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Acid-catalyzed rearrangement of α-hydroxytrialkylsilanes

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Abstract—Cationic rearrangement of several α-hydroxysilanes is described. Treatment of both (1*R*,1′*R*,2′*S*)-α-hydroxycyclopropylsilane *syn*-**9** and (1*S*,1′*R*,2′*S*)-*anti*-**9** under aqueous H_2SO_4 underwent rearrangement via a common α-silyl cation intermediate **A** to give a mixture of the ring-opened (*R*)-vinylsilane **13**, the tandem [1,2]-CC bond migration product (1*R*,2*S*,1′*R*)-**14**, and its 1′*S* isomer **15**. On the other hand, the acidic treatment of (*R*,*E*)-α-hydroxyalkenylsilane **8** or (*R*,*Z*)-**8** was each accompanied with partial racemization to give an enantiomeric isomer of allylic alcohol **23** via a preferential *syn*-facial S_N2' reaction, respectively. Both α-hydroxyalkynylsilane **6** and α-hydroxyalkylsilane **12** were inert to the acidic conditions; however, treatment of (*R*)-α-mesyloxyalkynylsilane **26** under aqueous H_2SO_4 gave a mixture of the optically active rearranged allene **27**, α,β-unsaturated ketone **28**, and (*S*)-α-hydroxyalkynylsilane **6** with partial racemization. Comparisons of the reactivities of these α-hydroxysilanes under acidic conditions are also disclosed.

1. Introduction

It is well-known that carbocation β to silicon is stabilized by σ-π hyperconjugation (the β-effect), and various synthetic applications have been provided (Scheme 1).[1] On the contrary to the β-silyl cation, carbocation α to silicon (α-silyl cation) has not been well investigated because of its presumed chemical instability which is indicated by MP2/6-31G*//3-21G calculations; a carbocation a to the SiH_3 group is 18.3 kcal/mol less stable than the corresponding carbocation α to a methyl group.[2] To date, no systematic investigations regarding the generation of the α-silyl cation and its synthetic applications have been reported.[1a,3] During the course of our recent studies regarding syntheses and reactions using optically active α-hydroxysilane, we found that the α-hydroxycyclopropylsilane **1** underwent acid-catalyzed rearrangement via a putative α-silyl cation intermediate to give a mixture of products, which were composed of the ring-opened vinyl silane **2**, silylcyclopropane **3**, and its C1′-diastereomer **4** (Scheme 2).[4] Since the previous work dealt preliminarily with only one diastereomer of α-hydroxycyclopropylsilane (*syn* form), the stereochemical outcome from the other diastereomer (*anti* form) remained to be examined. Furthermore, it is of interest to investigate acid-catalyzed reactions of α-hydroxysilanes having an α-alkenyl, an α-alkynyl or an α-alkyl group to establish whether the α-silyl cation can be generated (Scheme 3). Herein, we wish to report acid-catalyzed rearrangement of several α-substituted α-hydroxysilanes.

2. Results and discussion

2.1. Preparation of α-hydroxysilanes

Since in the previous studies difficulty was incurred in handling the TMS-substituted α-hydroxysilanes during its preparation and the product analysis due to its instability against acidic conditions, a chemically more stable *tert*-butyldimethylsilyl (TBDMS) group was used for the present study. Preparation of the enantiomers and diastereomers of α-hydroxysilanes **6**, **8**, **9** and **12** are summarized in Scheme 4 where racemic **6**, prepared from 2-butyn-1-ol (**5**) in one pot (86%),[5,6] was used as the common synthetic precursor except for (*R*,*E*)-**8**. Jones oxidation of **6** gave silyl ketone **7** whose enantioselective reduction with (−)-B-chloro diisopinocamphenylborane (DIP-Cl)[7] afforded optically active α-hydroxyalkynylsilane (*R*)-**6** (86% yield, >95% ee).[8] *Z*-α-Hydroxyalkenylsilane (*R*,*Z*)-**8** was prepared from (*R*)-**6** by hydrogenation using the Lindlar catalyst (81%). Stereoselective cyclopropanation of (*R*,*Z*)-**8** was performed using Et_2Zn–CH_2I_2 to give (1*R*,1′*R*,2′*S*)-α-hydroxycyclopropylsilane *syn*-**9**.[9] Its 1*S* isomer *anti*-**9** was prepared by the following two-step reaction: (1) PDC oxidation of *syn*-**9** (72%) and (2) reduction with DIBAL-H (76%, *anti*/*syn*=20/1). α-Hydroxyalkenylsilane (*R*,*E*)-**8** (90% ee)[8] was prepared from (*E*)-silyl ketone **11**[10] by enantioselective reduction using (−)-DIP-Cl (63%).[11] An α-hydroxysilane (*R*)-**12** having an alkyl group was prepared from (*R*)-**6** by hydrogenation using the Willkinson catalyst.[12]

Keywords: α-hydroxysilane; α-silyl cation; acid-catalyzed rearrangement; tandem [1,2] shift.

