajima

Department of Chemistry and Chemical Engineering, Faculty of Technology,
Kanazawa University, Kodatsuno, Kanazawa 920, Japan

Key Words: selenoaldehyde; electron-withdrawing group; Diels-Alder reaction; cycloadduct; regioselectivity

Abstract: *Several selenoaldehydes substituted with electron-withdrawing groups were synthesized by the reaction of the corresponding gem-dichlorides with selenium dianion, generated by the treatment of bis(tributyltin) selenide and tetrabutylammonium fluoride trihydrate, and were in situ trapped by 1,3-dienes to give Diels-Alder adducts.*

During the past decade, there has been great interest in the chemistry of reactive carbon-chalcogen double bonds.[1] We have previously reported simple and convenient methods for the direct conversion of aromatic and aliphatic aldehydes or ketones into the corresponding chalcogenocarbonyl compounds.[2] However, these methods are inapplicable to the preparation of electron-withdrawing substituted chalcogenoaldehydes because of the unstability of the starting aldehydes. Though the syntheses of reactive selenoaldehydes substituted with electron-withdrawing groups have been reported in recent years,[3] these methods have required the multi-step process to prepare the selenoaldehyde precursors[3a,b] or some reactions have been accompanied with the formation of by-products.[3c] In this letter we present a novel and useful one-step route to such reactive selenoaldehydes, which contains the reaction of geminally substituted dichlorides (EWG-$CHCl_2$) with Se^{2-} as shown in eq. 1. The starting dichlorides are commercially available or readily prepared by double chlorination of the hydrogen precursors.

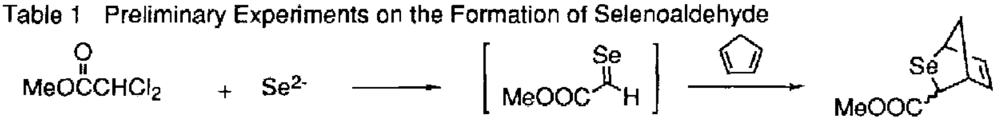


$$\mathrm{EWG{-}CHCl_2} + \mathrm{Se^{2-}} \longrightarrow \mathrm{EWG{-}\overset{\overset{\textstyle Se}{\|}}{C}{-}H} + 2\mathrm{Cl^-} \qquad (\text{eq. } 1)$$

EWG : electron-withdrawing group

There are several methods for generation of Se^{2-} species. So, at first we undertook preliminary experiments to find out optimal conditions for the formation of selenoaldehydes, in which methyl dichloroacetate and cyclopentadiene were used as a substrate and a trapping agent for selenoaldehydes, respectively. The results are shown in Table 1. Procedures using strong bases such as BuLi[4] resulted in moderate yields of the selenoaldehyde cycloadduct and concomitant side-reactions[5] (entries 1~3). In the case of Se^{2-} generation by a desilylation reaction of bis(trimethylsilyl) selenide with fluoride ion, the desired cycloadduct was little obtained (entry 4). On the other hand, application of a fluorodestannylation reaction by the combination of organotin selenide and fluoride ion[6] led to satisfactory yields of the cycloadduct (entries 5~12). Particularly, the combination of bis(tributyltin) selenide and tetrabutylammonium fluoride trihydrate is

Table 1 Preliminary Experiments on the Formation of Selenoaldehyde



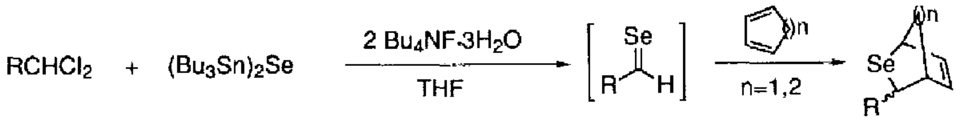
entry	method of Se^{2-} generation	solvent	temp. (°C)	yield of cycloadduct (%)[a]
1	Se / $LiBHEt_3$	THF	25	47
2	$(Me_3Si)_2Se$ / n-BuLi	THF	25	54
3	$(Bu_3Sn)_2Se$ / n-BuLi	THF	25	48
4	$(Me_3Si)_2Se$ / $Bu_4NF{\cdot}3H_2O$	THF	25	——[b]
5	$(Bu_3Sn)_2Se$ / $Bu_4NF{\cdot}3H_2O$	THF	25	79
6		THF	50	62
7		CH_3CN	25	77
8		DMF	25	82
9		C_6H_6	25	48
10	$(Bu_3Sn)_2Se$ / Bu_4NF-anhyd.	THF	25	75
11	$(Bu_3Sn)_2Se$ / CsF,18Crown6	THF	25	58
12		THF/CH_3CN	25	72

