[3 + 2] Annulation of β-Heteroatom-Substituted α,β-Unsaturated Acylsilanes with Methyl Ketone Enolates: Scope and Investigation of the Reaction Course

Kei Takeda,*,† Kenji Yamawaki, and Noriaki Hatakeyama

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan

takedak@hiroshima-u.ac.jp.

Received August 9, 2001

A new route to (*Z*)-β-silylacryloylsilanes **10** and the improved conditions for the [3 + 2] annulation using **10** and alkyl methyl ketone enolates are reported. Also, details of investigations defining a reaction course of the [3 + 2] annulation using β-phenylthio- and β-trimethylsilyl-acryloylsilanes **1** (X = SPh, $SiMe_3$) and alkyl methyl ketone enolates are described.

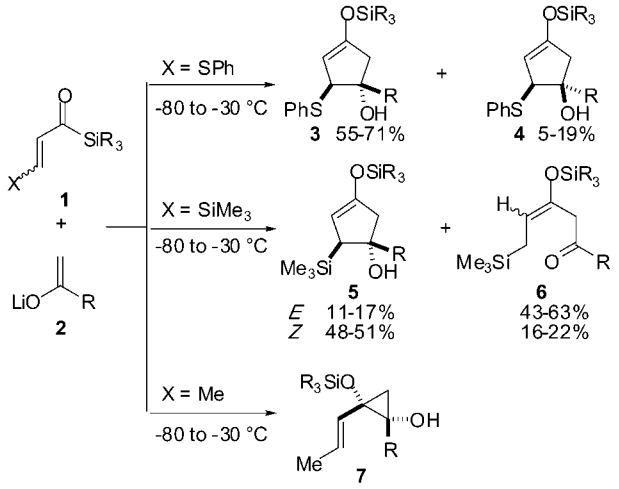
Introduction

The development of synthetic methodologies for the highly efficient and stereoselective construction of five-membered rings has been a very active area of research.[1] In 1993 we reported a novel [3 + 2] annulation approach to obtain cyclopentenol derivatives that involves the reaction of β-heteroatom-substituted acryloylsilanes with ketone enolates.[2] The synthetic utility of the reaction has been successfully demonstrated in the synthesis of natural products, including untenone A[3] and clavulones (claviridenones).[4]

An intriguing feature of the reaction of acryloylsilanes with ketone enolates is that the products and the product distributions depend on the β-substituent of the acryloylsilanes. Thus, in contrast to the observation with (*E*)- and (*Z*)-β-phenylthio derivatives **1** (X = SPh) in which isomeric cyclopentenols **3** (major) and **4** (minor) were obtained in almost the same ratio irrespective of the acylsilane geometry, the trimethylsilyl derivative **1** (X = $SiMe_3$) afforded cyclopentenols **5** and uncyclized enol silyl ether **6** in a ratio depending on the vinylsilane geometry (Scheme 1). Thus, cyclopentenol **5** was a major product from (*Z*)-acylsilane, whereas (*E*)-acylsilane afforded uncyclized enol silyl ether **6** as a major product. On the other hand, crotonoylsilane **1** (X = Me) did not afford cyclopentenol but cyclopropanol derivative **7**.[5]

In this paper, we present additional information on the reaction pathway depending on the β-substituent as well as the scope of the [3 + 2] annulation.

Scheme 1



Results and Discussion

[3 + 2] Annulation Using (β-(Trimethylsilyl)- and β-(Dimethylphenylsilyl)acryloyl)silanes. Although the [3 + 2] annulation methodology using (β-(phenylthio)-acryloylsilanes **1** (X = SPh) has proved to be very efficient for the synthesis of highly functionalized five-membered carbocycles, the process of preparing the acryloylsilanes produces the unpleasant-smelling byproduct thiophenol. Consequently, we decided to reinvestigate the [3 + 2] annulation using (β-(trimethylsilyl)acryloyl)silane, which we previously reported to afford a cyclopentenol derivative in lower yields relative to the corresponding β-phenylthio derivative and in a better yield from (*Z*)-**1** (X = $SiMe_3$) than from (*E*)-**1** (X = $SiMe_3$). Our first task was to find a stereoselective route to (*Z*)-**10a**, because the reported procedure provides only (*E*) or a mixture of (*E*) and (*Z*) derivatives[6] and to optimize the conditions for the annulation process using (*Z*)-**10a** leading to **5**. Also, we examined [3 + 2] annulation using (*Z*)-β-(dimethyl-(phenyl)silyl)acryloylsilane (*Z*)-**10b**, which would signifi-

† Current address: Institute of Pharmaceutical Sciences, Faculty of Medicine, Hiroshima University, 1−2−3, Kasumi, Minami-Ku, Hiroshima 734-8551, Japan.

(1) (a) Ramaiah, M. *Synthesis* **1984**, 529−570. (b) Hudlicky, T.; Rulin F.; Lovelace, T. C.; Reed, J. W. In *Studies in Natural Products Chemistry*; Attaur-Rahman, T., Ed.; Elsevier Science: Essex, U.K. 1989; pp 3−72. (c) Ho, T.-L. *Carbocycle Construction in Terpene Synthesis*; VCH: New York, 1988.

(2) (a) Takeda, K.; Fujisawa, M.; Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc.* **1993**, *115*, 9351−9352. (b) Takeda, K.; Ohtani, Y.; Ando, E.; Fujimoto, K.; Yoshii, E.; Koizumi, T. *Chem. Lett.* **1998**, 1157−1158.

(3) Takeda, K.; Nakayama, I.; Yoshii, E. *Synlett* **1994**, 178−178.

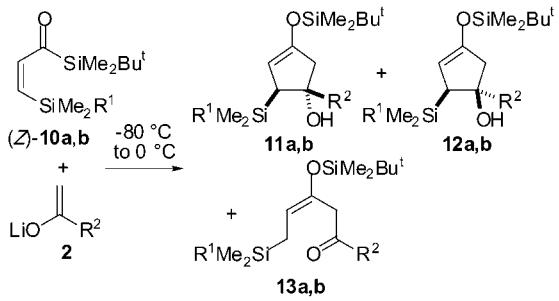
(4) Takeda, K.; Kitagawa, K.; Nakayama, I.; Yoshii, E. *Synlett* **1997**, 255−256.

(5) Takeda, K.; Nakatani, J.; Nakamura, H.; Sako, K.; Yoshii, E.; Yamaguchi, K. *Synlett* **1993**, 841−843.

(6) (a) Reich, H. J.; Kelly, M. J.; Olson, R. E.; Holtan, R. C. *Tetrahedron* **1983**, *39*, 949−960. For stereoselective preparation of (*E*)-**10a**, see: (b) Takeda, K.; Nakajima, A.; Takeda, M.; Yoshii, E.; Zhang, J.; Boeckman, R. K., Jr. *Org. Synth.* **1999**, *76*, 199−213.

