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The first isolation of allenylselenonium salts: their synthesis and properties as electrophiles

Shin-ichi Watanabe,[a,*] Yukio Miura,[b] Tatsunori Iwamura,[b] Hideko Nagasawa[b] and Tadashi Kataoka[c]

[a]*College of Pharmacy, Kinjo Gakuin University, 1723 Omori 2 chome, Moriyama-ku, Nagoya 463-8521, Japan*
[b]*Gifu Pharmaceutical University, 6-1 Mitahora-higashi 5 chome, Gifu 502-8585, Japan*
[c]*Yokohama College of Pharmacy, 601 Matanocho, Totsuka-ku, Yokohama 245-0066, Japan*

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Abstract—The first synthesis of allenylselenonium salts and their reactivities are described. The corresponding allenyl methyl selenides were alkylated with methyl trifluoromethanesulfonate to afford the desired compounds. Their reactions with active methylene carbanions produced furan, dihydrofuran or methylene cyclopropane derivatives via the Michael addition of nucleophiles to the selenonium salts.

The addition of nucleophiles to electron deficient allene compounds is one of the most widely used construction methods in organic synthesis.[1] In particular, stabilized carbon nucleophiles undergo the Michael-type addition toward allenes to afford highly functionalized materials[2] as well as heteronucleophiles.[3] Although the study on the reactivity of allenes bearing electron withdrawing groups has been fairly often reported, there are few examples of their reaction as Michael acceptors of allenylchalcogenonium salts.[4] For the reported reactions of allenylsulfonium salts with active methylene carbanions, the salts were generated in situ from the corresponding propargylic salts. Thus, the isolation of allenylchalcogenonium salts has not yet been achieved.

During the course of our work to investigate selenonium salts bearing unsaturated carbon–carbon bond groups, we developed alkynyl and alkenylselenonium salts as versatile synthons for organic synthesis.[5] Notably, their reactions with active methylene carbanions produced highly functionalized furan and cyclopropane derivatives, respectively, through the tandem Michael addition–cyclization routes.[5b,j] Therefore, these selenonium salts act as useful Michael acceptors. Due to their interesting features, allenylselenonium salts, which have still not been synthesized, should be targeted to determine their properties. We now report the first synthesis of the allenylselenonium salts and the study of their reactions with active methylene carbanions.

We planned the synthesis of the dimethylallenylselenonium salts by alkylation of the allenyl methyl selenide precursors. The racemic allenylselenonium salt **1a** was prepared as shown in Scheme 1. The reaction of (3-bromo-1-propynyl)benzene, which was produced from phenyl acetylene in high yield and in two steps,[6] with lithium methaneselenolate that had been generated from methyllithium and elemental selenium, gave methyl 3-phenyl-2-propynyl selenide **2** in a good yield. Although the isomerization of **2** to an allene did not proceed in good yield with various bases at room temperature, the desired allenyl selenide **3** could be obtained in 69% by the treatment with potassium *tert*-butoxide at 60 °C for 4 h. The methylation of the selenium atom in **3** with methyl triflate in ether at −40 °C for 72 h formed the allenylselenonium salt **1a** in 61% yield.[7] This salt **1a** was isolated as an oil, however, it was too hygroscopic to be isolated as stable crystals. Next, the preparation of an achiral one was examined in order to obtain a stable allenylselenonium salt. The reaction of 1-propyneselenolate with methyl iodide afforded methyl 1-propynyl selenide **4** in high yield. Allenyl selenide **5** was formed by the reaction of **4** with LDA followed by a treatment

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* Corresponding author. Tel.: +81 52 798 0180; fax: +81 52 798 0754; e-mail: swatana@kinjo-u.ac.jp