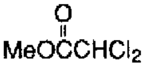
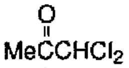
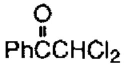
a) Isolated yield. b) Complex mixture was obtained.

a best choice (entries 5, 7, and 8). In this case, the use of polar solvents such as THF, CH_3CN, or DMF was effective, which suggests that this reaction involves an ionic pathway. Accordingly, on the basis of the results of preliminary experiments we chose a fluorodestannylation technique using $(Bu_3Sn)_2Se$ and $Bu_4NF{\cdot}3H_2O$ in THF as a method of Se^{2-} generation in the following experiments for the synthesis of several selenoaldehydes.

In an illustrated experimental procedure, a THF (10 ml) solution of $Bu_4NF{\cdot}3H_2O$ (1.0 mmol) was added slowly dropwise to a solution of $(Bu_3Sn)_2Se$ (0.5 mmol), methyl dichloroacetate (0.55 mmol), and cyclopentadiene (7.0 mmol) in THF (20 ml) at room temperature under an argon atmosphere. After stirring for 3 h, the reaction mixture was worked up with water. Extraction with ether and concentration *in vacuo*, followed by flash column chromatography on silica gel (hexane:dichloromethane=1:2 as eluent), gave the Diels-Alder adduct of the corresponding selenoaldehyde with cyclopentadiene in 79% yield. The results on the trapping of several selenoaldehydes by cyclopentadiene or cyclohexadiene are summarized in Table 2.[7] Selenoaldehydes substituted with electron-withdrawing groups such as MeOCO, MeCO, PhCO, or CN were efficiently trapped by cyclopentadiene to yield the cycloadducts, whereas, in the case when R is Ph or MeO, the generation of selenoaldehydes was unsuccessful under the same reaction conditions (entries 6 and 7). The *endo*/*exo* ratios were determined by integration of ^1H NMR signals corresponding to the proton α to selenium in the adduct. The specific proton in the *endo* adduct appears as a doublet having a *ca.* 3~4 Hz coupling with the adjacent bridgehead proton, whereas in the *exo* adduct, the corresponding proton is a singlet at higher field. In the present reaction except for entry 4, the *endo* isomer predominated, which is consistent with the results on stereochemistry of selenoaldehyde cycloadditions so far reported.[1] The *exo* preference (*endo*:*exo*=14:86, entry 4) observed in the cycloadduct of the PhCO-substituted selenoaldehyde with cyclopentadiene may result from the isomerization of the epimeric center adjacent to selenium under the basic reaction condition. For *endo*/*exo* ratios of seleno- and thioaldehyde cycloadducts with cyclopentadiene, in general, a thermodynamic mixture

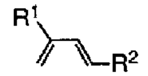
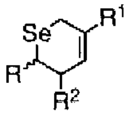
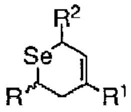
Table 2 Cycloaddition Reaction of Selenoaldehydes with Cyclic Dienes



entry	$RCHCl_2$	temp. (°C)	diene	cycloadduct yield(%)[a]	cycloadduct *endo* : *exo*[b]
1	 $\mathrm{MeO\overset{O}{\overset{\|}{C}}CHCl_2}$	25		79	59 : 41
2		50		24	80 : 20
3	 $\mathrm{Me\overset{O}{\overset{\|}{C}}CHCl_2}$	25		75	71 : 29
4	 $\mathrm{Ph\overset{O}{\overset{\|}{C}}CHCl_2}$	25		77	14 : 86
5	$NCCHCl_2$	25		70	56 : 44
6	$PhCHCl_2$	60		trace	——
7	$MeOCHCl_2$	65		——[c]	——

a) Isolated yield. b) Determined by ^{1}H NMR. c) Cycloadduct was not obtained.

Table 3 Cycloaddition Reaction of Selenoaldehydes with Unsymmetrical Acyclic Dienes

entry	dichloride	diene		cycloadduct yield(%)[a]	cycloadduct regioisomer ratio[b]		
	$RCHCl_2$ R =	 R^1=	R^2=		 "*ortho-para*"	:	 "*meta*"
1	-COOMe	Me	Me	55	86	:	14
2		H	Me	22	82	:	18
3		Me	H	30	63	:	37
4	-COMe	Me	Me	71	94	:	6
5	-COPh	Me	Me	64	86	:	14
6	-CN	Me	Me	26	89	:	11

a) Isolated yield. b) Determined by ^{1}H NMR.

contains more of an *exo* isomer than a kinetic mixture.[8]