10.1021/jo0160219 CCC: $22.00
Published on Web 02/26/2002

Table 1.



			yield (%)		
	R^1	R^2	11	12	13
10a	Me	Et	75	5	9
10a	Me	*n*-Pr	70	4	19
10a	Me	*i*-Pr	76	9	10
10b	Ph	Et	72	3	10
10b	Ph	*n*-Pr	71	3	10
10b	Ph	*i*-Pr	80	4	5

cantly enhance the synthetic versatility of the process because of the ability of the silyl group to act as a hydroxyl surrogate in combination with Fleming's oxidative desilylation protocol.[7] The new route to (*Z*)-**10a**,**b** started from *O*-protected propargyl alcohol **8**,[8] which was converted to **9a**,**b** by a 2-fold silylation followed by deprotection. Transformation of **9a**,**b** into acryloylsilanes **10a**,**b** was carried out with hydroboration[9] followed by Swern oxidation.[10]

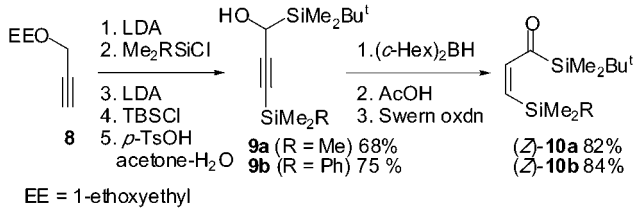
Having developed an efficient route to (*Z*)-**10**, we optimized the reaction conditions for [3 + 2] annulation using (*Z*)-**10**. The best results were obtained when the reaction mixture was warmed to 0 °C. A trace amount of diastereomeric cyclopentenol **12** was detected in addition to **11**, in contrast to the results obtained in our previous study,[2a] in which **11a** was formed exclusively (Table 1). Also, unlike in our previous study in which (*E*)- and (*Z*)-**13** were obtained in various proportions, (*E*)-**13** was formed exclusively.

Although we also reexamined the reaction using (*E*)-**10a** by elevating the reaction temperature to 0 °C, no improvement in the yield of **11a** and no formation of cyclopentenol **12a** were observed. The difference in the product distribution of *E* and *Z* derivatives will be discussed later.

A Mechanistic Proposal for [3 + 2] Annulation. In an earlier stage of this research, as a mechanism to explain the reaction outcome outlined in Scheme 1, we proposed the reaction mechanism illustrated in Scheme 3, which involves two competing pathways.[11]

The first one, path a, involves delocalized allylic carbanion intermediate **15** that is derived from the 1,2-adduct **14** by way of Brook rearrangement.[12] Path b involves the cyclopropanolate intermediate **16** that is generated by internal attack on the carbonyl group by the carbanion derived by Brook rearrangement. We considered that the reaction proceeds through either path a or path b, depending on the α-carbanion-stabilizing ability of the β-substituent of the acryloylsilanes. In the case of an anion-stabilizing substituent such as a phenylthio group, the carbanion **17** (X = SPh) generated by Brook rearrangement immediately delocalizes to give an intermediate **15**. Consequently, the olefin geometry of **15** arising from (*E*)- and (*Z*)-**1** can be the same if conformational interconversion occurs faster than cyclization. On the other hand, in the case of a methyl group, which does not have α-carbanion-stabilizing ability, carbanion **17** (*X* = Me) attacks the β-carbonyl group before allylic delocalization to give **7** via **16**. If it is assumed that a trimethylsilyl group has less ability to stabilize the α-carbanion than does a phenylthio group, the results with (β-(trimethylsilyl)acryloyl)silane **1** (X = $SiMe_3$) could be explained as being due to the formation of vinylcyclopropanolate followed by oxyanion-accelerated vinylcyclopropane rearrangement[13] to cyclopentenone (**16** → **5**) in which (*E*)- and (*Z*)-**16** can retain their geometries in **1** (X = $SiMe_3$) and possibly have different reactivities. This hypothesis is based on the fact that **3**, **4**, and **5** were recovered unchanged after treatment with LDA (1 equiv) in THF at −80 to 0 °C, respectively, and the fact that the reaction of **1** (X = SPh) with lithium enolate **18** of alkenyl methyl ketone produces [3 + 2] annulation product **19** in sharp contrast with the reaction of **1** (X = $SiMe_3$) that affords cycloheptenone derivatives, **21**, a [3 + 4] annulation product (Scheme 4). Our previous study[14] has established that the latter process proceeds via anionic oxy-Cope rearrangement of divinylcyclopropanolate **20**.

Scheme 2



It seemed that verification of the proposed mechanism would require (1) comparison of relative α-carbanion-stabilizing abilities of trimethylsilyl and phenylthio groups, (2) verification of the stereochemical integrity of the starting acryloylsilanes under the reaction conditions, and (3) examination of whether the vinylcyclopropane−cyclopentene rearrangement (**16** → **5**) proceeds at temperatures below −30 °C.

(7) Fleming, I.; Henning, R. Parker, D. C.; Plaut, H. E.; Sanderson, P. E. *J. Chem. Soc., Perkin Trans. 1* **1995**, 317−337.

(8) Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 916. Also, see ref 6b.

(9) Denmark, S. E.; Herbert, B. *J. Org. Chem*. **2000**, *65*, 2887−2896.

(10) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165−185.

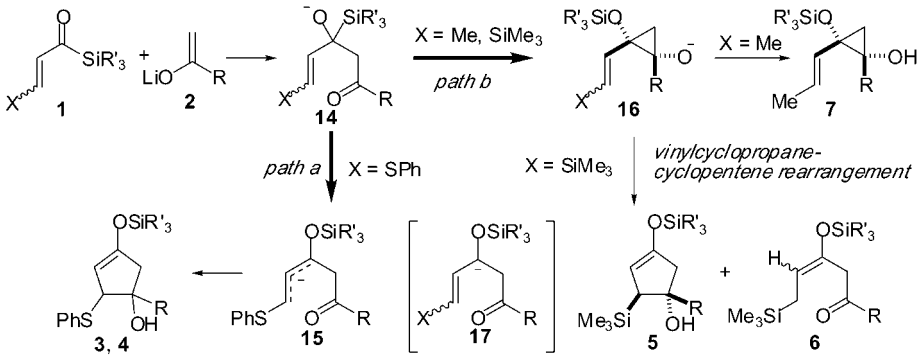
(11) Takeda, K. *J. Synth. Org. Chem. Jpn*. **1997**, *55*, 774−784.