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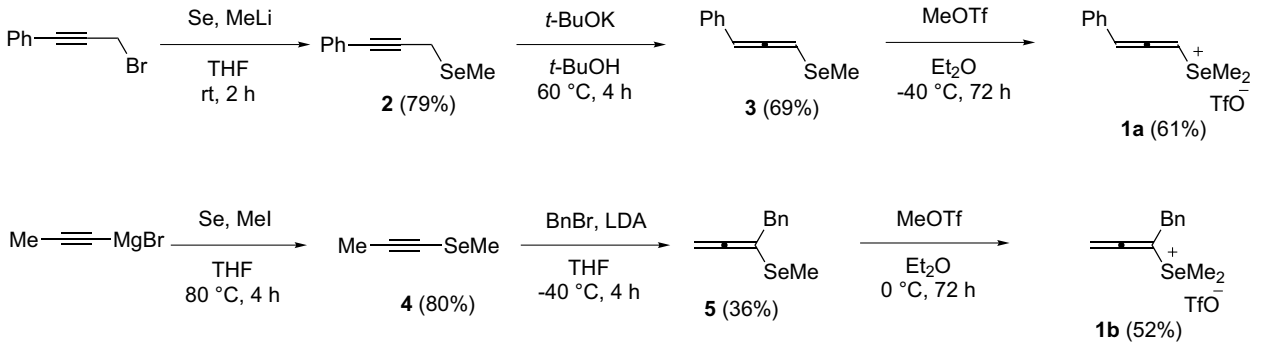
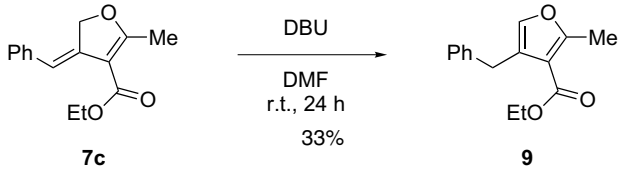


Scheme 1. Synthesis of allenylselenonium salts.

with benzyl bromide.[8] Selenide **5** reacted with methyl triflate to give the desired selenonium salt **1b** in 52% yield.[9] The structures of **1** were determined from its spectral data. The ^{13}C NMR spectrum indicated the presence of the quaternary carbons in the allenic moieties at δ 203.8 of **1a** and 202.5 of **1b**, respectively. In particular, two singlet peaks (δ 2.87 and 2.86) of diastereotopic methyl protons on the selenium atom in **1a** showed the existence of a chiral allenyl group.

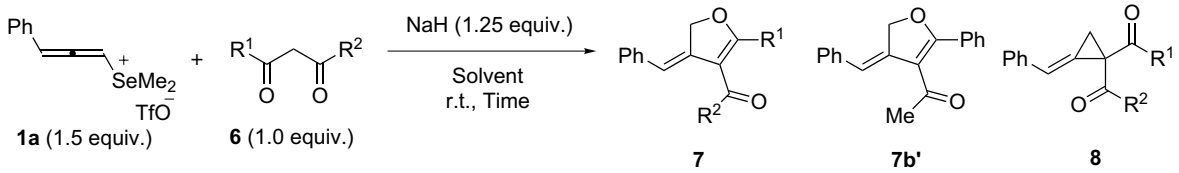
Table 1 shows the reactions of the allenylselenonium salt **1a** with active methylene carbanions.[10] We first conducted the reaction of **1a** with acetylacetone (**6a**) in DMF (entry 1) and *t*-BuOH (entry 2) at room temperature for 3 h to afford the dihydrofuran derivative **7a** in 32% and 42%, respectively, together with allenyl selenide **3** formed by the demethylation of the selenonium salt **1a** with a nucleophile. The benzoylacetone (**6b**) reacted with **1a** in *t*-BuOH to form the 4-benzylidene-3-benzoyl-2-methyl-4,5-dihydrofuran **7b** in moderate yield as a major product accompanied by a small amount of isomer **7b′** (entry 3). The reaction with ketoester **6c** in the mixture of *t*-BuOH and DMF gave **7c** in a better yield (entry 4). On the other hand, the methylene cyclopropane derivatives **8** were obtained from the reaction with the dibenzyl and diethyl malonates (entries 5 and 6). The structures of **7** and **8** were determined on the basis of their spectral data. The isomerization of compound **7c** under basic conditions produced a known furan derivative **9** in 33% yield and this transformation also supported the fact that **7** had a dihydrofuran skeleton (Scheme 2).[11] The stereochemistry of the exo double bond in compound **7** was determined to be the (*Z*)-geometry by the NOE enhancement between the methylene protons of the dihydrofuran ring and the *ortho*-protons of the *cis*-phenyl group (23%). On the other hand, the (*E*)-configuration of the methylene cyclopropane derivatives **8** was determined by the NOE experiment of **8b** showing the enhancement of the *ortho*-protons of the *cis*-phenyl group (5%) upon the irradiation of the cyclopropane's methylene protons.