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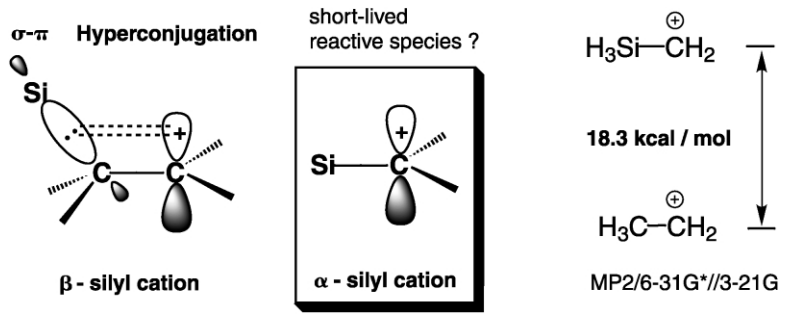
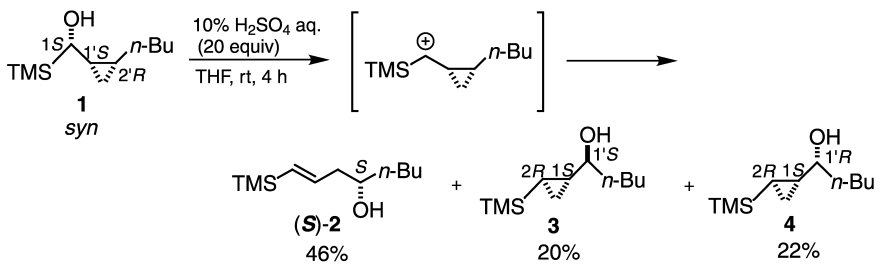
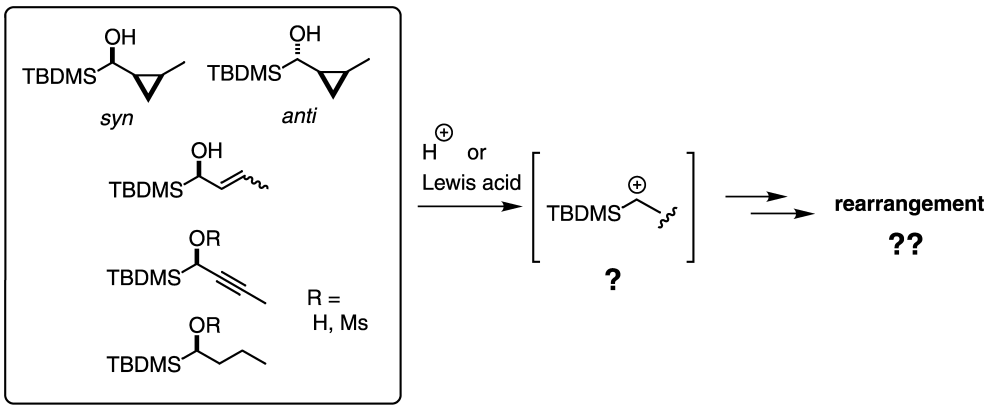


Scheme 1.



Scheme 2.

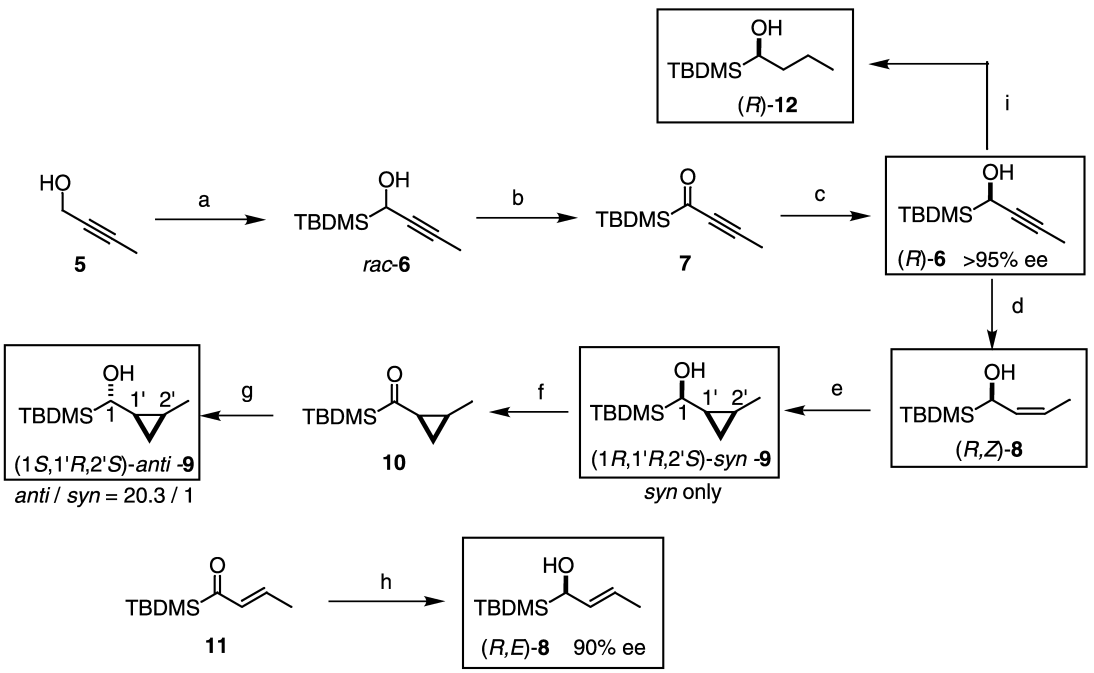


Scheme 3.

2.2. Acid-catalyzed rearrangement of α-hyroxycyclopropylsilanes

To test the effect of the sterically bulky TBDMS group under the cationic rearrangement, *syn*-**9** (>95% ee) which is the same diastereomer as the TMS substrate, *syn*-**1**, was subjected to acidic conditions (Scheme 5). The reaction using 10% H_2SO_4 (THF, rt, 1 h) gave a mixture of (*R*)-vinylsilane **13** (Julia-type rearrangement product, 38%),[13] (1*R*,2*S*,1′*R*)-silylcyclopropane **14** (16%) and its 1′*S* diastereomer **15** (14%) whose composition was almost identical with that of products from *syn*-**1**.[4] The optical purity of the starting *syn*-**9** was completely retained in the rearranged products (>95% ee).[8] A trace amount of the primary alcohol **16** was a by-product which would be produced by a nucleophilic attack of 1,4-butanediol derived from THF. On the other hand, the hydroxy diastereomer, *anti*-**9** (>95% ee), was completely consumed within 4 h to give a mixture of (*R*)-**13** (39%), **14** (20%) and **15** (26%) in an optically active form (>95% ee).[8] Thus, it was found that *anti*-**9** gave not only the same rearrangement products as those from *syn*-**9** but also their product ratios were almost similar to that of each diastereomer. Interconversion between the rearranged products (*R*)-**13**, **14** and **15** was not observed under the reaction conditions.[14]

