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Novel generation of (α-ketovinyl)thioketenes as intermediates through tandem [2,3]/[3,3] sigmatropic rearrangement of alkynyl propargyl sulfoxides

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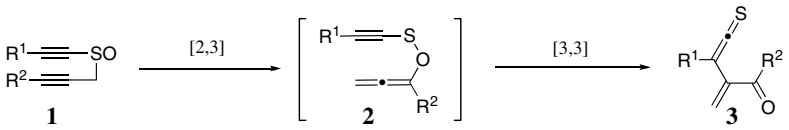
Abstract—Thermal reaction of alkynyl propargyl sulfoxides **1** afforded novel highly reactive (α-ketovinyl)thioketenes **3**. Trapping experiments using a primary or secondary amine, formation of furanophane **4**, through head-to-tail type dimerization, as well as direct observation using ^{1}H NMR elucidated the generation pathway of **3** through sequential [2,3]/[3,3] sigmatropic rearrangement.

In these decades, much attention has been focused on generation of chalcogenoketenes because of their attractive reactivities intrinsic to the heterocumulene structure as well as their potential in organic synthesis.[1–5] Among the research works concerning chalcogenoketenes, generation and trapping of allenylchalcogenoketenes through [3,3] sigmatropic rearrangement of alkynyl propargyl chalcogenides were widely studied,[5] and synthetic application of allenylthioketenes for natural products was also accomplished in our laboratory.[5e,f] Moreover, we established generation and trapping of a novel sulfene-type reactive species, allenylthioketene *S*,*S*-dioxides, by thermal reaction of alkynyl propargyl sulfones.[6] As a part of our research works on generation of highly reactive species from alkynyl propargyl chalcogenides and their oxidized forms, we were urged to investigate thermal reaction of alkynyl propargyl sulfoxides, which are assumed to undergo in two possible reaction modes, that is, [3,3] sigmatropic rearrangement[7] to give allenylthioketene *S*-oxides and [2,3] sigmatropic rearrangement[8] to give alkynesulfenates. Generally, [2,3] sigmatropic rearrangement of sulfoxide proceeds smoothly at relatively low temperature and in thermal reaction of alkynyl propargyl sulfoxide the latter reaction mode to give **2** is assumed to be preferable. Actually, tandem [2,3]/[3,3] sigmatropic rearrangement of aryl propargyl sulfoxides to give benzothiophene derivatives was reported by Majumdar.[9] On the basis of these results, alkynyl propargyl sulfoxides **1** were expected to undergo similar sequential rearrangements to give (α-ketovinyl)thioketene **3** as shown in Eq. 1. In this Letter, we wish to describe thermal reaction of alkynyl propargyl sulfoxides **1** to generate (α-ketovinyl)thioketenes **3**. Trapping and direct observation of reactive species **3**, as well as dimerization of **3** bearing silyl substituents to form furanophanes **4** are also reported.

Alkynyl propargyl sulfoxides **1** were prepared by treatment of alkynyl propargyl sulfides[5d] with *m*CPBA (1.1 equiv) in CH_2Cl_2 at 0 °C for 30 min and were



1 **2** **3** (1)

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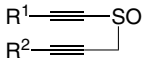
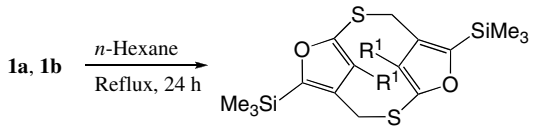


1a (R^1= Me_3Si, R^2 = Me_3Si); 79%
1b (R^1= *t*-$BuMe_2Si$, R^2 = Me_3Si); 88%
1c (R^1= Me_3Si, R^2 = Ph); 88%
1d (R^1= *t*-$BuMe_2Si$, R^2 =Ph); 85%
1e (R^1= *t*-Bu, R^2 = Me_3Si); 66%
1f (R^1= Ph, R^2 = Me_3Si); 78%

Figure 1. Alkynyl propargyl sulfoxides **1**.

