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An Efficient Construction of a Selenocarbonyl Unit by the Reaction of Acetal Derivatives with Bis(dimethylaluminum) Selenide

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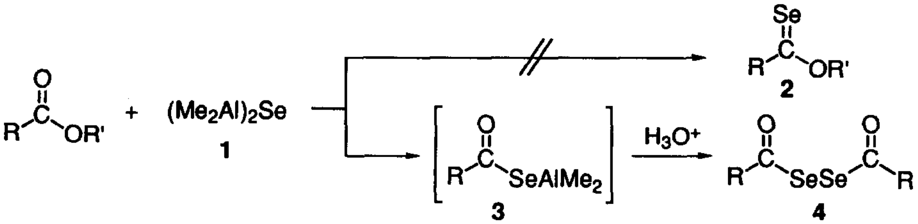
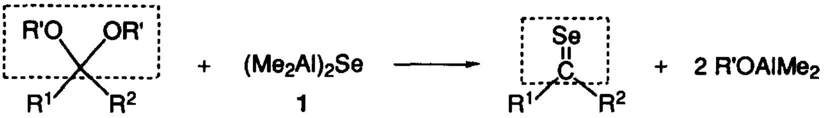
Key Words: selenocarbonyl group; selenoaldehyde; selenonester; selenocarbonate; bis(dimethylaluminum) selenide

Abstract: *The construction of a carbon-selenium double bond was achieved by the reaction of acetal derivatives with bis(dimethylaluminum) selenide, and a variety of selenocarbonyl compounds containing selenoaldehydes, selenoformamides, and selenonesters were efficiently synthesized.*

It is of considerable interest to study the synthesis and the reactivity of highly reactive compounds involving multiple bonds of heteroatoms in the chemistry of recent organic synthesis.[1] One of them is a series of compounds with a carbon-selenium double bond, a so-called selenocarbonyl group, which have been noted as building blocks in organic synthesis or important intermediates in the synthesis of selenium-containing molecules.[2] Recently, we have reported efficient and simple methods to directly convert a carbonyl group into a seleno- or tellurocarbonyl group using bis(dimethylaluminum) chalcogenides, $(Me_2Al)_2E$ (E=Se, Te), as a chalcogenating reagent.[3] However, the reaction of esters with $(Me_2Al)_2Se$ (**1**) did not give the desirable selenonesters (**2**) having a carbon-selenium double bond but gave bis(acyl) diselenides (**4**) which may be formed through acyl aluminum selenide intermediates (**3**) (eq. 1). This means that an aluminum atom in **1** functions effectively for the elimination of an alkoxy group. This result prompted us to investigate the construction of a carbon-selenium double bond by the reaction of acetal derivatives with $(Me_2Al)_2Se$ (eq. 2). In this letter, we describe a new and useful method for the synthesis of a variety of selenocarbonyl compounds such as selenoaldehydes, selenoformamides, and selenonesters.



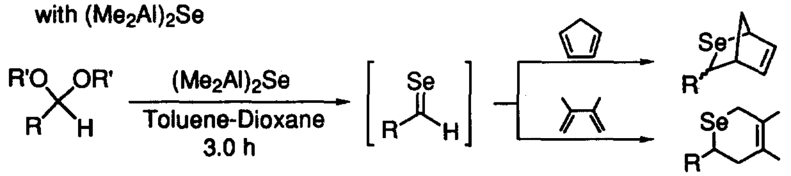
(eq. 1)



(eq. 2)

R^1 and/or R^2 = H, alkyl, aryl, amino, alkoxy, etc.

Table 1 Generation and Cycloaddition of Selenoaldehydes by the Reaction of Acetals with $(Me_2Al)_2Se$