(12) For reviews on the Brook rearrangement, see: (a) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; John Wiley & Sons: 2000. (b) Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; pp 149−221. (c) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77−84. For the use of the Brook rearrangement in tandem bond formation strategies, see: (d) Moser, W. H. *Tetrahedron* **2001**, *57*, 2065−2084. Also, see: (e) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647−660. (f) Bulman Page, P. C.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev*. **1990**, *19*, 147−195. (g) Qi, H.; Curran, D. P. In *Comprehensive Organic Functional Group Transformations*, Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W.; Moody, C. J., Eds.; Pergamon: Oxford, 1995; pp 409−431. (h) Cirillo, P. F.; Panek, J. S. *Org. Prep. Proc. Int*. **1992**, *24*, 553−582. (i) Patrocinio, A. F.; Moran, P. J. S. *J. Braz. Chem. Soc*. **2001**, *12*, 7−31.

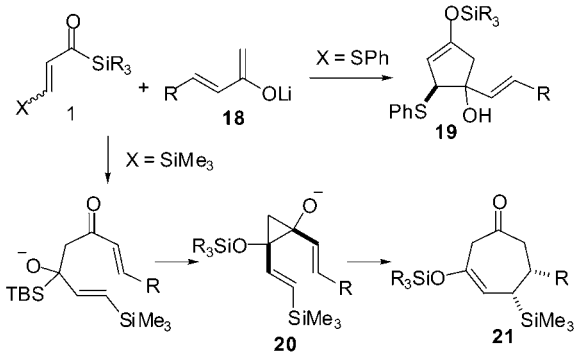
(13) (a) Denheiser, R. L.; Martinez-Davila, C.; Morin, J. M., Jr. *J. Org. Chem*. **1980**, *45*, 1340−1341. (b) Danheiser, R. L.; Martinez-Davila, C.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 2443−2446. For a carbanion-accelerated version, see: Danheiser, R. L.; Bronson, J. J.; Okano, K. *J. Am. Chem. Soc.* **1985**, *107*, 4579−4581.

(14) Takeda, K.; Nakajima, A.; Takeda, M.; Okamoto, Y.; Sato, T.; Yoshii, E.; Koizumi, T.; Shiro, M.*J. Am. Chem. Soc*. **1998**, *120*, 4947−4959.

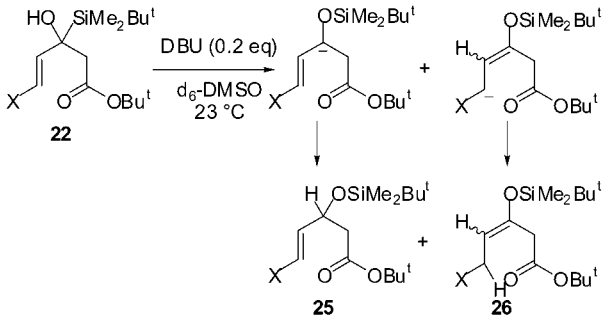
Scheme 3



Scheme 4



Scheme 5

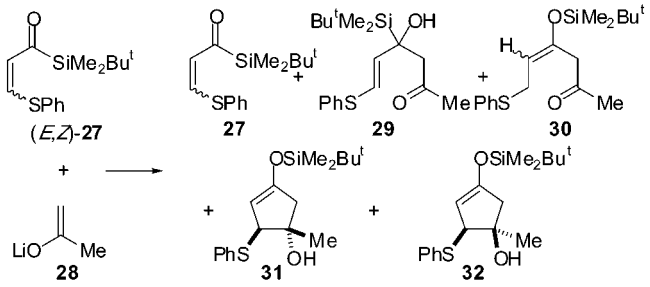


X	product	$t_{1/2}$ (min)
22a SPh	**26**	3.2
22b $SiMe_3$	**25**, **26** (*ca* 2:1)	27.5

Comparison of α-Carbanion-Stabilizing Abilities of the Phenylthio and Trimethylsilyl Groups. We compared the α-carbanion-stabilizing abilities of the two groups based on the relative rates of the base-catalyzed Brook rearrangement of the *β*-heteroatom-substituted α-silylallyl alcohol **22** to **25** and **26**.[15] This stems from the fact that the Brook rearrangement is facilitated by electron-withdrawing substituents.[12] Thus, the rates of formation of **25** and **26** would increase as the α-carbanion-stabilizing ability of the substituent X increases. The result that the half-life of **22a** is much shorter than that of **22b** suggests that the phenylthio group stabilizes α-carbanion more strongly than does the trimethylsilyl group, at least in this system (Scheme 5), thus, providing good support for the above-postulated mechanism.

Low-Temperature Quenching of the Reaction of *β*-(Phenylthio)- and (*β*-(Trimethylsilyl)acryloyl)-silanes and Lithium Enolate of Acetone. To verify whether the stereochemical integrity of the acryloylsilanes **27** was preserved under the reaction conditions, low-temperature quenching experiments were carried out, and the results are shown in Table 2. Loss of the olefin geometry of **27** was observed in all cases in which the starting material was recovered. The possibility that isomerization occurred during the workup/purification process was ruled out by subjecting **27** without **28** to the same workup conditions and purification process.

Table 2.



		yield (%)				
27	conditions	**27** (*E*:*Z*)	29	**30** (*E*:*Z*)	31	32
E	−80 °C, 10 min	23 (1:1.4)	14	12 (1:1.3)	33	-
E	−80° to −70 °C	20 (1:1.2)	-	17 (1:1.2)	53	-
E	−80° to −60 °C	12 (1:1.2)	-	24 (1:1)	48	1
E	−80° to −50 °C	-	-	-	63	1
E	−80° to −30 °C	-	-	-	68	2
Z	−80 °C, 10 min	73 (1:1.9)	-	3 (1:3.3)	8	2
Z	−80° to −70 °C	66 (1:1.2)	-	9 (1:2.4)	21	2
Z	−80° to −60 °C	38 (1:1.2)	-	12 (1:1.9)	40	2
Z	−80° to −50 °C	24 (1:1.3)	-	8 (1:1.2)	42	2
Z	−80° to −30 °C	-	-	-	73	5

The fact that the stereochemical outcome was almost the same irrespective of the olefin geometry in the [3 + 2] annulation of **27** can be partly attributed to the loss of the stereochemical integrity of the starting acylsilanes. To obtain information on the origin of the *E*−*Z* isomerization, reaction of (*E*)-**29** with LDA at −80 °C for 10 min was carried out, and the results are shown in Scheme 6.

The nearly stereorandom formation of acryloylsilanes **27** suggests that a retro-aldol process (**29** → **27** + **28**) exists in the [3 + 2] annulation in which isomerization of the double bond can occur; however, the mechanism is not clear.

On the other hand, the corresponding reaction of *β*-trimethylsilyl derivative **10a** with **28** was found to be different from that of *β*-phenylthio derivative **27** (Table 3). In the reaction of (*E*)-**10a**, **10a** was not recovered; instead, **33**, a reduction product by a slight excess of LDA,

(15) Takeda, K.; Ubayama, H.; Sano, A.; Yoshii, E.; Koizumi, T. *Tetrahedron Lett.* **1998**, *39*, 5243−5246.