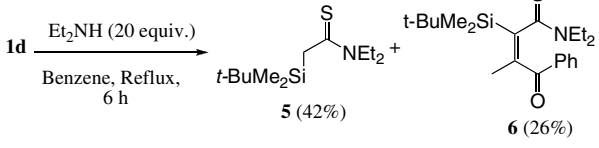
purified by column chromatography on silica gel (Fig. 1). Thermal reaction of **1** was carried out in hexane at refluxing temperature for 24 h and the crude mixture was subjected to column chromatography on silica gel. When both R^1 and R^2 were silyl groups, novel furanophanes **4**, which would be derived through dimerization of (α-ketovinyl)thioketenes **3** in head-to-tail mode, were afforded in good yields (Eq. 2). In contrast, thermal reaction of **1c**–**f**, bearing no silyl group as the R^1 or R^2 substituent, only gave insoluble polymeric matter in place of furanophanes **4**. Therefore, silyl group at R^1 stabilizing thioketene moiety of **3**[3a,5d] and silyl group at R^2, which induce nucleophilicity of oxygen atom through interaction of Si–C σ bond and carbonyl π orbital,[10] would be essential for the formation of furanophanes **4**. The structures of **4a** and **4b** were fully characterized by MS, IR, ^{1}H NMR, ^{13}C NMR and elemental analysis.[11] The dimeric structure of **4b** was finally determined by X-ray crystallographic analysis and an ORTEP drawing of **4b** is shown in Figure 2.[12] Interestingly, two furan rings tethered by $–CH_2S–$ moieties are distorted. C(1), O(1), C(4) and C(3) atoms are located almost on a same plane (C(1)–O(1)–C(4)–C(3) = 1.5(3)°) and C(2) atom bearing a TBDMS group is flipped to avoid the steric repulsion. Two double bonds of furan rings are distorted (C(3)–C(2)–C(1)–S(1) = 22.8(2)°; C(5)*–C(3)–C(4)–O(1) = 19.6(3)°). However, no significant change of line shape in ^{1}H NMR of **4b** in benzene-d_6 up to 100 °C suggests the rigid structure of **4b**, in spite of their plausible ring strain.

Direct observation of intermediate **3c** was also successfully carried out by ^{1}H NMR monitoring. When a $CDCl_3$ solution of **1c** was heated at 60 °C for 15 min



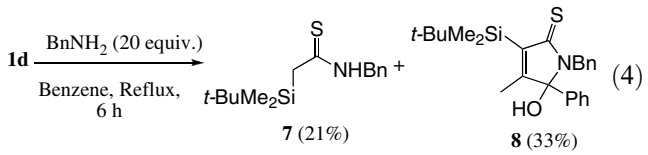
4a (R^1= Me_3Si); 82%
4b (R^1= *t*-$BuMe_2Si$); 61%

(2)



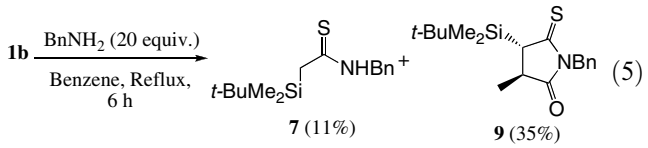
5 (42%) **6** (26%)

(3)



7 (21%) **8** (33%)

(4)



7 (11%) **9** (35%)

(5)

in an NMR tube, a set of new signals assignable to **3c** emerged at δ 0.36 (s, 9H; Me_3Si), 5.42 (s, 1H; *exo*-methylene), 5.69 (s, 1H; *exo*-methylene), and 7.79 (d, *J* = 8.6 Hz, 2H; *o*-H of phenyl group) along with those of precursor **1c**. However, the NMR signals became complicated along with diminishing the signals of **3c** through further heating of the solution. In contrast to thermal reaction of alkynyl propargyl sulfides,[5d] cyclobutenethione, a possible product through ring closure of **3c**, was not found at all in the resulting crude mixture.

