

Preparation and Synthetic Utility of 2-Methylselenomethyl Allyl Methyl Selenide. A Valuable Precursor to 2-Silylmethylallyllithiums

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Abstract: 3-Lithio-2-[silylmethyl]propenes, easily prepared from 3-methylseleno-2-[silylmethyl]propenes by the cleavage of the C-Se bond, are useful intermediates for the preparation of a variety of functionalised allylsilanes. These allylsilanes are interesting building blocks, used for example, as annelating agents in the efficient synthesis of spiroketals by the Intramolecular Silyl-Modified Sakurai (ISMS) cyclisation. The methodology described in this article provides also an expedient route to a range of heterosubstituted methylselenopropenes, which are valuable precursors to a range of useful heterosubstituted allyllithium reagents. Finally, a one-step preparation of functionalised allylsilanes from readily available 3-methylseleno-2-[methylselenomethyl]propene is reported.

Some time ago, we reported the smooth reaction of 3-methylseleno-2-[trimethylsilylmethyl]propene **2a** with butyllithium to produce the lithiated allylsilane **3a** (Scheme 1).^[1]

This valuable intermediate has since been used for the synthesis of various annelating agents such as **5** required for the Intramolecular Silyl Modified Sakurai (ISMS) reaction. Condensation of silyl ether **5** with ortholactones has been shown to provide an efficient approach to spiroketals (Scheme 1).^[1] This flexible methodology has been applied to the synthesis of several natural products including insect pheromones and antiparasitic agents.^[2]

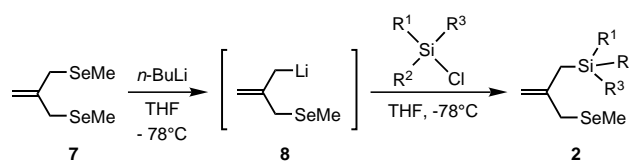
We were therefore rather surprised by a recent paper from Livinghouse^[3a] which described the transformation of **2a** to **3a** as a novel reaction, and quoted only one of our previous references in the field of allyl selenides, neglecting to mention our more recent publications.^[1,4] In order to emphasize our previous contributions to this area we would now like to describe some of our new results.

Although the synthesis of allylselenide **2a** can be easily achieved from sodium methylselenolate (from (MeSe)₂ and NaH, DMF, 20°C, 75%) and commercially available, but rather expensive, 3-chloro-2-

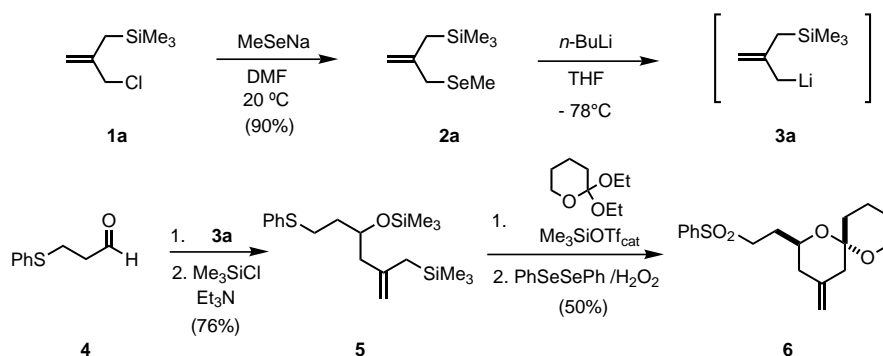
[trimethylsilylmethyl]propene **1a** (Scheme 1), we decided to develop a less expensive and more flexible route (Table 1, Entry 1) starting from 3-methylseleno-2-[methylselenomethyl]propene **7**.^[1] Addition of 1 equivalent of *n*-BuLi (THF, -78°C, 0.25h) smoothly generated the allyllithium species **8** by selective cleavage of one of the C-Se bonds. Subsequent trapping with a range of silylchlorides efficiently produced a variety of substituted allylsilanes **2** in excellent overall yield (Table 1).^[5]

3-Methylseleno-2-[triisopropylsilylmethyl]propene **2c** proved to be particularly acid sensitive and could only be purified by distillation after washing the crude reaction mixture with a saturated solution of aqueous sodium bicarbonate.