Scheme 6

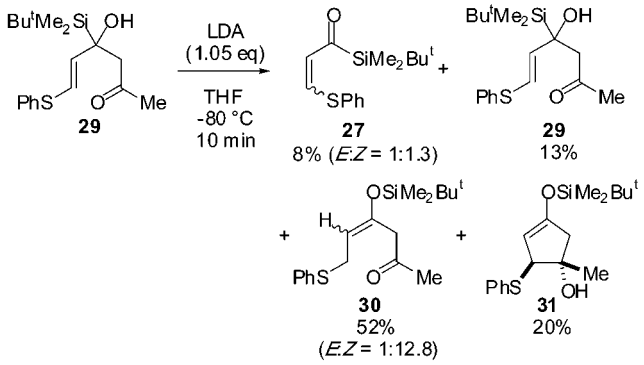
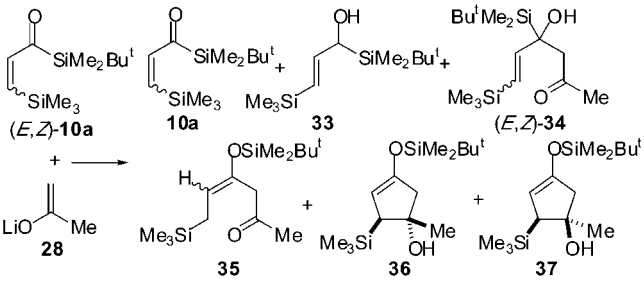


Table 3.



		yield (%)				
10a	conditions	**10a** (**33**)	34	**35** (*E*:*Z*)	**36**	**37**
E	−80 °C, 10 min	11[a]	31[c]	30 (1:1.8)	6	-
E	−80° to −70 °C	9[a]	18[c]	35 (1:1.5)	9	-
E	−80 to −60 °C	6[a]	8[c]	35 (1.7:1)	12	-
E	−80 to −50 °C	4[a]	-	35 (3.5:1)	15	-
E	−80 to −30 °C	-	-	34 (5.6:1)	17	-
E	−80 to 0 °C	-		34 (6.2:1)	19	-
Z	−80 °C, 10 min	65[b]	12[d]	2 (1:1.9)	6	-
Z	−80 to −70 °C	61[b]	14[d]	3 (1:1.8)	7	-
Z	−80 to −60 °C	56[b]	-	7 (1.3:1)	12	-
Z	−80 to −50 °C	57[b]	3[d]	6 (2.0:1)	16	3
Z	−80 to −30 °C	32[b]	-	7 (only *E*)	42	5
Z	−80 to 0 °C	-	-	20 (only *E*)	60	6

[a] Yield of **33**. [b] Yield of (*Z*)-**10a**. [c] Yield of (*E*)-**34**. [d] Yield of (*Z*)-**34**.

was obtained.[16] In contrast, in the reaction of (*Z*)-**10a**, a significant amount of **10a** was recovered without *E*/*Z* isomerization. Moreover, since we previously showed that (*Z*)-**10a** cannot be reduced by LDA, in contrast to the fact that reduction of (*E*)-**10a** by LDA is a rapid process even at −80 °C, the fact that **33** was not obseved in the reaction of (*Z*)-**10a** suggests that a detectable amount of (*E*)-**10a** was not formed and, hence, that *E*/*Z* isomerization did not occur.

Also, the reaction of (*E*)- and (*Z*)-**34** with LDA afforded **33** and (*Z*)-**10a**, respectively, without *E*/*Z* isomerization (Scheme 7).

The slower reaction of (*Z*)-**10a** with **28** relative to (*E*)-**10a** is attributed in part to an unfavorable equilibrium of 1,2-adduct (*Z*)-**34** toward the starting materials, which can be ascribed to the relatively severe steric repulsions in the (*Z*)-1,2-adduct. A similar trend was previously observed for reactions of (*E*,*Z*)-**10a** with lithium enolate of alkenyl methyl ketone.[14]

There are several possibilities concerning the origin of **35** in Table 3, including protonation during workup of cyclopropanolate intermediates **38** or of allyllithium derivatives **39** and **42**, and an intermolecular protonation of **41** (Scheme 8). The allyllithium derivatives **39** and **41** may also arise from ring-opening of **38** and/or directly from **14** (X = $SiMe_3$). Protonation of **38** followed by a ring-opening would provide both (*E*)- and (*Z*)-**35**. On the other hand, while protonation of **39** should afford some amount of 1,3-silyl-migration product **40**[17] in addition to (*Z*)-**35**, (*E*)-**35** would become a major product upon protonation of **42**. In the reaction of both (*E*)- and (*Z*)-**10a**, the greater formation of (*E*)-**35** with increase in reaction temperature and with progress of the reaction and no formation of detectable amounts of **40** suggests that **35** could come from both unreacted **38** and dienolate **42** at lower temperatures and that **42** becomes a major precusor for **35** with increasing temperature.

Low-Temperature Oxyanion-Accelerated Vinylcyclopropane−Cyclopentene Rearrangement. Although the vinylcyclopropane−cyclopentene rearrangement only proceeds at high temperatures, usually at tempertures over 250 °C,[18] Danheiser found that an oxyanion substituent on the cyclopropane ring dramatically accelerated the rearrangement.[13a,b,19] However, even in these cases, a temperature in excess of 25 °C is required for the reaction. Consequently, in our case (**16** → **11**, **12**), it was questionable whether the rearrangement would proceed at a temperature below −30 °C. We decided to prepare four diastereomeric vinylcyclopropanolate intermediates **16** (X = $SiMe_3$, R = Me) by an independent route and to examine the reactivity to the cyclopentene derivatives and the stereochemistry of the reaction. We sought a synthetic route that would permit the rapid generation of cyclopropanolate even at −80 °C, and we found that the reaction of 2 equiv of MeLi with the corresponding cyclopropyl acetates **45** was suitable for this purpose. The acetates **45** were prepared by the reaction of dienol silyl ethers **43**[14] with acetoxy carbene complex **44** (Chart 1).[20,21] The dienol silyl ethers, in turn, were prepared from the corresponding acylsilanes and lithiomethyl phenyl sulfone utilizing the Brook rearrangement according to Reich's method.[22]

The reaction of **45** with MeLi (2.2 equiv) was carried out in both THF and toluene at −80 °C for 30 min and followed by elevation of the temperature (from −80 ° to −50 °C and −30 °C) over a 30-min period and then

(16) (a) Takeda, K.; Ohnishi, Y. *Org. Lett.* **1999**, *1*, 237−239. For a review of reduction with lithium dialkylamides including LDA, see: (b) Majewski, M.; Gleave, D. M. *J. Organomet. Chem.* **1994**, *470*, 1−16.