Trapping of intermediary **3** was carried out using primary and secondary amines. Heating of a solution of **1d** in the presence of diethylamine (20 equiv) in refluxing benzene for 6 h afforded thioamide **5** and γ-keto-α,β-unsaturated thioamide **6** in 42% and 26% yields, respectively (Eq. 3). The (*E*) geometry of **6** was determined by NOE (25%) between the *t*-Bu of TBS group and the methyl group. When a benzene solution of **1d** was heated to reflux in the presence of benzylamine (20 equiv), thiolactam **8** was given in 33% yield along with thioamide **7** in 21% yield (Eq. 4). The structure of thiolactam **8** was confirmed by X-ray crystallographic

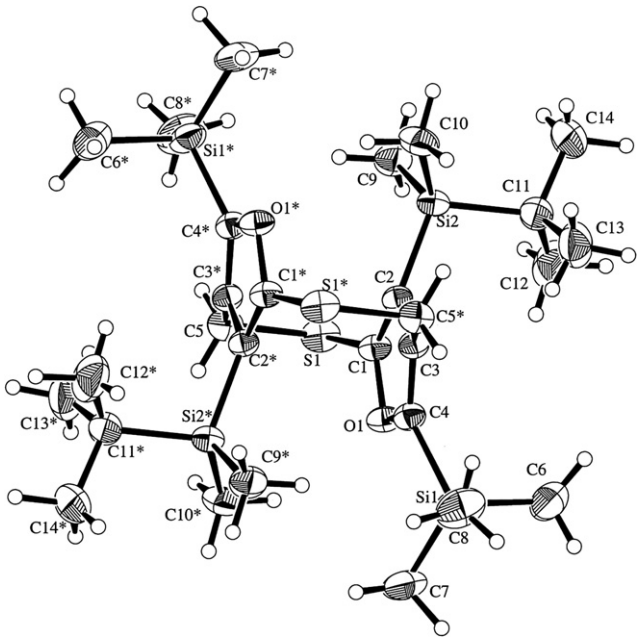


Figure 2. ORTEP drawing of **4b**.

analysis (Fig. 3).[13] Heating of a solution of **1b** in the presence of benzylamine (20 equiv) in refluxing benzene for 6 h afforded thioamide **7** and monothiosuccinimide **9** in 11% and 35% yield, respectively (Eq. 5). Trans configuration of TBS and Me groups of **9** was determined by the coupling constant ($J = 1.9$ Hz) of the protons at 3 and 4 positions as well as NOE (12%) between the hydrogen at the 3-position and methyl group. Products **6**, **8** and **9** were assumed to be trapping products of (α-ketovinyl)thioketenes **3** generated through tandem [2,3]/[3,3] sigmatropic rearrangement of **1**. Thermal reaction of **1e** bearing *t*-Bu which would stabilize the thioketene moiety in the presence of Et_2NH (20 equiv) in refluxing benzene for 6 h only gave *N*,*N*-diethyl-3,3-dimethybutanethioamide in 43% yield in place of a trapping product of **3e**. Analogous reaction of **1f** in the presence of Et_2NH gave a complex mixture including an enamine formed through Michael addition of amine to **1f**. In contrast, attempts for trapping of **3** using *N*-benzylbenzylideneimine, 2-methypyrroline, DMAD, DEAD or azobenzene afforded neither [4+2] nor [2+2] cycloadduct derived from (α-ketovinyl)thioketene **3**.