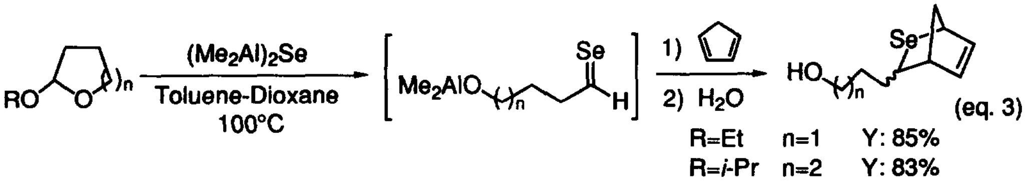


entry	acetal		diene	temp. (°C)	cycloadduct	
	R =	R' =			yield (%) c)	*endo* : *exo* d)
1	Ph	Me	CP a)	100	93	75 : 25
2	Ph	Me	CP	25	18	78 : 22
3	Ph	Me	DMB b)	100	95	——
4	$PhCH_2$	Me	CP	100	88	74 : 26
5	$PhCH_2$	Me	DMB	100	80	——
6	Me	Me	CP	100	51	71 : 29
7	Me	Me	CP	65	0 e)	——
8	*i*-Pr	Et	CP	100	80	80 : 20
9	*i*-Pr	Et	DMB	100	81	——
10	C_7H_{15}	Me	CP	100	86	77 : 23
11	C_7H_{15}	Me	DMB	100	96	——
12	$(CH_2O)_n$		DMB	100	78	——
13	$(CH_3CHO)_3$		CP	100	92	70 : 30
14	$(CH_3CHO)_3$		DMB	100	71	——

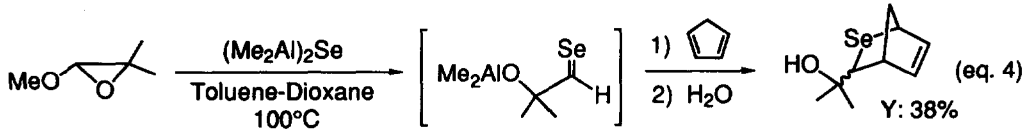
a) Cyclopentadiene. b) 2,3-Dimethyl-1,3-butadiene. c) Isolated yield.
d) Determined by ^1H NMR. e) Complex mixture was obtained.

The reaction of aromatic and aliphatic acetals with **1** in the presence of cyclopentadiene or 2,3-dimethyl-1,3-butadiene yielded Diels-Alder adducts of the corresponding selenoaldehydes and the diene in good yields.[4] The results are summarized in Table 1.[5] In all reactions, the yield of cycloadducts remarkably depended upon the reaction temperature, that is, these reactions necessitated such a high reaction temperature as around 100°C (entries 1, 2, 6, and 7). Diels-Alder reaction of a selenoaldehyde with a diene, in general, readily proceeds itself even at 0°C.[6] Accordingly, in the present reaction the step of the carbon-selenium bond formation by the nucleophilic attack of the electronegative selenium atom in **1** to the aluminum-coordinated acetal carbon may probably require a high reaction temperature. The cycloaddition reaction with cyclopentadiene preferentially gave the *endo* isomer, kinetically favorable isomer, in all cases as shown in Table 1, and this result means generation of a monomeric selenoaldehyde. When paraformaldehyde or paraldehyde was used as a substrate, the efficient generation of the corresponding selenoformaldehyde, the simplest selenoaldehyde, or selenoacetaldehyde was confirmed by good yields of cycloadducts with a diene, respectively (entries 12~14). Thus, this method is also useful for the synthesis of volatile selenoaldehydes. In this connection, our methods for the direct synthesis of selenoaldehydes from aldehydes as a starting material resulted in the low yields of the above cycloadducts because of the intractable volatile aldehydes.[7]

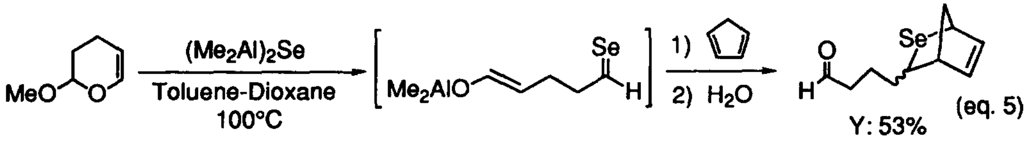
Cyclic acetals with one exocyclic acetal oxygen atom reacted with **1** in the presence of cyclopentadiene at 100°C to afford the cycloadducts of selenoaldehydes having a hydroxy group at the terminal position in good yields (eqs. 3 and 4). Similarly the reaction of dihydropyranyl methyl ether with **1** in the presence of cyclopentadiene at 100°C gave the Diels-Alder adduct with a side chain having a terminal formyl group in 53% yield (eq. 5). Thus the reaction of cyclic acetals with **1** made it possible to generate functionalized



(eq. 3)



(eq. 4)

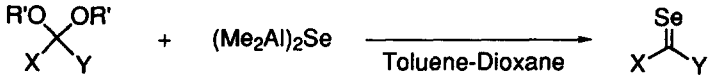


(eq. 5)

selenoaldehydes.