These results suggest that the reactions of both *syn*- and *anti*-**9** proceed via the common α-silyl cation intermediate **A** having a stable anti conformation as compared with an unfavorable eclipsed conformation **A′** to give the rearrangement products as shown in Scheme 6. The formation of the vinylsilane (*R*)-**13** would be a stereospecific process via the transition state structure **C** where the positive charge is located at the more substituted C2′ (secondary carbocation, path a) than the less substituted C3′ in **B** (primary carbocation, path b). Thus, the reaction proceeded via path a in an S_N2' manner to give (*R*)-**13**. On the other hand, the formation of a mixture of diastereomeric **14** and **15** would be attributed to the tandem [1,2]-CC bond migration from the α-silyl cation **A** via a putative cyclobutyl cation

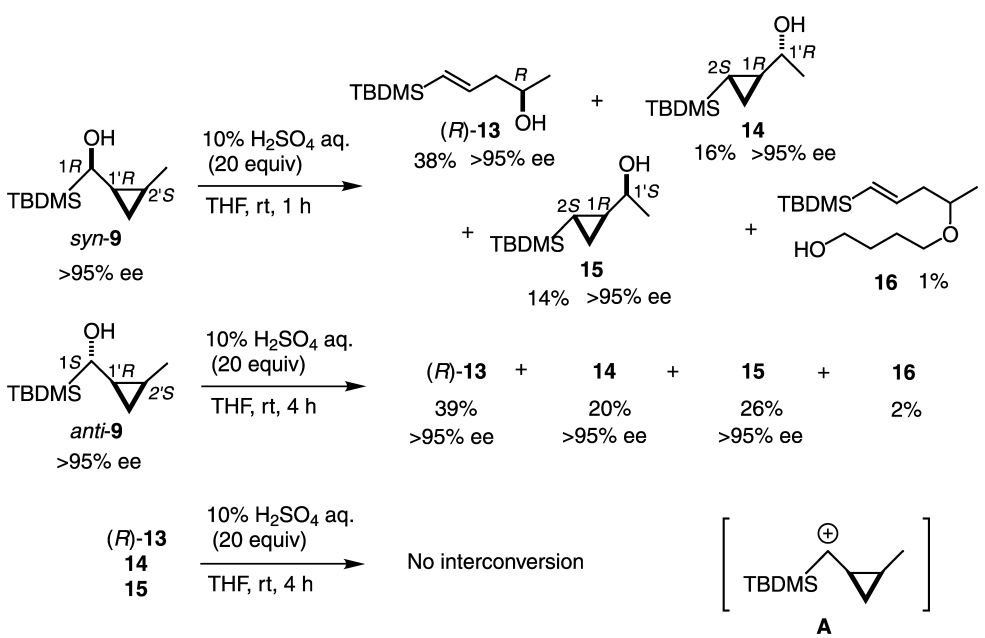


Scheme 4. Conditions. (a) (one-pot) (1) *n*-BuLi (1.05 equiv.), TBDMSCl (1.05 equiv.), THF, 0°C, 2 h. (2) *n*-BuLi (1.2 equiv.), THF, −45°C, 1.5 h, then AcOH, −78°C, 86%. (b) Jones oxidation, 91%. (c) (−)-DIP-Cl (1.5 equiv.), THF, −40°C, 2 h, 86%. (d) H_2, Lindlar cat., AcOEt, rt, 1 h, 81%. (e) Et_2Zn, CH_2I_2, CH_2Cl_2, −20°C, 3 h, 75%. (f) PDC, CH_2Cl_2, rt, 1 h, 72%. (g) DIBAL-H, CH_2Cl_2, −78°C, 30 min, 88%. (h) (−)-DIP-Cl (1.5 equiv.), THF, rt, 2 h, 63%. (i) H_2, $(PPh_3)_3RhCl$, benzene, rt, 1 h, 69%.