Table 3[7] shows the results of Diels-Alder reaction of electron-withdrawing substituted selenoaldehydes with unsymmetrical acyclic 1,3-dienes, together with regioisomer ratios of the cycloadducts. The ratios were determined by integration of suitable resonances in the ^{1}H NMR spectrum. The cycloaddition of electron deficient selenoaldehydes with a methyl-substituted 1,3-butadiene yielded "*ortho-para*" type adducts, relative to substituent R, as the predominant products. These regiochemical results are consistent with those reported by Meinke and Krafft.[9] Cycloadducts shown in Table 3 except for entry 3, in fact, are a mixture of four isomers arising from both regioselectivity and facial selectivity in the cycloaddition reaction. The facial selectivity, as a whole, was not appreciably observed under the present reaction conditions, with *ca.* 1:1.

In conclusion, for the synthesis of electron-withdrawing substituted selenoaldehydes the described method provides a novel and useful approach. The combination of this method and our previously reported methods[2] for alkyl and aryl substituted selenoaldehyde synthesis will facilitate further studies on the chemistry of selenoaldehydes containing a variety of functionalities. Furthermore, this method is applicable to the synthesis of electron deficient selenoketones[10] and sulfur homologs, which will be reported as a full paper in due course.

Acknowledgements: Financial support from Grant in-Aids (Nos. 01750780 and 01550663) for Scientific Research from the Ministry of Education, Science and Culture of Japan and Research Aid of Inoue Foundation for Science (to M. S.) is greatly acknowledged. We also thank Nitto Kasei Co. Ltd. for the gift of tributyltin chloride.

References and Notes

1. For reviews on seleno- and tellurocarbonyl compounds, see the following. Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Baldwin, J. E.; Pergamon Press: **1986**; pp. 58-83. Guziec, Jr., F. S. *Organoselenium Chemistry*; Liotta, D., Ed.; John Wiley & Sons: **1987**; pp. 277-324. Guziec, Jr., F. S. *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; John Wiley & Sons: **1987**; Vol. 2; pp. 215-273. Okazaki, R. *Yuki Gosei Kagaku Kyokai Shi* **1988**, *46*, 1149-1163.
2. a) Segi, M.; Nakajima, T.; Suga, S.; Murai, S.; Ryu, I.; Ogawa, A.; Sonoda, N. *J. Am. Chem. Soc.* **1988**, *110*, 1976-1978. b) Segi, M.; Koyama, T.; Nakajima, T.; Suga, S.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1989**, *30*, 2095-2098. c) Segi, M.; Koyama, T.; Takata, Y.; Nakajima, T.; Suga, S. *J. Am. Chem. Soc.* **1989**, *111*, 8749-8751. d) Segi, M.; Kojima, A.; Nakajima, T.; Suga, S. *Synlett* **1991**, 105-106.
3. a) Meinke, P. T.; Krafft, G. A. *J. Am. Chem. Soc.* **1988**, *110*, 8671-8679. b) Kirby, G. W.; Trethewey, A. N. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1913-1922. c) Okuma, K.; Komiya, Y.; Kaneko, I.; Tachibana, Y.; Iwata, E.; Ohta, H. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1653-1657. d) Nakayama, J.; Akimoto, K.; Niijima, J.; Hoshino, M. *Tetrahedron Lett.* **1987**, *28*, 4423-4426.
4. We have reported the synthesis of unsymmetrical selenides utilizing a desilylation reaction of $(Me_3Si)_2Se$ with BuLi. Segi, M.; Kato, M.; Nakajima, T.; Suga, S.; Sonoda, N. *Chem. Lett.* **1989**, 1009-1012.
5. The side reactions are condensation of cyclopentadiene with aldehydes and vague reactions.
6. Harpp, D. N.; Gingras, M. *J. Am. Chem. Soc.* **1988**, *110*, 7737-7745.
7. All new compounds prepared by the present study exhibited satisfactory spectra (^{1}H NMR, IR, and MS).
8. For the *endo/exo* selectivity of selenoaldehyde cycloadditions, see Refs. 3a and 3b. For that of thioaldehyde cycloadditions, see Vedejs, E.; Stults, J. S.; Wilde, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 5452-5460.
9. Meinke, P. T.; Krafft, G. A. *Tetrahedron Lett.* **1987**, *28*, 5121-5124.
10. The reaction of dimethyl dichloromalonate with Se^{2-} in the presence of 2,3-dimethyl-1,3-butadiene in THF at 65°C for 4 h gave the cycloadduct of the corresponding selenoketone with the diene in 94% yield.

(Received in Japan 26 September 1991)