Table 1. Preparation of substituted allylselenides **2**



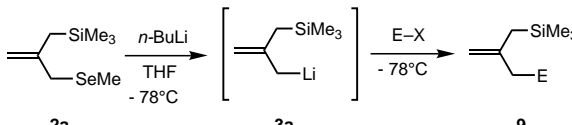
Entry	R ¹	R ²	R ³	Product	Yield
1	Me	Me	Me	2a	70 %
2	Me	Me	<i>t</i> -Bu	2b	73 %
3	<i>i</i> -Pr	<i>i</i> -Pr	<i>i</i> -Pr	2c	80 %
4	Me	Me	Ph	2d	77 %
5	Ph	Ph	Ph	2e	70 %



Scheme 1

The remaining C-Se bond of the selenopropenes **2** is efficiently cleaved in THF at -78°C upon reaction with *n*-butyllithium. The intermediate 3-lithio-2-[silylmethyl]propenes **3** have been quenched with a variety of electrophiles, affording the desired adducts in high yields, as shown in Tables 2 and 3. As can be seen from Table 2, 3-lithio-2-[trimethylsilylmethyl]propene **3a** has been reacted with a range of aldehydes and ketones, including those with α,β -unsaturation, as well as with epoxides. The silyl-functionalized unsaturated alcohols **9a-9h** have been obtained in good to excellent yields. Interestingly, enones were found to undergo exclusive 1,2-addition. No Michael-type products could be detected using the *in situ* generated allyllithium **3a**. Finally, condensation between sulfide **4** and reagent **3a** proceeded smoothly, affording the desired silylether **5** in excellent overall yield (Scheme 1). It is important to note that this transformation can not be effected successfully with a range of other organometallic derivatives akin to **3a**, thus demonstrating the synthetic value of allyllithium species such as **3**.

Table 2. Condensation of **3a** with various electrophiles



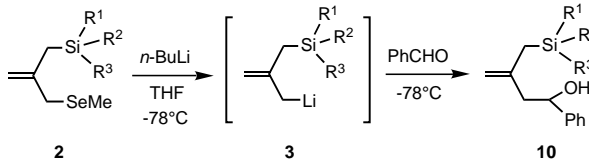
Entry	E-X	Product	Yield ^(a)
1	PhCHO		70 %
2			66%
3			78 %
4	TIPSO		41 %
5			73 % (b)
6			87 % (b)
7			79 %
8	HCHO		80 %

(a) All yields are for pure, isolated compounds. (b) Only the 1,2-adduct is formed

Furthermore, allylsilanes possessing different substituents on the silicon atom also underwent smooth metallation with *n*-BuLi to generate the corresponding allyllithium reagents **3**. Trapping with benzaldehyde

afforded the homoallylic alcohols **10** in excellent overall yields (Table 3).

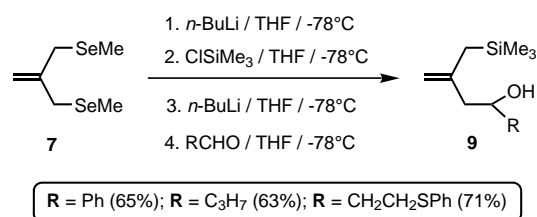
Table 3. Condensation of **3** with benzaldehyde



Entry	R ¹	R ²	R ³	Product	Yield ^(a)
1	Me	Me	<i>t</i> -Bu		87 %
2	Me	Me	Ph		72 %
3	Ph	Ph	Ph		82 %
4	<i>i</i> -Pr	<i>i</i> -Pr	<i>i</i> -Pr		80 %

(a) All yields are for pure, isolated products

It is worth noting that, in some cases, the direct transformation of *bis*-selenide **7** into either **9** or **10** could be realized in a single operation by the sequential addition of the previous reagents. Such a one-pot procedure results in increased overall yields compared to the two-step protocol (Scheme 2).



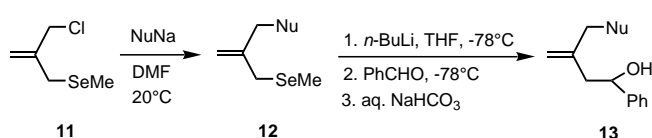
Scheme 2


Our results compare most favorably with alternative routes previously reported in the literature. For example, compound **9a** (Table 2, entry 1) has already been prepared by the thermally induced condensation of 3-tributylstannyl-2-(trimethylsilylmethyl)propene with benzaldehyde (150°C , 24h, 61%).^[6] The same reaction can be performed at much lower temperature, promoted by triethylaluminum (Et_3Al , -78 to 0°C , 42%).^[5] The reaction between the allylstannane, generated *in situ* from 3-iodo-2-trimethylsilylpropene and SnF_2 , and polycarbonyl compounds has been also reported.^[7]