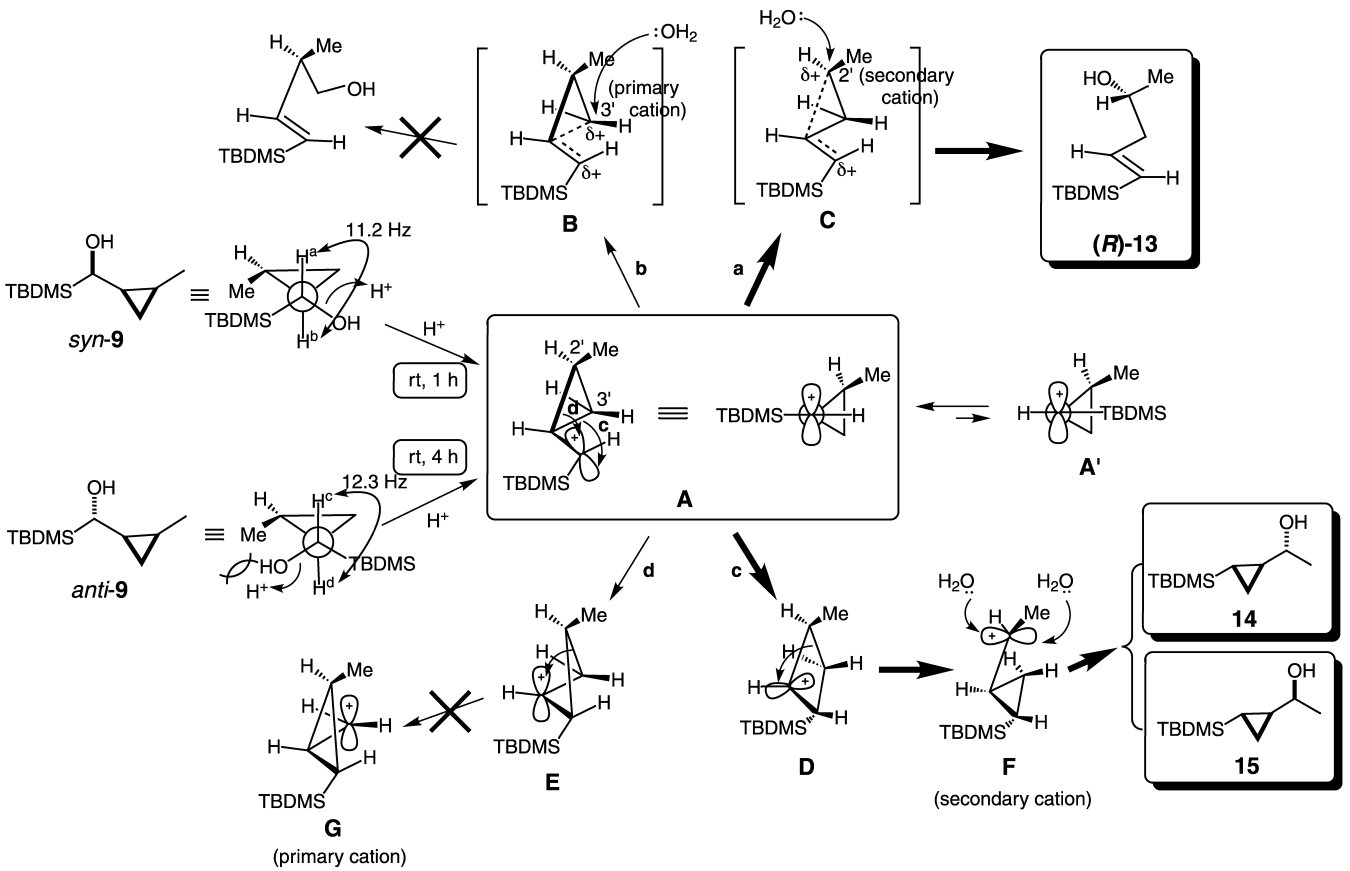
D[15] (path c), which immediately rearranged to a stable cyclopropylcarbinyl cation **F**. H_2O attacks the cationic center from the *re*- or *si*-face in a non-stereoselective manner to give a mixture of **14** and **15**. Since none of the rearranged products derived from the primary cation **G** (path d) was obtained, path c to form **D** would be the favored rearrangement process. As the result, the reaction proceeded in a competitive manner between the hydroxy attack to the C2′ position (path a) and the CC bond migration from **A** (path c).

The fact that *anti*-**9** required longer reaction time (4 h) than *syn*-**9** (1 h) would be attributed to the ease of protonation to the hydroxy group of **9**. Conformation analysis of *syn*-**9** and *anti*-**9** using ^1H NMR revealed that the hydroxy group of *anti*-**9** was sterically more hindered (J_{Hc-Hd}=12.3 Hz) than that of *syn*-**9** (J_{Ha-Hb}=11.2 Hz). Therefore, elimination of H_2O to produce **A** in *anti*-**9** would be slower than that of *syn*-**9**.

Next, we examined the mode of rearrangement using a



Scheme 5.



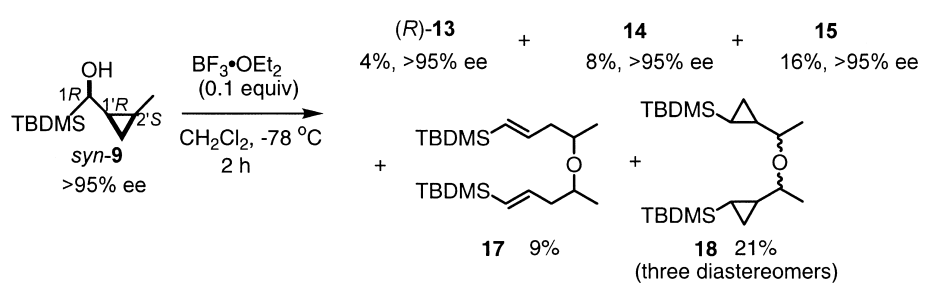
Scheme 6.

Lewis acid in an aprotic solvent. The reaction of *syn*-**9** with BF_3OEt_2 (0.1 equiv.) in CH_2Cl_2 was completed within 2 h at −78°C to give a mixture of (*R*)-**13** (4%, >95% ee), 14 (8%, >95% ee), **15** (16%, >95% ee), and the dimeric products **17** (9%) and **18** (21% as a mixture of three diastereomers) (Scheme 7). The fact that the reaction gave the same rearranged products **13**–**15** in optically active form as those from sulfuric acid indicates that the rearrangement proceeded in the same manner as that using aqueous sulfuric acid. Presumably, dimeric products **17** and **18** were derived from **13** and a mixture of **14** and **15**, respectively.

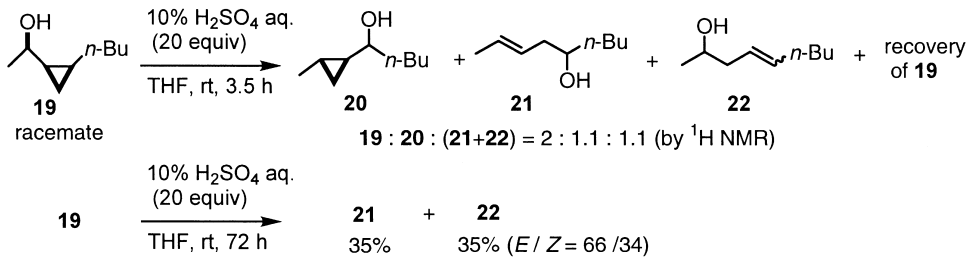
The remaining question is whether the present rearrangement is specific to the α-trialkylsilylcyclopropyl system. Thus, we examined the reaction of an analogous substrate **19** having a methyl group instead of a trialkylsilyl group (Scheme 8). The reaction of **19** with 10% H_2SO_4 in THF at room temperature was monitored using ^1H NMR and was found to proceed slowly to give after 3.5 h a mixture of cyclopropane **20** (a mixture of diastereomers at the hydroxy group) and homoallyl alcohols **21** and **22** and unreacted starting material **19** [**19**: **20**: (**21**+**22**)=2:1.1:1.1]. Upon standing the reaction for 72 h, both **19** and **20** disappeared to give a mixture of **21** (35%) and **22** (35%, *E*/*Z*=66/34).[16] From these results, it was clearly understood that (1) tandem [1,2] CC-shift occurs in both the α-silyl and the α-methyl substrates, (2) the rate of the rearrangement of α-hydroxysilanes **1** and **9** is 10–70 times faster than that of the methyl derivative **19**, and (3) the rearranged cyclopropylcarbinol having a trialkylsilyl group is stable under the reaction conditions for 20 h,[14] while the methyl derivative undergoes rapid ring-opening to give the homoallyl alcohols.