As mentioned above, it was turned out that two alkoxy groups of an acetal were substituted for a selenium atom by the use of **1** as a selenating reagent. Therefore, it is suggested that the reaction of orthoesters with **1** leads to the formation of selenonesters. As we would expect, triethyl orthobenzoate reacted with **1** at 50°C to give the corresponding *O*-ethyl selenobenzoate in 91% yield (Table 2, entry 16). As this compound is unstable to acidic media and light, the rapid isolation by flash column chromatography on florisil must be performed. Similarly, an aliphatic selenonester was also prepared in good yield (entry 17). In addition, the reaction of tetraethyl orthocarbonate with **1** afforded *O,O*-diethyl selenocarbonate in 74% yield as a liquid (entry 18). Though several methods for the synthesis of selenonesters have been reported,[8] in which the reactions of iminium esters with sodium hydrogen selenide or imidate esters with hydrogen selenide are involved, these methods have required the multi-step process or the use of poisonous reagents such as H_2Se. Our procedure described here provides a novel and practical approach to selenonester synthesis. Moreover, taking into account the result that the direct selenation of esters with **1** did not yield the desirable selenonesters as shown in eq. 1, the present method is of great value. A nitrogen substituted acetal reacted with **1** at 80°C to give the corresponding selenoformamide in a quantitative yield (entry 19). This method is as excellent for the preparation of selenoformamides as one reported in our previous paper.[3c]

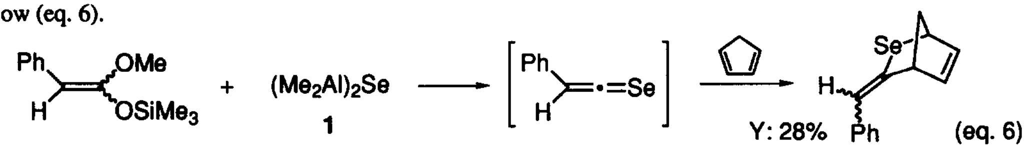
Table 2 Synthesis of Selenonesters, a Selenocarbonate, and a Selenoformamide



entry	substrate X =	substrate Y =	substrate R' =	temp. (°C)	time (h)	yield (%)[a]
15	Ph	MeO	Me	50	3.0	88 [b]
16	Ph	EtO	Et	50	3.0	91 [b]
17	Bu	MeO	Me	65	4.0	67 [b]
18	EtO	EtO	Et	80	2.5	74 [b]
19	Me_2N	H	Me	80	3.0	96 [c]

a) Isolated yield. b) Isolated by flash column chromatography on florisil.
c) Isolated by flash column chromatography on silica gel.

On the basis of this strategy for construction of a carbon-selenium double bond, next we tried to generate a selenoketene through the reaction of a ketene silyl acetal, readily prepared by silylation of ester enolates, with **1**. In the presence of cyclopentadiene, the expected selenoketene was trapped by the diene, but the yield was low (eq. 6).



(eq. 6)

In summary, the methodology presented here allows for the preparation of various selenocarbonyl compounds. Investigations into the scope and limitations of this methodology are in progress.

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4. A typical experimental procedure is exemplified by the synthesis of a selenobenzaldehyde cycloadduct. Trimethylaluminum (1.0 M solution in hexane, 1.1 ml, 1.1 mmol) was added to a solution of bis(tributyltin) selenide (215 mg, 0.5 mmol) in toluene (10 ml) under argon atmosphere, and the mixture was stirred for 3 h at 80°C. After the addition of dioxane (10 ml) as a co-solvent, cyclopentadiene (165 mg, 2.5 mmol) and benzaldehyde dimethylacetal (91 mg, 0.6 mmol) were added in that order. The mixture was subsequently heated at 100°C for 3 h and poured into water. Extraction with ether (20 ml x 3), drying over $MgSO_4$, and evaporation of the solvent followed by flash column chromatography on silica gel (hexane:dichloromethane=4:1) furnished the Diels-Alder adduct of selenobenzaldehyde in 93% yield.
5. All new compounds prepared by the present study exhibited satisfactory spectra (^{1}H NMR, IR, and MS).
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