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Trialkylsilyl Group-Directed Regioselective Transformations of 2-(Alk-1-yn-1-yl)-2-(trialkylsilyl)-1,3-dithianes to Alkynylcyclopropanes and Enynes

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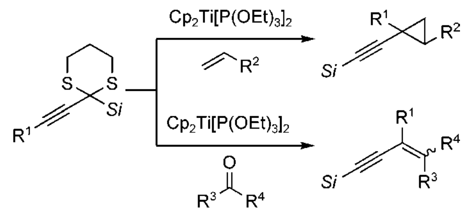
ABSTRACT

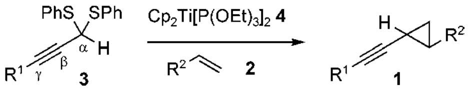


The Cp$_2$Ti[P(OEt)$_3$]$_2$-promoted reaction of 2-(alk-1-yn-1-yl)-2-(trialkylsilyl)-1,3-dithianes with 1-alkenes regioselectively produced [(trialkylsilyl)-ethynyl]cyclopropanes with a formal allylic rearrangement. The reaction of the thioacetals with ketones proceeded with the same regioselectivity to produce 1-(trialkylsilyl)alk-3-en-1-ynes predominantly. It is suggested that these reactions proceed via the formation of titanium α-(silylethynyl)-carbene complexes Cp$_2$Ti=C(R)C≡C*Si* in preference to their regioisomers, α-silylalkynylcarbene complexes Cp$_2$Ti=C(*Si*)C≡CR.

We have developed a variety of synthetic reactions utilizing a thioacetal−titanocene(II) system, in which titanium carbene complexes are assumed to be formed as active intermediates.[1] This methodology, however, suffers the drawback that the formation of intermediary organotitanium species is seriously affected by steric hindrance;[2] hence thioacetals prepared from ketones cannot be employed except for those of less hindered ketones such as cyclobutanone.[3]

Recently, we reported the preparation of alkynylcyclopropanes **1** by the reaction of terminal olefins **2** with the alkynylcarbene complexes generated by the desulfurization of thioacetals of α,*β*-acetylenic aldehydes **3** with the titanocene(II) species Cp$_2$Ti[P(OEt)$_3$]$_2$ **4** (Scheme 1).[4] We expected that the cyclopropanation could be extended to the α-substituted alkynyl thioacetals because a less bulky alkynyl group would alleviate the steric crowding of the thioacetals. After several attempts, we found that the reaction proceeded to afford the alkynylcyclopropanes **5** even in the case when the thioacetals **6** bearing a bulky trialkylsilyl group at the α-position were employed (Scheme 2).

Scheme 1



The treatment of 2-(5-phenylpent-1-yn-1-yl)-2-(trimethylsilyl)-1,3-dithiane **6a** with 2 equiv of titanocene(II) reagent

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(1) (a) Takeda, T. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, 2002; p 480. (b) Takeda, T.; Tsubouchi, A. In *Modern Carbonyl Olefination*; Takeda, T., Ed.; Wiley-VCH: Weinheim, 2004; p 178.

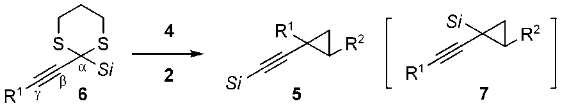
(2) Takeda, T.; Sasaki, R.; Fujiwara, T. *J. Org. Chem.* **1998**, *63*, 7286.

(3) Fujiwara, T.; Iwasaki, N.; Takeda, T. *Chem. Lett.* **1998**, 741.

(4) Takeda, T.; Kuroi, S.; Yanai, K.; Tsubouchi, A. *Tetrahedron Lett.* **2002**, *43*, 5641.