2.3. Acid-catalyzed rearrangement of α-hyroxyalkenylsilanes

Next, we turned our attention to the acid-catalyzed

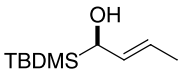
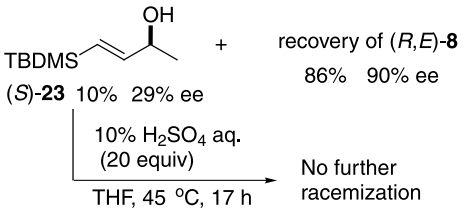
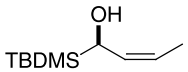
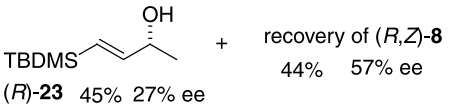
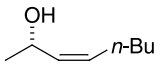
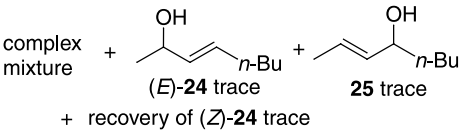


Scheme 7.

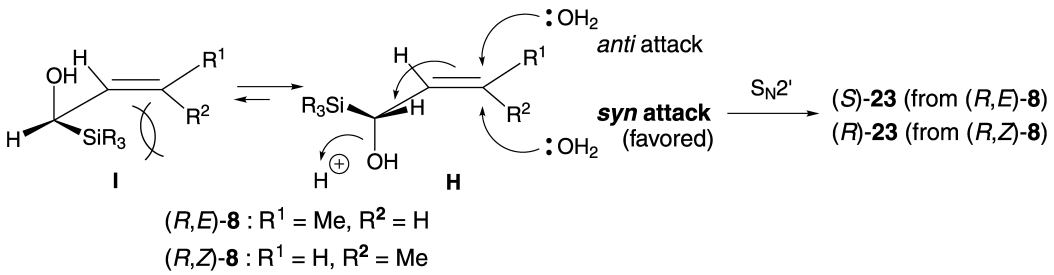


Scheme 8.

Table 1. Reactions of α-hydroxyalkenylsilanes and their analogs under acidic conditions

Entry	Substrate	Method[a]	Condition	Results
1	 (*R*,*E*)-**8** 90% ee	A	rt, 21 h	 (*S*)-**23** 10% 29% ee + recovery of (*R*,*E*)-**8** 86% 90% ee; 10% H_2SO_4 aq. (20 equiv), THF, 45 °C, 17 h → No further racemization
2	 (*R*,*Z*)-**8** >95% ee	A	rt, 23 h	Recovery of (*R*,*Z*)-**8** 85%, 94% ee
3	(*R*,*Z*)-**8** >95% ee	A	45°C, 41 h	 (*R*)-**23** 45% 27% ee + recovery of (*R*,*Z*)-**8** 44% 57% ee
4	(*R*,*Z*)-**8** >95% ee	B	rt, 8 h	(*R*)-**23** 19%, 48% ee + recovery of (*R*,*Z*)-**8** 57%, 93% ee
5	 (*S*,*Z*)-**24** >95% ee	A	rt, 22 h	 complex mixture + (*E*)-**24** trace + **25** trace + recovery of (*Z*)-**24** trace; (*E*)-**24** : **25** : (*Z*)-**24** = 20 : 8 : 100 (by 1H NMR)

[a] (a) Method A: 10% H_2SO_4 aq. (20 equiv.) in THF; method B: $BF_3{\cdot}OEt_2$ (1.5 equiv.) in CH_2Cl_2.

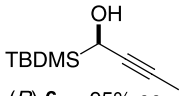
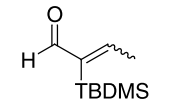
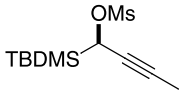
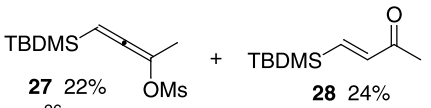
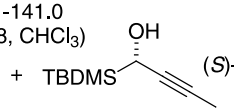
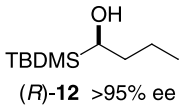
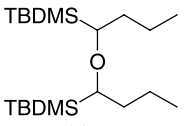
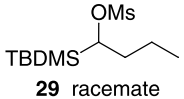
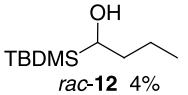
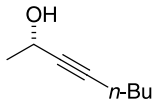
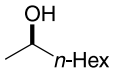
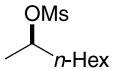
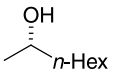


Scheme 9.

rearrangement of optically active α-hydroxyalkenylsilanes (Table 1). Treatment of α-hydroxysilane (*R*,*E*)-**8** (90% ee) with 10% H_2SO_4 in THF at room temperature for 21 h gave a mixture of *trans*-vinylsilane (*S*)-**23** (10%) and the starting (*R*,*E*)-**8** (86%) (entry 1). The optical purity of the recovered (*R*,*E*)-**8** was the same as that of the starting **8**, while the optical purity of the rearranged (*S*)-**23** was 29% ee where the ee of the starting **8** was much decreased. Treatment of (*S*)-**23** (28% ee) under warm-up conditions (45°C, 17 h) resulted in the exclusive recovery of (*S*)-**23** whose ee was the same as that of the starting **23**.