Next, the reactions of the allenylselenonium salt **1b** with active methylene carbanions were carried out (Table 2).[10] Interestingly, the reactions of **1b** gave different products from those of **1a**. The tetra substituted furan derivative **10a** was produced in 60% yield by the reaction



Scheme 2. Isomerization of **7c** into **9**.

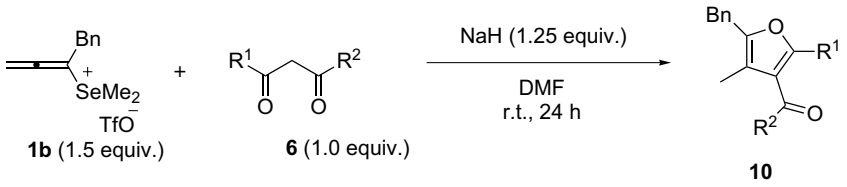
Table 1. Reactions of **1a** with active methylene carbanions



Entry	6	Solvent	Time (h)	Products	Yield (%)
1[a]	**6a**: $R^1 = R^2 =$ Me	DMF	3	**7a**	32
2	**6a**	*t*-BuOH	3	**7a**	42
3	**6b**: $R^1 =$ Me, $R^2 =$ Ph	*t*-BuOH	24	**7b**, **7b′**[b]	41, 7
4	**6c**: $R^1 =$ Me, $R^2 =$ OEt	*t*-BuOH–DMF (3:1)	24	**7c**	42
5	**6d**: $R^1 = R^2 =$ OBn	*t*-BuOH	12	**8a**	50
6	**6e**: $R^1 = R^2 =$ OEt	*t*-BuOH	24	**8b**	29

[a] NaH (1.0 equiv) was used.
[b] Determined by ^1H NMR.

Table 2. Reactions of **1b** with active methylene carbanions



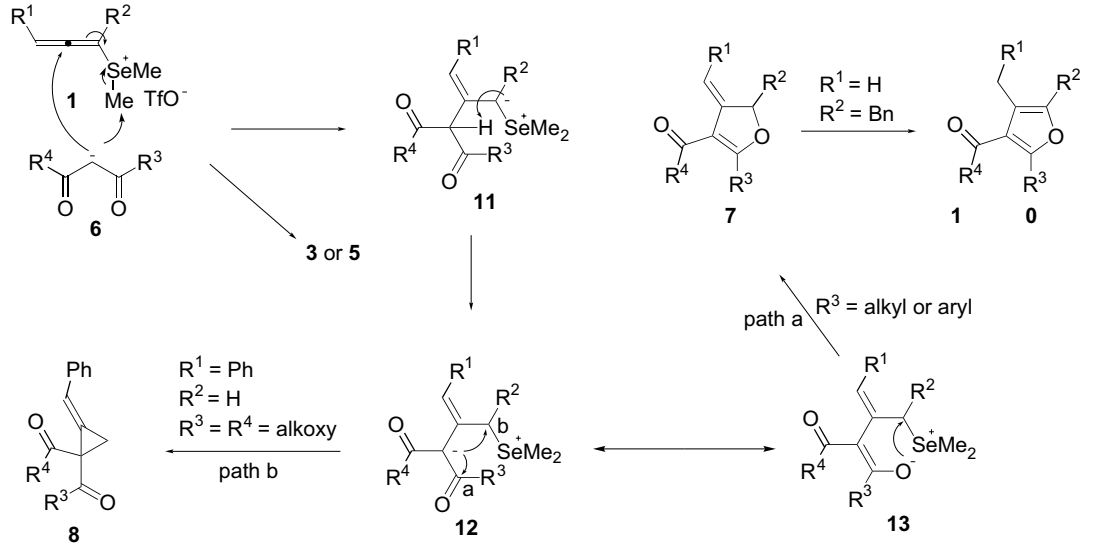
Entry	6	Products	Yield (%)
1	**6a**: $R^1 = R^2 = Me$	**10a**	60
2[a]	**6c**: $R^1 = Me$, $R^2 = OEt$	**10b**	56
3	**6d**: $R^1 = R^2 = OBn$	**10c**	47
4	**6e**: $R^1 = R^2 = OEt$	**10d**	39