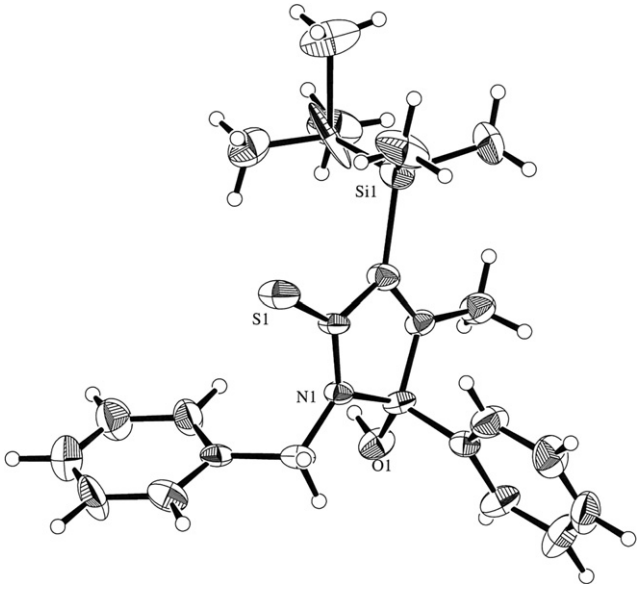
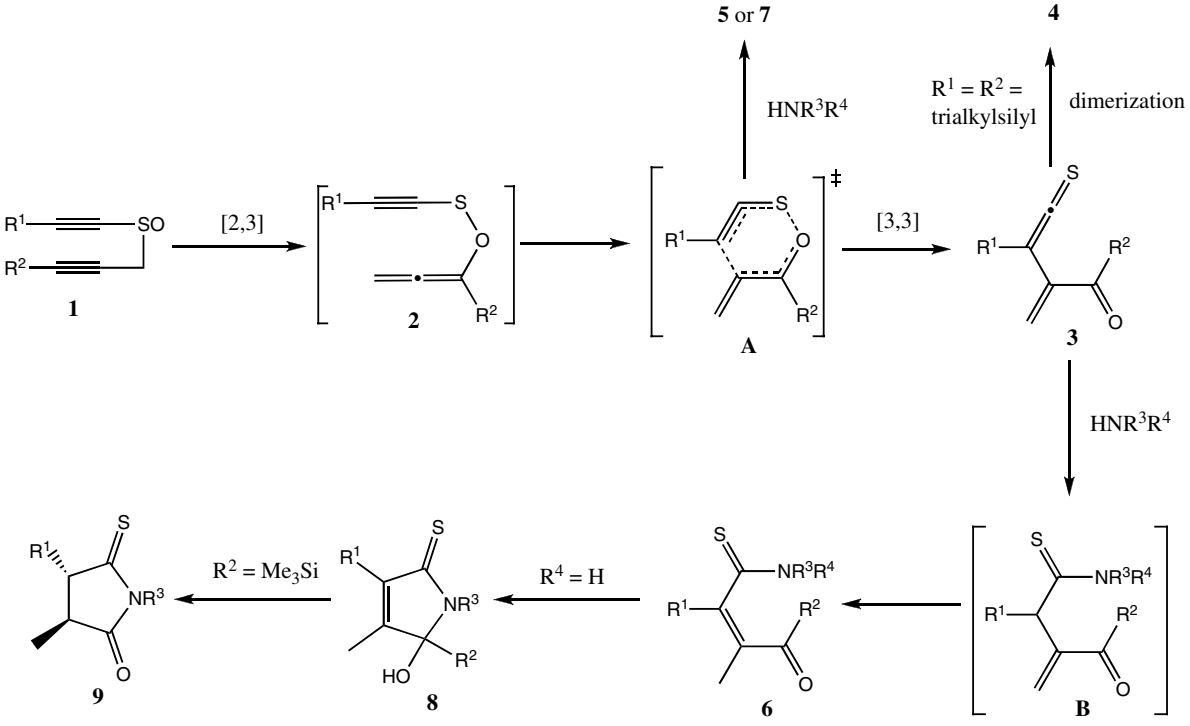


Figure 3. ORTEP drawing of **8**.