The same acidic treatment of the *Z*-isomer, (*R*,*Z*)-**8** (>95% ee), as above was very slow and none of the rearranged product was produced (entry 2). Since the ee of the recovered (*R*,*Z*)-**8** was 94%, no racemization was observed in (*R*,*Z*)-**8**. On the other hand, upon warming to 45°C the reaction gradually proceeded to give, after 41 h, a mixture of vinylsilane (*R*)-**23** (45% yield, 27% ee[8]) and the starting (*R*,*Z*)-**8** (44% yield, 57% ee[8]) (entry 3). Since **23** is optically stable under the warm-up conditions, partial racemization occurred at the α position of the *Z*-isomer **8**. Lewis acid treatment (BF_3, CH_2Cl_2, room temperature, 8 h) of (*R*,*Z*)-**8** afforded a mixture of the

Table 2. Reactions of α-hydroxyalkynylsilanes, α-hydroxyalkylsilanes, and their analogs under acidic conditions

Entry	Substrate	Method[a]	Condition	Results
1	 (*R*)-**6** >95% ee	A	Reflux, 19 h	Recovery of (*R*)-**6** 88% >95% ee
2	(*R*)-**6**>**95**% ee	B	rt, 2 h	 + recovery of (*R*)-**6** 49%, >95% ee **30** 9%, *E* / *Z* = 1 / 2.1
3	 (*R*)-**26** >95% ee	A	Reflux, 21 h	 **27** 22% $[\alpha]_D^{26}$ -141.0 (*c* 1.68, $CHCl_3$) +  (*S*)-**6** 36%, 22% ee
4	 (*R*)-**12** >95% ee	A	Reflux, 18 h	Recovery of (*R*)-**12** 96% >95% ee
5	(*R*)-**12** >95% ee	B	Reflux, 24 h	 + recovery of (*R*)-**12** 27% >95% ee **31** 37% $[\alpha]_D^{27}$ -9.9 (*c* 3.25, $CHCl_3$)
6	 **29** racemate	A	Reflux, 18 h	 + recovery of **29** 90% *rac*-**12** 4%
7	 (R)-**32** >95% ee	A	Reflux, 21 h	Recovery of (*S*)-**32** 73% 87% ee
8	 (*R*)-**33** >95% ee	A	Reflux, 21 h	Recovery of (*R*)-**33** 73% 87% ee
9	 (*R*)-**34** >95% ee	A	Reflux, 19 h	 (*S*)-**33** 46% >95% ee

[a] (a) Method A: 10% H_2SO_4 aq. (20 equiv.) in THF; method B: $BF_2{\cdot}OEt_2$ (0.1 equiv.) in CH_2Cl_2.

rearrangement product (*R*)-**23** (19%, 48% ee[8]) and the starting (*R*,*Z*)-**8** (57%, 93% ee[8]) (entry 4).

From these results, acid-catalyzed rearrangement of α-hydroxyalkenylsilane is summarized by the following points. (1) Both (*R*,*E*)-**8** and (*R*,*Z*)-**8** are optically stable alcohols under the reaction conditions at room temperature, since the recovered **8** showed the same ee values, respectively (entries 1, 2, and 4). (2) Under the warm-up conditions, the ee of **23** was completely retained. (3) The (*R*,*E*)-isomer gave (*S*)-**23** containing 36% of its *R*-isomer, and the (*R*,*Z*)-isomer gave (*R*)-**23** containing 37% of the corresponding *S*-isomer while the reaction of the *Z*-isomer was much slower than that of the *E*-isomer (entries 1 and 2). (4) None of the rearranged *Z*-vinylsilane was produced in all cases. (5) Partial racemization occurred upon warming (*R*,*Z*)-**8** to 45°C (entry 3). (6) Aprotic conditions using BF_3 gave the same (*R*)-**23** in 48% ee (entry 5).

These experimental results led us to propose the following reaction pathway (Scheme 9): (1) A trigonal α silyl cation which gives a completely racemized product did not form except under the warm-up conditions of (*R*,*Z*)-**8** where formation of a delocalized allylic cation is also possible. (2) The reaction proceeded from conformer **H** with the least allylic strain among other conformers where the hydroxy group locates perpendicular to the CC double bond plane. Conformer **I** would be eliminated due to the fact that the *Z*-vinylsilane was not obtained. (3) Based on this assumption, *syn*-S_N2' reaction would be the major pathway to produce (*S*)-**23** from (*R*,*E*)-**8** or (*R*)-**23** from (*R*,*Z*)-**8**. The reaction also involved an *anti*-S_N2' reaction that contributes to a decrease in ee of the product. However, we have not reached a conclusion regarding the preference of the *syn* attack over the anti attack. (4) Lewis acid-catalyzed reaction of (*R*,*Z*)-**8** would involve internal migration of the hydroxy group that gives (*R*)-**23**, since the product ee (48%) was higher than that obtained using protic conditions.

Next, we examined acid-catalyzed rearrangement of the α methyl substrate, (*S*,*Z*)-3-octen-2-ol (**24**, >95% ee),[17] to compare the results obtained by the use of the TBDMS substrate **8**. Treatment of (*S*,*Z*)-**24** using 10% H_2SO_4, THF, room temperature, 24 h gave an unidentifiable mixture of products which contained only trace amounts of (*E*)-**24**, **25** and the starting (*Z*)-**24**. The product mixture was analyzed by ^1H NMR indicating that the ratio of (*E*)-**24**:**25**:(*Z*)-**24** was 20:8:100. Because the reaction is sluggish and only trace amounts of the products mixture were isolated, the ee values of the products could not be obtained. However, we found that the reaction involves allylic rearrangement together with double bond isomerization. From these results, it is seen that α-hydroxyalkenylsilane **8** gradually rearranges to the *trans*-vinylsilane **23**; however, **8** is much less reactive than its methyl-substituted analog contrary to the case of the α cyclopropyl substrates **9** and **19**.