10.1021/ol0486066 CCC: $27.50

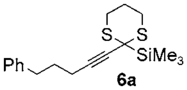
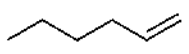
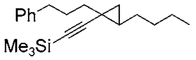
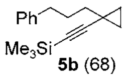
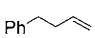
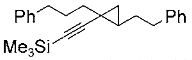
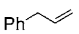
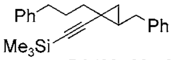
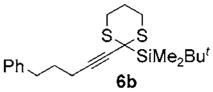
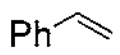
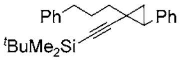
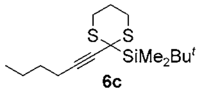
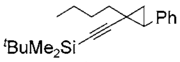
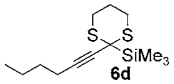
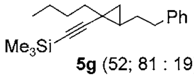
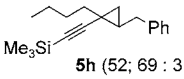
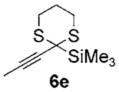
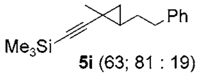
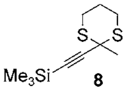
Scheme 2



Si = Me$_3$Si or *t*BuMe$_2$Si

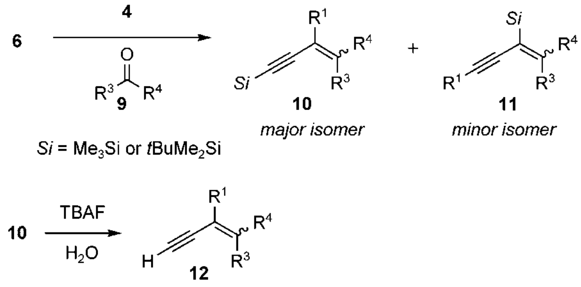
4 in the presence of 1-hexene **2a** (8 equiv) at 25 °C for 1 h gave the [(trimethylsilyl)ethynyl]cyclopropane **5a** in 67% yield (Table 1, entry 1). Interestingly the cyclopropanation took place exclusively at the γ-position of **6a** in contrast to the reaction of α-unsubstituted thioacetals **3**, the cyclopropanation of which proceeded at the α-position. When an excess amount of the low-valent titanium **4** was used, the reduction of the triple bond partly proceeded to give the corresponding alkenylcyclopropane as a byproduct. The reaction of organotitanium species generated from several acetylenic thioacetals **6** with various terminal olefins **2** gave the alkynylcyclopropanes **5** with excellent regioselectivity. In all of the reactions examined, formation of the other possible regioisomer, (trimethylsilyl)cyclopropane **7**, was not observed. When styrene was used as the olefin component, reduction of the carbon−carbon triple bond partially proceeded to produce the alkenylcyclopropanes as byproducts. We found that use of bulky *tert*-butyldimethylsilyl-substituted acetylenic thioacetals could eliminate the reduction of the triple bond, giving [(*tert*-butyldimethylsilyl)ethynyl]cyclopropanes **5** as sole products in good yields (entries 5 and 6). The cyclopropane **5i** was regioselectively produced by both the reactions of α-(trimethylsilyl)-β,γ-acetylenic thioacetal **6e** and its isomer, γ-(trimethylsilyl)-β,γ-acetylenic thioacetal **8** (entries 7 and 8). These results indicate that the regioselectivity of the cyclopropanation depends on the relative steric bulkiness of α (R^1)- and γ (R^2)-substituents of acetylenic thioacetals $R^2C{\equiv}CC(SR)_2R^1$.

Table 1. Regioselective Formation of the (Silylethynyl)cyclopropanes **5**

entry	acetylenic thioacetal **6**	olefin **2**	(silylethynyl)cyclopropane **5** (yield / %; ratio of diastereomers)
1	 **6a**	 **2a**	 **5a** (67; 57 : 43)
2[a]	**6a**	 **2b**	 **5b** (68)
3	**6a**	 **2c**	 **5c** (67; 61 : 39)
4	**6a**	 **2d**	 **5d** (69; 62 : 38)
5[b]	 **6b**	 **2e**	 **5e** (75; >99 : 1)
6[b]	 **6c**	**2e**	 **5f** (75; >99 : 1)
7	 **6d**	**2c**	 **5g** (52; 81 : 19)
8	**6d**	**2d**	 **5h** (52; 69 : 31)
9	 **6e**	**2c**	 **5i** (63; 81 : 19)
10	 **8**	**2c**	**5i** (70; 80 : 20)

[a] Carried out under ethylene. [b] Performed with 3 equiv of **4** and 4 equiv of styrene.