Plausible formation pathway of all products are shown in Scheme 1. Initially, [2,3] sigmatropic rearrangement of **1** occurred to generate sulfenic ester **2**. Then [3,3] sigmatropic rearrangement of **2** via transition state **A** proceeded to give intermediary (α-ketovinyl)thioketenes **3**. In the absence of amine, dimerization of **3** having silyl groups at both R^1 and R^2 proceeded to furnish furanophane **4**. On the other hand, when the similar heating was carried out in the presence of a primary or secondary amine, **3** reacted with amine to afford intermediary thioamide **B** and following isomerization gave **6**. Especially, in the case using a primary amine as a trapping reagent, **6** underwent cyclization leading to thiolactam **8.** Moreover, Brook-type rearrangement and isomerization of olefin into silyl enol ether followed by desilylation would occur to afford monothiosuccinimide **9**, when R^2 was silyl group. Low yields of trapping products **6**, **8** and **9** were presumably due to competitive attack of the amine to **A** of biradical character leading to thioamide **5** and **7**. In conclusion, thermal reaction of alkynyl propargyl sulfoxides **1** afforded novel (α-ketovinyl)thioketenes **3** via tandem [2,3]/[3,3] sigmatropic rearrangement. All the results of trapping experiments using amine, formation of furanophanes **4** through



Scheme 1. Plausible formation mechanism of products.

head-to-tail type dimerization, as well as direct NMR observation elucidated the generation of **3**. Further investigation on synthetic aspect of **3** as key intermediates for heterocyclic compounds is in progress in our laboratory.

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11. Compound **4a**: Colorless prisms: mp 153.2 °C (dec). MS (*m*/*z*): 512 (M^+, 37%), 439 (M^+-Me_3Si, 12%), 241 ($M^+/2-Me$, 64%), 73 (Me_3Si, bp). IR (KBr): 2958, 2897, 1423, 1248, 1114, 829, 633 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 18H), 0.34 (s, 18H), 3.81 (d, $J = 10.8$ Hz, 2H), 4.28 (d, $J = 10.8$ Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 0.0 (q), 2.2 (q), 35.9 (t), 137.0 (s), 138.7 (s), 150.1 (s), 162.5 (s). Anal. Calcd for $C_{22}H_{40}O_2S_2Si_4$: C, 51.51; H, 7.86. Found: C, 51.60; H, 7.98.
Compound **4b**: Colorless prisms: mp 166.9–168.3 °C (dec). MS (*m*/*z*): 596 (M^+, 5%), 73 (Me_3Si, bp). IR (KBr): 2954, 1471, 1416, 1248, 1032, 782 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.32 (s, 18H), 0.35 (s, 6H), 0.50 (s, 18H), 0.57 (s, 6H), 3.83 (d, $J = 10.8$ Hz, 2H), 4.26 (d, $J = 10.8$ Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −4.6 (q), −2.8 (q), −0.3 (q), 17.8 (s), 25.9 (q), 36.4 (q), 131.9 (s), 138.8 (s), 151.6 (s), 161.9 (s). Anal. Calcd for $C_{28}H_{52}O_2S_2Si_4$: C, 56.32; H, 8.78. Found: C, 56.52; H, 8.83.
12. *Crystal data for* **4b**: $C_{28}H_{52}O_2S_2Si_4$, $M_w = 597.18$, colorless prism, triclinic, $P\bar{1}$(#2), $a = 11.062(3)$ Å, $b = 16.75(1)$ Å, $c = 9.986(3)$ Å, $\alpha = 91.86(4)°$, $\beta = 106.12(2)°$, $\gamma = 93.99(5)°$, $V = 1771(1)$ Å^3, $Z = 2$, $D_{calcd} = 1.090$ g/cm^3, μ(Mo Kα) = 3.04 cm^{-1}, $R = 0.043$, $R_w = 0.043$. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC633770.
13. *Crystal data for* **8**: $C_{24}H_{31}NSiSO{\cdot}0.5C_6H_6$, $M_w = 448.72$, yellow needle, monoclinic, $P2_1/c$(#14), $a = 10.5585(8)$ Å, $b = 22.857(2)$ Å, $c = 11.938(1)$ Å $\beta = 106.933(3)°$, $V = 2756.2(4)$ Å^3, $Z = 4$, $D_{calcd} = 1.081$ g/cm^3, μ(Mo Kα) = 1.78 cm^{-1}, $R = 0.091$, $R_w = 0.089$. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC633771.