2.4. Acid-catalyzed rearrangement of α-alkynyl and α-alkyl α-hyroxysilanes

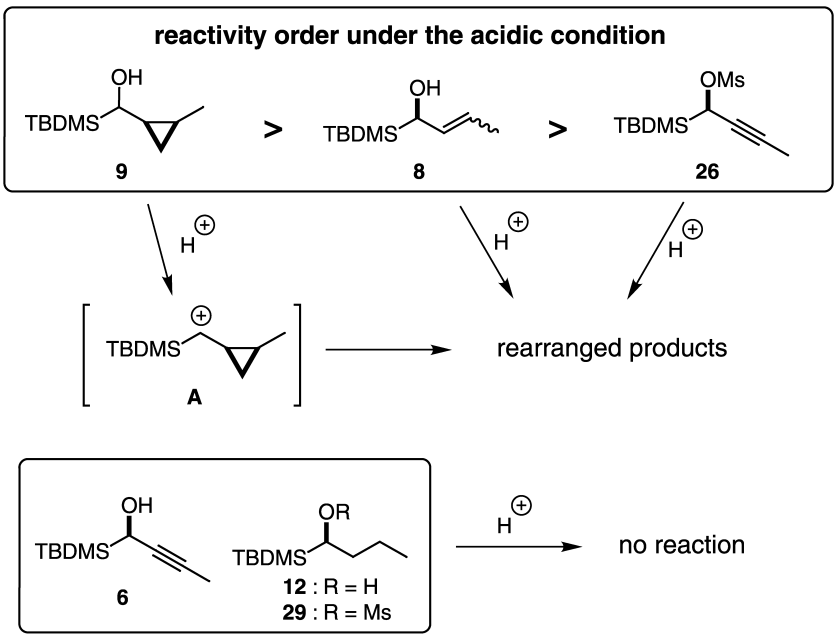
Next, we examined acid-catalyzed rearrangement of α-alkynyl or α-alkyl substituted α-hydroxysilanes. These results are summarized in Table 2. The reaction of α-hydroxyalkynylsilane (*R*)-**6** with 10% H_2SO_4 in THF at room temperature did not proceed at all and even under reflux for 19 h resulted in complete recovery of the starting material (entry 1). On the other hand, treatment of its mesylate (*R*)-**26**[18] under the same conditions gave a mixture of the optically active allene **27** {22%, $[\alpha]_D^{26}=-141.0$ (*c* 1.68, $CHCl_3$)},[19] the unsaturated ketone **28** (24%) and α-hydroxysilane (*S*)-**6** (36%, 22% ee[8]) (entry 3). The allenyl mesylate **27** would be produced via [3,3] sigmatropic rearrangement of (*R*)-**26**. The ketone **28** would be formed by a nucleophilic attack of H_2O (S_N2'). The hydrolyzed product (*S*)-**6** showed 22% ee suggesting that competitive hydrolysis of the mesyl group and nucleophilic substitution with H_2O occurred. Lewis acidic treatment of (*R*)-**6** (BF_3OEt_2) afforded a mixture of unsaturated ketone **30** (9%, *E*/*Z*=1/2.1) and the starting material (*R*)-**6** (49%, >95% ee) (entry 2). The formation of **30** would be the result of a [1,2]-silyl shift. Silyl migration similar to that of **30** has been reported by Schaumann et al.[6]

Treatment of the α-hydroxyalkylsilane (*R*)-**12** (10% H_2SO_4, THF, reflux, 18 h) resulted in complete recovery of the starting material without loss of its ee (entry 4). Its mesylate gave a small amount of a hydrolyzed product (entry 6). On the other hand, treatment of (*R*)-**12** (>95% ee) with BF_3OEt_2 afforded dimerized product **31** in 37% yield which showed $[\alpha]_D^{27}=-9.9$ (*c* 3.25 $CHCl_3$). Although its ee could not be estimated, **31** would contain a significant amount of the optically active (*R*,*R*)-enantiomer, i.e., the α-silyl cation from **12** would be attacked by the hydroxy group of (*R*)-**12** in an S_N1 manner, since S_N2 reaction would give the (*R*,*S*)-enantiomer which is a mesomeric form (entry 5).

We, next, examined the acidic treatment of analogous substrates having a methyl group instead of the TBDMS group. Treatment of (*R*)-3-octyn-2-ol (**32**, >95% ee)[20] (10% H_2SO_4, THF, reflux, 21 h) resulted in recovery of (*R*)-**32** in 73% yield, but its optical purity was reduced to 87% ee[8] (entry 7). Treatment of (*R*)-2-octanol (**33**, >95% ee)[21] under the same conditions also resulted in recovery of partially racemized (*R*)-**33** (entry 8, 73% yield, 87% ee[8]). On the contrary to this, the reaction of the mesylate (*R*)-**34**[22] (10% H_2SO_4, THF, reflux, 19 h) gave (*S*)-2-octanol in 46% yield with >95% ee (S_N2 reaction) (entry 9). These results indicate that α-hydroxyalkynylsilane **6**, α-hydroxyalkylsilane **12** or its mesylate **29** is each much less reactive than the corresponding methyl-substituted analog **32**, **33** or **34** under acidic conditions (10% H_2SO_4), respectively.