[a] **1b** (1.1 equiv) and NaH were used.

of **1b** with acetylacetone in the presence of sodium hydride in DMF for 24 h (entry 1). Ketoester **6c** also reacted with **1b** to afford the corresponding furan **10b** in 56% yield (entry 2). Furthermore, the reactions with the dialkyl malonates produced the furan derivatives **10c** and **10d** (entries 3 and 4) different from the reaction forming methylenecyclopropanes **8** from **1a**. Selenide **5** generated through the pathway similar to the reaction with **1a** was detected by TLC as a by-product in all the reactions.

A plausible reaction mechanism of the allenylselenonium salts **1** with the carbanions is shown in Scheme 3. The selenonium ylides **11** are formed from the Michael addition of carbanion **6** to the allenylselenonium salt **1** followed by the deprotonation of an active methyne proton to generate betaine **12**. In the case of selenonium salt **1a**, the intramolecular nucleophilic attack of the enolate occurs to afford dihydrofuran derivatives **7** (path a) when the active methylene compound possesses not less than one acyl group. On the other hand, an active methyne carbanion of the ester derivatives **12** ($R^3 = R^4 =$ alkoxy) which has the greater electron density on the carbon attacks the primary α-carbon ($R^2 = H$) of the selenonio group to give methylene cyclopropane derivatives **8**, in spite of the ring strain of them (path b). Since carbanions **6** attack the center carbon of the allenyl moiety in **1** from the backside of the R^1 (phenyl) group, the geometry of R^1 and the nucleophiles is the *Z* (**7**) or *E* (**8**) configuration, respectively. Meanwhile, the reactions of **1b** with **6** proceed through path a regardless of the structure of the active methylene compounds. Due to the steric hindrance of the secondary α-carbon ($R^2 = Bn$) of the selenonio group, path b is inhibited and the enolization predominantly proceeds (path a) to produce the unstable dihydrofurans, which are easily transformed into the more stable furan derivatives **10** under the given reaction conditions.

In conclusion, the first synthesis and isolation of allenylselenonium salts **1** have been achieved by the alkylation of the corresponding allenyl methyl selenides with methyl triflate. The reactions of **1** and active methylene carbanions produced highly functionalized furan or dihydrofuran derivatives via the tandem Michael-intramolecular cyclization reaction. In particular, we developed a novel synthetic method of methylene cyclo-



Scheme 3. Plausible mechanism for the reactions of **1** with **6**.

propanes. Utilization of the allenylselenonium salts is currently under investigation.

Acknowledgments

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7. *Dimethyl(3-phenylpropa-1,2-dienyl)selenonium trifluoromethanesulfonate* (**1a**): To a solution of [3-(methylseleno)propa-1,2-dienyl]benzene (4.9 g, 23 mmol) in ether (50 mL) at −40 °C was slowly added methyl trifluoromethanesulfonate (5.1 mL, 46 mmol). The mixture was stirred for 72 h at the same temperature. Filtration of the precipitate and several washings with ether gave **1a** (2.60 g, 61%) as a pale yellow oil. This compound was pure enough for its analysis and subsequent reactions: ^{1}H NMR ($CDCl_3$) δ: 2.86 (3H, s, CH_3), 2.87 (3H, s, CH_3), 6.90 (1H, d, $J = 6.0$ Hz, CH), 6.96 (1H, d, $J = 6.0$ Hz, CH), 7.30–7.38 (5H, m, ArH); ^{13}C NMR δ: 23.9 (q), 24.2 (q), 86.4 (d), 105.2 (d), 120.4 (q), 128.0 (d), 129.3 (d), 129.6 (d), 129.8 (s), 203.8 (s); FABMS *m*/*z* 225 [$(M-TfO)^+$]; HRFABMS calcd for $C_{11}H_{13}Se$ [$(M-TfO)^+$] 225.0183, found 225.0188.
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10. *Caution*: Dimethyl selenide evolved by the reaction is a toxic material. All the operations should be carried out in a well-ventilated hood wearing appropriate protection.
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