3-Chloro-2-[trimethylsilylmethyl]propene **1a** is also a potential precursor of **3a**. Condensation of **1a** with cyclohexanone can be effected using lithium naphthalenide under Barbier-type conditions.^[8] However, the authors reported^[8] that the synthesis of **3a** could not be accomplished if cyclohexanone was omitted as the allylic reagent readily dimerized under these conditions. The use of selenium now allows the efficient synthesis of a whole series of 3-lithio-2-[silylmethyl]propenes **3** and their further use in synthesis. It is interesting to note that 3-chloro-2-[trimethylsilylmethyl]propene **1a** has been widely used in organic synthesis but most of the reactions described so far involve the substitution of either the allylsilane moiety^[9] or the halogen atom thereby introducing this four-carbon unit as an electrophilic species.^[9,10,11,12]

Our preparation of bis-selenide **7** from the corresponding dichloride and sodium methylselenolate (2 equiv., DMF) obviously implies the intermediate formation of 3-chloro-2-[methylselenomethyl]propene **11**. This monosubstitution product is isolated in good yield upon reaction of the dichloride **8** with methylselenol and potassium hydroxide in THF.^[4b] We felt that **11** could also be a valuable precursor to a series of related heterosubstituted propenes **12** and their subsequent condensation products **13** (Table 4).^[8]

Table 4. Synthesis and Condensation of Allylselenides **12**



Entry	Nu	Yield of 12		Yield of 13
1	MeO	80%	12a	90% 13a
2		60%	12b	60% 13b
3	EtS	92%	12c	81% 13c

Reaction of allylselenide **11** with O-, N- and S-nucleophiles smoothly afforded a range of 3-methylseleno-2-[heterosubstituted-methyl]propenes **12** (Table 4). All these derivatives reacted readily with *n*-butyllithium (1 equiv.) to produce the corresponding homoallylic alcohols **13** in good to excellent yield upon quenching with benzaldehyde.^[11,12]

In summary, we have shown that readily available 3-methylseleno-2-[methylselenomethyl]propene **7** is a useful precursor to a variety of silylsubstituted allyllithium reagents. These can be efficiently reacted with a range of electrophiles to afford the corresponding adducts with excellent chemoselectivity and high yields. Further work is directed towards broadening the scope of these useful reactions and using allyl selenides **2** as precursors of the corresponding radicals by cleavage of their C-Se bond. Full experimental details including further reactions of these interesting intermediates will be reported in a forthcoming publication.

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- All yields refer to pure, homogeneous compounds which were fully characterised by spectroscopic and analytic techniques. Typical spectroscopic data are:
Compound **2**: ¹H NMR (200 MHz; CDCl₃), δ (ppm) 1.65 (CH₂Si), 3.06 (CH₂Se), 4.5-4.6 (C=CH₂). ¹³C NMR (50 MHz, CDCl₃), δ (ppm) 24.8 (CH₂Si), 33.1 (CH₂Se), 110 (C=CH₂), 143 (C=CH₂).
Compound **9**: ¹H NMR (200 MHz; CDCl₃), δ (ppm) 1.4-1.5 (CH₂Si), 2.0 (CH₂CHOH), 2.85 (CHOH), 4.6 (C=CH₂). ¹³C NMR (50 MHz, CDCl₃), δ (ppm) 26.5 (CH₂Si), 46.4 (CH₂CHOH), 67.3 (CHOH), 110 (C=CH₂), 144 (C=CH₂).
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General procedure for the preparation of allylsilanes from 3-silyl-2-(methylselenomethyl)prop-1-ene **2 and carbonyl compounds or epoxides.**

n-Butyllithium (1.6 N in hexanes, 1.25 ml, 2 mmol) was slowly

added to a cooled (-78°C) solution of the 3-silyl-2-(methylselenomethyl)prop-1-ene (2 mmol) **2** in anhydrous THF (3 ml) under argon. The resulting yellow solution was stirred for 0.5 h at -78°C and then quenched by slow addition of a solution of the electrophile in anhydrous THF (2 ml). The mixture was stirred for 0.5 h at -78°C and then treated with a saturated aqueous sodium bicarbonate solution (2 ml). The mixture was allowed to warm to room temperature and extracted with ether (3 x 20 ml). The

combined organic extracts were washed with water (2 x 5 ml) and dried (MgSO₄). The solvents were removed under reduced pressure to afford a crude mixture which was further purified by chromatography on buffered (pH 7) silica gel (eluant: pentane/ether: 9:1) to give the pure adducts **9**. Yields are quoted in Table 2.

Note: the TIPS derivative **9d** is especially sensitive to traces of acid leading to unidentified decomposition products.