(17) Nakahira, H.; Ryu, I.; Ogawa, A.; Kambe, N.; Sonoda, N. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3361−3363.

(18) For reviews on vinylcyclopropane-cyclopentene rearrangement, see: Hudlicky, T.; Reed, J. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 899−970. Hudlicky, T.; Kutchan, T. M.; Naqvi, S. M. *Org. React.* **1985**, *33*, 247−335. Also, see: Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165−198.

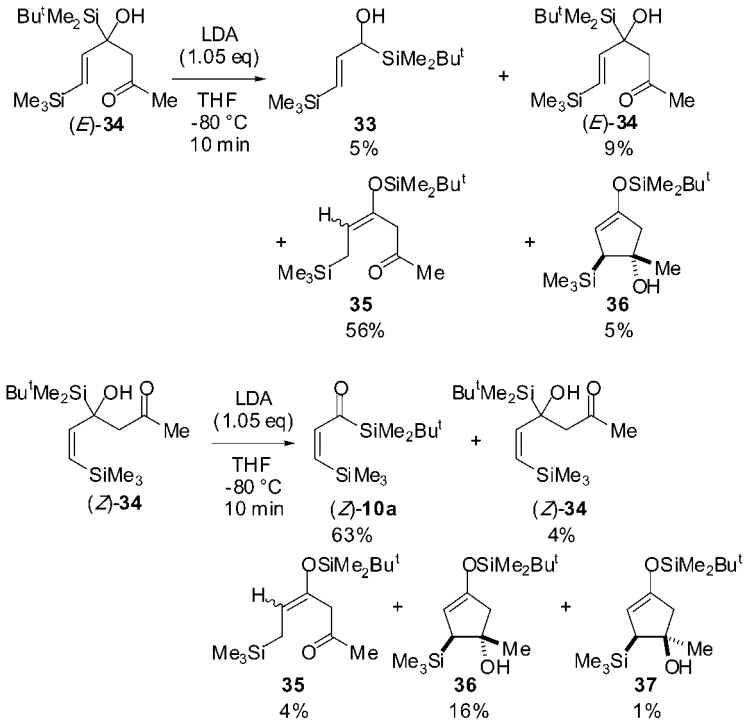
(19) For a review of charge-accelerated arrangement, see: (a) Bronson, J. J.; Danheiser, R. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 999−1036. (b) Wilson, S. R. *Org. React.* **1993**, *43*, 93−250.

(20) (a) Murray, C. K.; Yang, D. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1990**, *112*, 5660−5662. (b) Takeda, K.; Okamoto, Y.; Nakajima, A.; Yoshii, E.; Koizumi, T. *Synlett* **1997**, 1181−1183. For reviews on the synthetic applications of Fischer carbene complexes, see: (c) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1065−1113. (d) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Libeskind, L. S., Ed.; JAI Press Inc.; Greenwich, CT, 1989; Vol. 1, pp 209−393. (e) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587−608.

(21) The relative stereochemistry was assigned on the basis of results of NOESY experiments.

(22) Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609−5617.

Scheme 7



Scheme 8

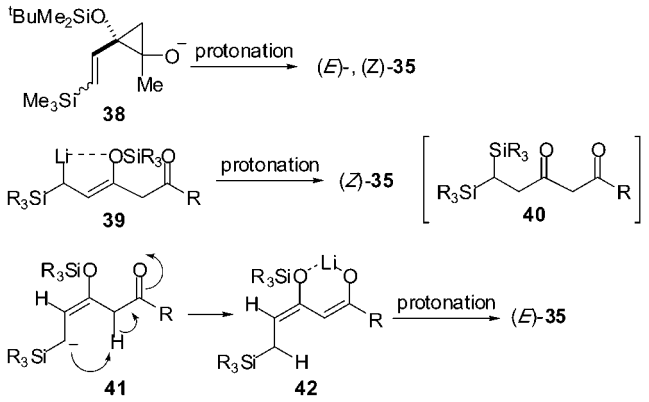
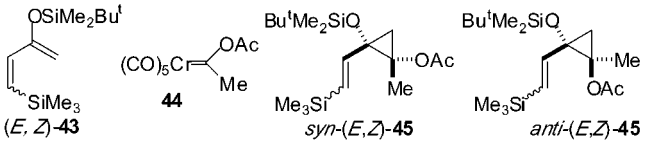


Chart 1



quenched with acetic acid (2.2 equiv). The results are shown in Table 4.[23]

When the reaction was performed in THF, in most cases, cyclopentenols **36** and **37**, which are exactly the same as those obtained in the [3 + 2] annulation, and a ring-opening product **35** were obtained.[24] The fact that the minor diasetereomer **37** was obtained only from (*Z*)-**45** is also consistent with the results of the [3 + 2] annulation. Particularly noteworthy is the substantial formation of cyclopentenol **36** from the (*Z*)-derivative even at −80 °C. This result indicates that oxyanion-accelerated vinylcyclopropane−cyclopentene rearrangement in the case of substrates having the substitution pattern shown in structure **16** (X = $SiMe_3$) (Scheme 3) can proceed at temperatures below −30 °C[25] and consequently provides support to our assumption of intermediacy of vinylcyclopropanolate derivative **16** in the [3 + 2] annulation. Furthermore, the same trend in product distribution and difference in reactivity depending on the vinylsilane geometry as that observed in the [3 + 2] annulation was observed. The greater formation of (*E*)-**35** with increases in reaction temperature and with progress of the reaction is also consistent with the results of [3 + 2] annulation. Although these results seem to support the proposed pathway involving cyclopropanolate (**16** (X = $SiMe_3$), Scheme 3), there remains the question of why cyclopentenol **36** was obtained as a major product irrespective of the stereochemistry of the vinylcyclopropanolates and the question of why (*Z*)-**45** gives more cyclopentenol **36** than does (*E*)-**45** under comparable conditions. To explain the stereochemistry of the process (**45** → **36**, **37**), we propose a mechanism in which cyclopentenol **36** is produced via a [1,3]-sigmatropic shift of the internally oxygen−silicon-coordinated *anti*-(*Z*)-**46** (Scheme 9).[26] The stereochemical course from *anti*-(*Z*)-**46** to the cyclopentenol **36** is in agreement with that predicted by orbital symmetry considerations (suprafacial-inversion). *Anti*-(*Z*)-**46** may be generated from three other diastereomers by a ring-opening, a geometric isomerization, and a ring-closure sequence via **47** and/or **48**. The intermediate should undergo more facile

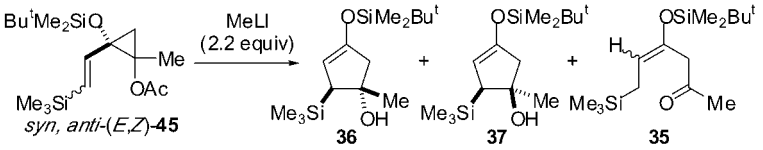
(23) Takeda, K.; Sakurama, K.; Yoshi, E. *Tetrahedron Lett.* **1997**, *38*, 3257−3260.