Scheme 3



Si = Me$_3$Si or *t*BuMe$_2$Si

Similar regioselectivity was also observed in the titanocene(II)-promoted reaction of the alkynyl thioacetals **6** with ketones **9** (Scheme 3, Table 2).[5] The successive treatment of the acetylenic thioacetal **6a** with the titanocene(II) reagent **4** (3 equiv) and 3-pentanone **9a** (1.2 equiv) produced the conjugated enyne **10a** as a major product along with the vinylsilane **11a** (entry 1). The formation of silylacethylene **10a** indicates that the process involves a formal allylic rearrangement. The reaction of more the sterically hindered *tert*-butyldimethylsilyl-substituted counterpart **6b** gave the enyne **10b** with higher regioselectivity (entry 2). Essentially complete regioselectivity was observed when less bulky ketones such as acetone and cyclohexanones were employed. Furthermore, even when the sterically hindered ketone **9e** was employed, the silylacetylene **10i** was produced with complete regioselectivity by use of the β,γ-acetylenic thioacetal **6d** bearing a less bulky methyl group at the γ-position (entry 9). Several enynes **10** possessing the (trialkylsilyl)acetylene moiety were protodesilylated to give the terminal alkynes **12** on treatment with TBAF in THF.

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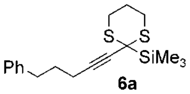
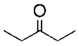
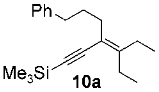
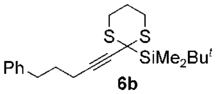
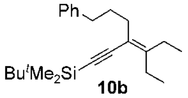
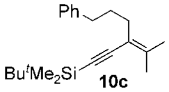
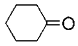
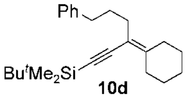
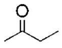
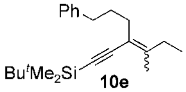
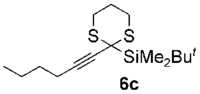
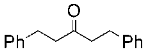
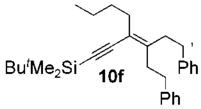
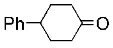
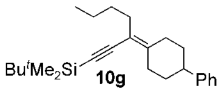
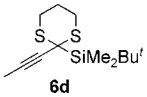
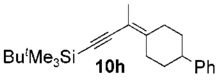
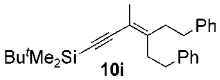
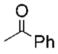
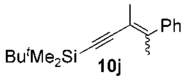
(5) In contrast to the reaction of **6**, a similar reaction of α-unsubstituted alkynyl thioacetals **3** with ketones **6** was complicated and no carbonyl olefination product was obtained under the same reaction conditions.

Table 2. Regioselective Formation of 1-(Trialkylsilyl)alk-3-en-1-ynes **10**

entry	acetylenic thioacetal **6**	ketone **9**	product	yield / % (**10** : **11**)	protodesilylated enyne **12** (yield / %)
1	 **6a**	 **9a**	 **10a**, **11a**	75 (80 : 20)	
2	 **6b**	**9a**	 **10b**, **11b**	72 (94 : 6)	**12a** (74)
3	**6b**	 **9b**	 **10c**	68	**12b** (76)
4	**6b**	 **9c**	 **10d**	72	**12c** (79)
5	**6b**	 **9d**	 **10e**	71 (83 : 17)[a]	**12d** (77; 82 : 18)[a]
6	 **6c**	 **9e**	 **10f**, **11f**	69 (87 : 13)	
7	**6c**	 **9f**	 **10g**	58	**12e** (93)
8	 **6d**	**9f**	 **10h**	66	
9	**6d**	**9e**	 **10i**	71	**12f** (76)
10	**6d**	 **9g**	 **10j**	68 (54 : 46)[a]	

[a] Ratio of stereoisomers.