(24) Although we previously reported in a preliminary communication (ref 23) that cyclopentenol **36** was the only cyclized product in the reaction of (*Z*)-**45**, reexamination of the original spectral data revealed the formation of a trace amount of **37**.

(25) For the effect of a substituent on the rate of thermal vinylcyclopropane−cyclopentene rearrangement, see: Trost, B. M.; Scudder, P. H. *J. Org. Chem.* **1981**, *46*, 506−509.

(26) For reviews of hypervalent silicon compounds, see: (a) ref 12a, chapter 4. (b) Kost, D.; Kalikhman, I. Hypervalent Silicon Compounds. In *The Chemistry of Organic Silicon Compounds*, Rappoport, Z., Apeloig, Y., Eds.; Wiley: Chichester, UK, 1998; Vol. 2, Chapter 23. (c) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371−1448.

Table 4.



			yield (%)					
			in THF			in toluene		
	45	conditions	**36**	**37**	**35** (*E*:*Z*)	**36**	**35** (*E*:*Z*)	**45**
	syn	−80 °C, 30 min	0	0	81 (1.1:1)	0	0	96
	syn	−80 to −50 °C	45	0	40 (2.9:1)	-	-	-
E	*syn*	−80 to −30 °C	54	0	31 (17:1)	0	13 (1.5:1)	83
	anti	−80 °C, 30 min	0	0	89 (1.1:1)	0	0	93
	anti	−80 to −50 °C	45	0	39 (3.3:1)	-	-	-
	anti	−80 to −30 °C	63	0	34 (only *E*)	0	44 (1.3:1)	53
	syn	−80 °C, 30 min	52	6	20 (1.7:1)	0	0	96
	syn	−80 to −50 °C	61	7	5 (3.9:1)	-	-	-
Z	*syn*	−80 to −30 °C	76	8	16 (only *E*)	7	54 (3.9:1)	35
	anti	−80 °C, 30 min	59	6	10 (1.7:1)	0	1	95
	anti	−80 to −50 °C	72	9	6 (2.8:1)	-	-	-
	anti	−80 to −30 °C	76	9	14 (5.7:1)	30	25 (1.8:1)	45

Scheme 9

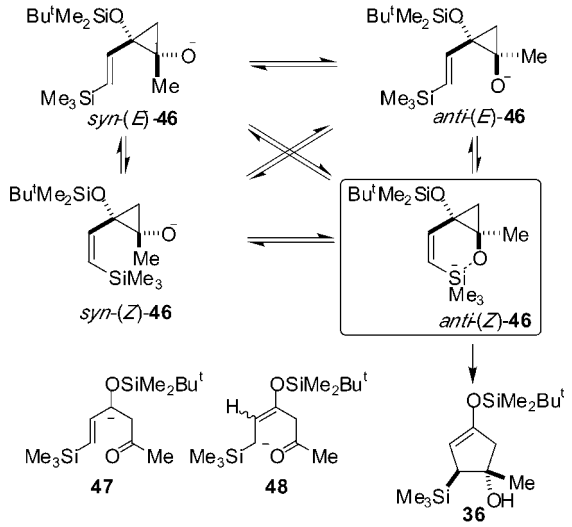
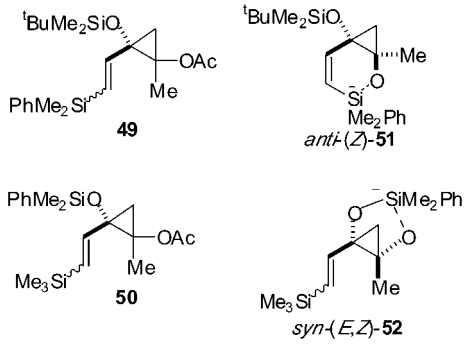


Chart 2



rearrangement to cyclopentenol than the other isomers presumably because of its fixed conformation that is suitable for the overlap of the orbitals required for the rearrangement. The observations that **35** is produced to a larger extent from the (*E*)-derivatives than from the (*Z*)-derivatives and that the products ratio is unaffected by the C-1 stereochemistry can be explained by assuming that the syn/anti isomerization proceeds much faster than does the *E*/*Z* isomerization. The assumption made above that the origin of (*E*)-**35** is **38** and/or **41** seems to rationalize the result that (*E*)-**46** produces more **35** than (*Z*)-**46** does.

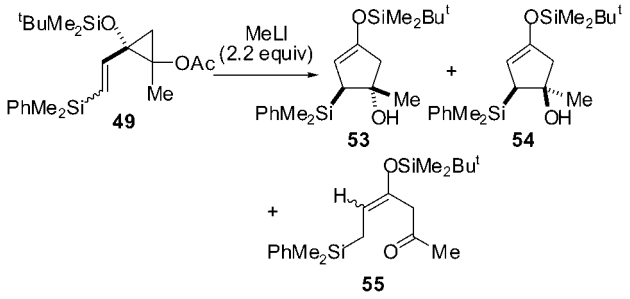
If interconversion between the four diastereomeric **46** via ionic intermediates **47** and/or **48** exists, as we assumed, the use of a less-polar solvent would cause a decrease in the rate of isomerization and would consequently result in decrease in the formation of **36** from *syn*-(*Z*)-**46** and (*E*)-**46** relative to *anti*-(*Z*)-**46**. In fact, when the reaction of **45** with MeLi was conducted in toluene, *syn*-(*Z*)-**45** afforded less cyclopentenol **36** than did *anti*-(*Z*)-**45**, and reaction of the (*E*)-derivatives resulted in recovery of the starting material (Table 4).

Next, to try to obtain further evidence supporting the assumption of a role of internal chelation of the silicon atom in Scheme 9, we carried out reactions of dimethylphenylsilyl derivatives **49** and **50** with MeLi, anticipating that, in both reactions, the syn isomers would afford less **36** analogue relative to the corresponding anti isomers because of internal chelation such as **51** and **52**, which can be more stabilized by the phenyl group than the corresponding trimethylsilyl and *tert*-butyldimethylsilyl derivatives, respectively (Chart 2).[27] Thus, if the assumption that the formation of **36** from *anti*-(*Z*)-**46** is faster than that from other isomers is correct, the rate from *anti*-(*Z*)-**51** and from *syn*-**52** would increase and decrease, respectively, owing to increased concentrations of *anti*-(*Z*)-**51** and *syn*-**52**. Consequently, in both cases, more **36** would be obtained from *anti*-(*Z*) derivatives relative to that from *syn*-(*Z*) derivatives.