On the basis of the regioselective formation of (silylethynyl)cyclopropanes **5** and enynes **10**, we tentatively propose that the reactions proceed via preferential formation of the intermediary α-(silylethynyl)carbene complexes **13** (Scheme 4). The reaction sequence involving the formation of the propargyltitanium intermediate **14** via the four-membered transition state **15** affords the cyclopropane **5** by further reductive elimination or the carbonyl olefination product **11** by metathesis-type degradation. In the case of the reaction of **13** with sterically hindered ketones, the transition state **15** is destabilized to a certain extent by steric repulsion between the α-substituent of **13** (R^1) and the substrate. As a result, the reaction partially follows the path involving the six-membered transition state **16**, and the metathesis-type degradation of the allenyltitanium intermediate **17** affords the minor product **11**. In the case of carbonyl olefination, a bulky *tert*-butyldimethylsilyl group in **13** disfavored the transition state **16**, and hence the reaction is more regioselective than that of the thioacetals bearing a trimethylsilyl group.

The mechanism for the formation of the carbene complex **13** from the thioacetal **6** is obscure at present; the isomerization of α-trialkylsilyl-substituted alkynylcarbene complexes $[\mathrm{Cp_2Ti{=}C}(\mathit{Si})\mathrm{C{\equiv}CR}]$, initially formed from the α-silyl thioacetal **6**, to **13** cannot be excluded because an equilibrium between the regioisomers of rhenium,[6] rhodium,[7] and manganese[8] alkynylcarbene complexes, $\mathrm{LnM{=}C(R^1)C{\equiv}CR^2}$ and $\mathrm{LnM{=}C(R^2)C{\equiv}CR^1}$, was observed.

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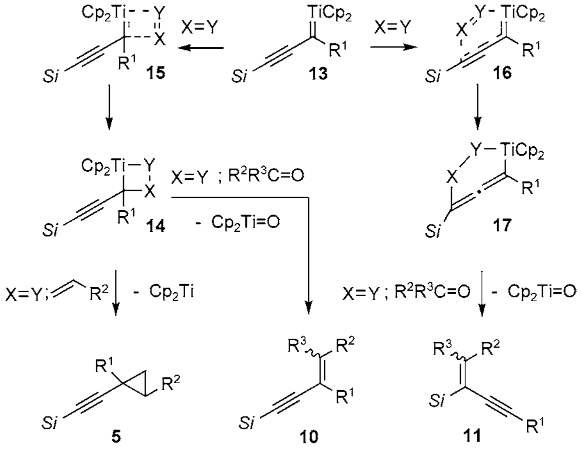
(6) (a) Casey, C. P.; Kraft, S.; Kavana, M. *Organometallics* **2001**, *20*, 3795. (b) Casey, C. P.; Kraft, S.; Powell, D. R. *J. Am. Chem. Soc.* **2001**, *124*, 2584.

(7) Padwa, A.; Austin, D. J.; Gareau, Y.; Kassir, J.; Xu, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 2637.

(8) Ortin, Y.; Coppel, Y.; Lugan, N.; Mathieu, R.; McGlinchey, M. J. *Chem. Commun.* **2001**, 1690.

Scheme 4



In summary, we have developed trialkylsilyl group-directed, highly regioselective transformations of α-silylalkynyl thioacetals into [(trialkylsilyl)ethynyl]cyclopropanes and 1-(trialkylsilyl)-3-en-1-ynes. These products were readily protodesilylated to give synthetically useful terminal alkynes. Further study on the reactions of (trialkylsilyl)ethynylcarbene complexes with a variety of organic molecules is currently in progress.

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research (No. 14340228) and Grant-in-Aid for Scientific Research on Priority Areas (A) “Exploitation of Multi-Element Cyclic Molecules” (No. 14044022) from the Ministry of Education, Culture, Sports, Science and Technology, Japan. This work was carried out under the 21st Century COE program of “Future Nanomaterials” at Tokyo University of Agriculture & Technology.

Supporting Information Available: Experimental procedures and characterization data for compounds **5a**−**i**, **10a**−**j**, **11a**, **11b**, **11f**, and **12a**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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