Although **49**[21] could be prepared from the corresponding dienol silyl ethers in a manner similar to that described for the preparation of **45**, in the case of **50**, the cyclopropanation step failed. We prepared **50**[21] via desilylation of **45** followed by dimethyl(phenyl)silylation. The results of the reactions of **49** and **50** with MeLi are shown in Tables 5 and 6, respectively. Replacement of the methyl group in the trimethylsilyl group with a

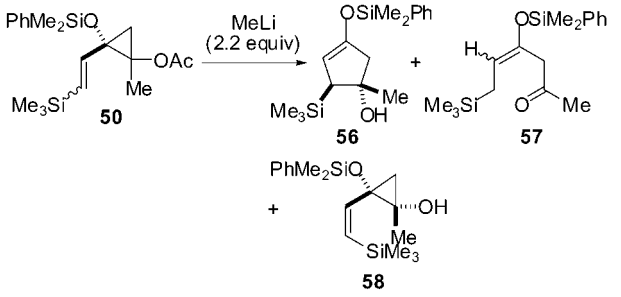
(27) Brook and coworkers reported the rate of C-to-O migration of silyl group in the reaction of diphenyl(trimethylsilyl)carbinol with diethylamine. Replacement of methyl on trimethylsilyl group by phenyl accelerates the 1,2-migration (the Brook rearrangement), which is believed to proceed via a pentavalent silicon intermediate, by a factor of about 6. Brook, A. G.; LeGrow, G. E.; MacRae, D. M. *Can. J. Chem.* **1967**, *45*, 239−253.

Table 5.



	49	conditions	yield (%) 53	54	55 (*E*:*Z*)
	syn	−80 °C, 5 min	16	0	80 (1.1:1)
	syn	−80 °C, 30 min	20	0	75 (1.6:1)
E	*syn*	−80° to −30 °C	80	0	12 (only *E*)
	anti	−80 °C, 5 min	18	0	77 (0.96:1)
	anti	−80 °C, 30 min	21	0	74 (0.92:1)
	anti	−80° to −30 °C	83	0	8 (only *E*)
	syn	−80 °C, 5 min	64	7	21 (1.4:1)
	syn	−80 °C, 30 min	70	9	19 (2.2:1)
Z	*syn*	−80° to 30 °C	81	8	6 (only *E*)
	anti	−80 °C, 5 min	66	8	16 (1.6:1)
	anti	−80 °C, 30 min	72	8	18 (1.7:1)
	anti	−80° to −30 °C	83	8	4 (only *E*)

Table 6.

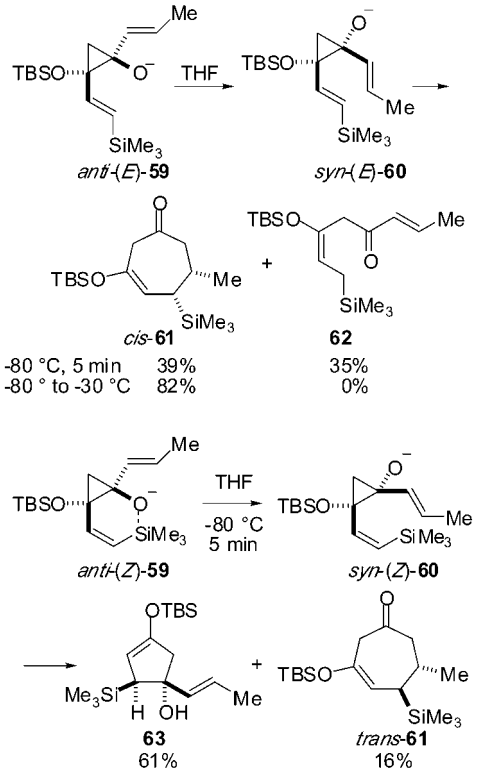


entry	50	conditions	yield (%) 56	57 (*E*:*Z*)	58
1	*syn*-(*E*)	−80 °C, 30 min	0	92 (1:5.8)	0
2	*syn*-(*E*)	−80 to −30 °C	4	90 (1:2.5)	0
3	*anti*-(*E*)	−80 °C, 30 min	0	96 (1:1.6)	0
4	*anti*-(*E*)	−80 to −30 °C	11	83 (1:1.5)	0
5	*syn*-(*Z*)	−80 °C, 30 min	8	40 (2.1:1)	43
6	*syn*-(*Z*)	−80 to −30 °C	28	65 (5.3:1)	0
7	*anti*-(*Z*)	−80 °C, 30 min	20	35 (2.6:1)	21
8	*anti*-(*Z*)	−80 to −30 °C	28	48 (only-*E*)	14

phenyl group resulted in a significant enhancement of the reaction rate in both (*E*)- and (*Z*)-**49**. As expected, there was little difference in the ratios of **53**/**55** between syn and anti derivatives. This is thought to be due to the delicate balance between enhanced reactivity and increased stabilization of the internal chelation induced by introduction of a phenyl group.

In contrast to the enhanced reactivity by introduction of a phenyl group in the vinylsilyl group, the introduction of a dimethyl(phenyl)siloxy group in place of the *tert*-butyldimethylsiloxy group resulted in a decrease in the rate of the reaction. Particularly noteworthy is that a more predominant formation of cyclopentenol **56** from *anti*-**50** than from *syn*-**50** was observed at −80 °C as expected (Table 6, entries 2, 4, 5, and 7). Moreover, *syn*-cyclopropandiol derivative **58** was obtained from both syn and anti derivatives **50**, suggesting facile interconversion between *syn*- and *anti*-cyclopropanolates and an important role of the stabilization by chelation involving pentacoordinate silicon species, as shown in Scheme 9.

Scheme 10



Furthermore, our previous observation on the reaction of 1,2-divinylcyclopropanolates **59** where the formation of seven-membered ring via [3 + 4] annulation can compete with the formation of five-membered ring via [3 + 2] annulation provides additional support for the chelation and the rapid interconversion between the syn and anti isomers (Scheme 10). Thus, the five-membered carbocycle **63** was obtained as a major product from *anti*-(*Z*)-**59**, which can involve a five-coordinated silicon atom, in contrast to the fact that no formation of detectable amounts of **63** was observed in the reaction of *anti*-(*E*)-**59** where chelation cannot take place.

Next, we turned our attention to [3 + 2] annulation using (*β*-(phenylthio)acryloyl)silanes **27**. Although the results of the low-temperature quenching experiments described above showed that the independence of the stereochemical outcome of [3 + 2] annulation using **27** to its olefin geometry is partly due to loss of the stereochemical integrity of **27** during the reaction, this does not tell us whether the annulation occurs via a cyclopropanolate intermediate. We decided to examine the reaction of the corresponding phenylthio derivatives **64**. Cyclopropyl acetates **64**[21] were prepared in a manner similar to **45**. Unfortunately, *syn*- and *anti*-(*E*)-**64** could not be separated. The results of the reaction with MeLi are shown in Table 7.

The remarkable difference between the [3 + 2] annulation using **27** and the reaction of **64** with MeLi was the product distribution depending on the olefin geometry of the starting materials, in addition to the enhanced reactivity in the latter case. Thus, the reaction of (*Z*)-**64** provided two diastereomers **31** and **32** in about a 5:4 ratio, while the reaction of (*E*)-**64** almost exclusively provided **31**. Also, since the change of the vinyl substituent in the vinylpropanolates from trimethylsilyl to di-

Scheme 11

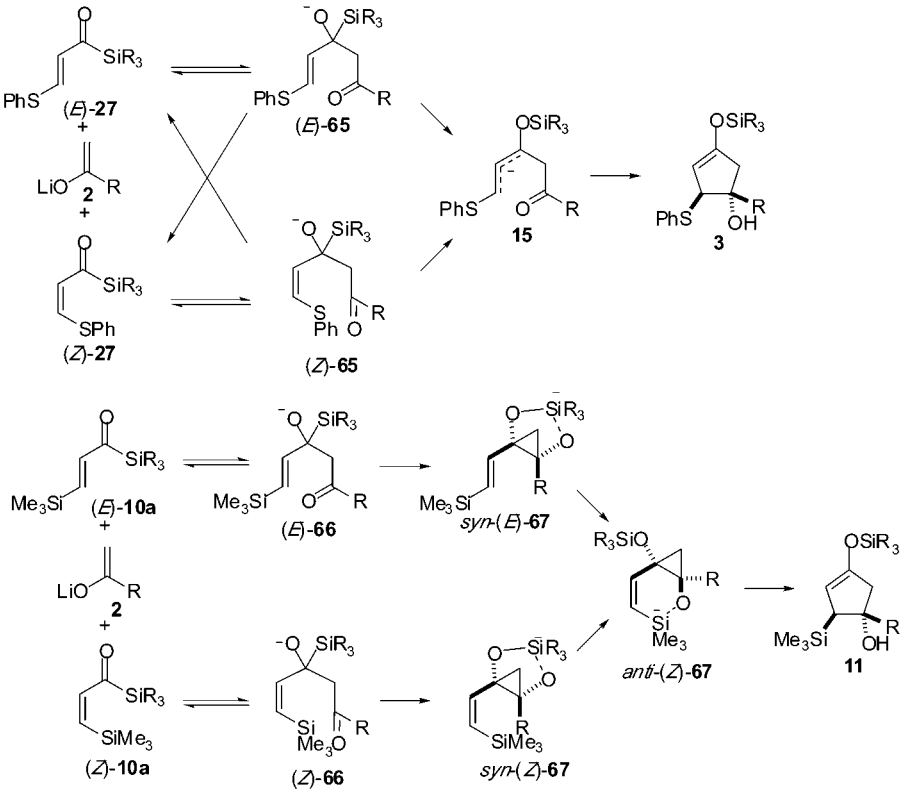
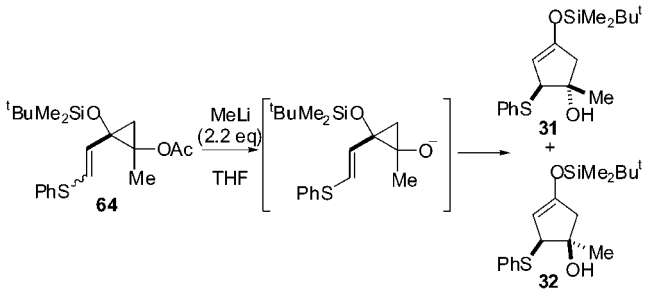


Table 7.



64	conditions	yield (%) **31**	**32**
anti-E	−80 °C, 30 min	84	2
	−80° to −30 °C	85	3
anti-E:*syn-E* (1:1.1)	−80 °C, 30 min	87	1
	−80 to −30 °C	87	2
anti-Z	−80 °C, 30 min	50	39
	−80 to −30 °C	48	39
syn-Z	−80 °C, 30 min	48	35
	−80 to −30 °C	48	40

methyl(phenyl)silyl and to phenylthio groups increased the reactivity of the rearrangement, it appears to be a general trend that the rate of the rearrangement increases, when the α-carbanion-stabilizing character of the substituent on the vinyl group increases. The enhanced reactivity is attributed to acceleration of the ring-opening of cyclopropane caused by the generation of a carbanion character at the α-position of the β-heteroatom substituent.

Although the origin of the observed stereoselectivity is not clear at present, the results rule out the possibility of the intermediacy of cyclopropanolate **16** (X = SPh) in the major reaction pathway of [3 + 2] annulation of **27**.

Conclusions

The results described above seem to indicate a need for a slight modification of the initially proposed mechanistic pathway for the [3 + 2] annulation shown in Scheme 3. (*E*)- and (*Z*)-**27** were found in equilibrium under the reaction conditions (Scheme 6 and Table 2). Although the possibility that either of (*E*)- or (*Z*)-**27** is the only precursor leading to cyclopentenols **3** and **4** cannot be entirely ruled out, the existence of the equilibrium does not necessarily mean that the delocalized allylic carbanion **15** is not involved as a common intermediate. The intermediacy of **15** is consistent with the failure in [3 + 4] annulation of **27**, which requires the formation of a cyclopropanolate intermediate. Consequently, we believe that delocalized allylic anion **15** is an intermediate in the major reaction pathway in the [3 + 2] annulation of **27** (Scheme 11). The reason for the preferential formation of **3**, which seems to be thermodynamically less stable than **4** due to steric repulsion between the phenylthio group and alkyl groups, is unclear at present because of potential complications associated with the structures of sulfur-stabilized allylic carbanions, their relative reactivities, and the relative conformation of the carbonyl group.

In the case of the trimethylsilyl derivatives **10a**, we propose a reaction pathway for the formation of **11** that involves the initial formation of vinylcyclopropanolate intermediates *syn*-(*E*)- and *syn*-(*Z*)-**67** followed by the isomerization to *anti*-(*Z*)-**67** and rearrangement to **11** via a 1,3-sigmatropic shift, although the mechanistic origin of the minor product **12** is still not clear.

Although a full understanding of the actual mechanism of the [3 + 2] annulation must await further detailed mechanistic experimentation, our current data have provided significant insights into the reaction sequence of the annulation.

Acknowledgment. This research was partly supported by a grant from the Takeda Science Foundation.

Supporting Information Available: Full experimental detail and characterization data for all new compounds described in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0160219