3. Conclusion

Systematic studies of the acid-catalyzed reactions of α-hydroxycyclopropylsilane **9**, α-hydroxyalkenylsilane **8**, α-hydroxyalkynylsilane **6**, α-mesyloxyalkynylsilane **26**, α-hydroxyalkylsilane **12**, and α-mesyloxyalkylsilane **29** were performed for the first time. From the mode of rearrangement using α-hydroxycyclopropylsilane it was well understood that the rearrangement involves an S_N2' cyclopropyl ring-opening and a tandem CC-migration reaction in a competitive manner. The alkenylsilanes **8** gave the allylic rearrangement product. Inspection of the products ee



Scheme 10.

suggested that the rearrangement involves a *syn*-S_N2' reaction as the major pathway. On the other hand, the reactions of alkynyl and alkyl substituted derivatives **6**, **12**, and **29** were inert under the reaction conditions, while the alkynyl mesylate **26** gave the rearranged products including optically active allene. The reactivity profile of the α-hydroxysilanes is depicted in Scheme 10. These results suggest that the putative α-silyl cation generated from the α-hydroxy or mesyloxy group is a short-lived species which rapidly migrates to the more stable cyclopropylcarbinyl, allyl, or allenyl cation to give the rearrangement product in all cases tested which is consistent with the calculation of the α-silyl cation.[2]

4. Experimental

4.1. General

All reagents and solvents were purchased from either Aldrich Chemical Company, Inc., Merck & Co., Inc., Nacalai Tesque Company, Ltd, Peptide Institute, Tokyo Kasei Kogyo Co., Ltd, or Wako Pure Chemical Industries, Ltd, and used without further purification unless otherwise indicated. Tetrahydrofuran (THF) was distilled under an argon atmosphere from sodium/benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from phosphoric pentaoxide (P_2O_5). Methanol (MeOH) was distilled from magnesium turnings and iodine. Diethyl ether (Et_2O) of anhydrous grade was used.

All reactions were monitored by thin layer chromatography (TLC), carried out on 2×5 cm precoated TLC plates (Merck Kieselgel gel 60F-254; layer thickness, 0.25 mm), with UV light (254 nm), $KMnO_4$ solution (0.5 g dissolved in 100 mL of water), ninhydrin solution (TCI N-094) and/or phosphomolybdic acid solution (10 g dissolved in 150 mL of EtOH). Silica gel (DAISO-GEL IR-60-63/210W or IR-60-40/63W) was used for column chromatography. Melting points (mp) were determined with a Yanaco MP-21 melting point apparatus and were uncorrected. Optical rotations ($[\alpha]_D$) were taken on a Perkin–Elmer 241 polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded on one of the following instruments: Varian Unity plus 500, JEOL JNM-LA400, JEOL JNM-GX-400 or JEOL JNM-LA300. Chemical shifts of ^1H NMR were reported as δ values in ppm relative to $CHCl_3$ (7.26) in $CDCl_3$, CH_3OH (3.30) in CD_3OD or HDO (4.80) in D_2O. Chemical shifts of ^{13}C NMR were reported as δ values in ppm relative to $CDCl_3$ (77.00) in $CDCl_3$, CH_3OH (49.00) in CD_3OD or dioxane (68.90) in D_2O. Infrared spectra (IR) were measured on either a Hitachi 270-30 or a JASCO FT/IR-420 spectrophotometer. High-resolution mass spectra (HRMS) were obtained on either a JEOL JMS-D300 or a JEOL JMS-AX500 spectrometer for electron ionization (EI), chemical ionization (CI) or fast atom bombardment ionization (FAB).

4.1.1. (*dl*)-1-*t*-Butyldimethylsilyl-2-butyn-1-ol (*rac*-6). To a solution of 2-butyn-1-ol (**5**, 15.0 g, 214 mmol) in THF (180 mL) was added *n*-BuLi in *n*-hexane (1.60 M solution; 161 mL, 257 mmol) at −78°C, and the mixture was stirred at 0°C for 30 min. To the solution was added a solution of TBDMSCl (35.48 g, 235 mmol) in THF (80 mL) at −78°C. After stirring at rt for 4 h, *n*-BuLi in *n*-hexane (1.60 M solution; 174 mL, 278 mmol) was added dropwise to the solution at −78°C, and the mixture stirred at −45°C for 2 h. The reaction was quenched by 10% AcOH in THF at −78°C. The mixture was extracted with Et_2O, and the organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/Et_2O=30/1) to give *rac*-**6** (34.86 g, 88%) as pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 4.17 (q, J=2.7 Hz, 1H), 1.87 (d, J=3.0 Hz, 3H), 1.34 (br, 1H, exchangeable with D_2O), 0.97 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 84.0, 80.2, 55.1, 26.9, 16.9, 3.8, −8.0, −8.6; IR (neat) 3448, 2960, 2900, 2864, 2310, 1696, 1590, 1466, 1250, 976, 838,

782 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{10}H_{20}OSi$ $(M)^+$ 184.1283, found 184.1264.

4.1.2. 1-*t*-Butyldimethylsilyl-2-butynone (7). To a solution of *rac*-**6** (32.00 g, 86.8 mmol) in acetone (100 mL) was added dropwise Jones reagent (110 mL, 27% solution) at 0°C until the reaction mixture became red. To the mixture was added isopropyl alcohol at 0°C until the reaction mixture became green. After removal of the solvent in vacuo, the reaction mixture was exposed to aqueous $NaHCO_3$ (350 mL) and was extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=50/1) to give **7** (27.22 g, 86%) as yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 3H), 0.96 (s, 9H), 0.21 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 226.0, 98.5, 85.0, 26.3, 16.8, 4.4, −7.5; IR (neat) 2960, 2936, 2892, 2864, 2280, 2192, 1594, 1466, 1252, 1142, 840, 820, 804, 780 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{10}H_{19}OSi$ $(M+H)^+$ 183.1205, found 183.1203.

4.1.3. (*R*)-1-*t*-Butyldimethylsilyl-2-butyn-1-ol {(*R*)-6}. To a solution of (−)-DIP-Cl (8.2 g, 26.3 mmol) in THF (25 mL) was added a solution of **7** (3.0 g, 16.5 mmol) in THF (20 mL) at −78°C under an argon atmosphere, and the reaction mixture was stirred at −35°C for 5 h. To the reaction mixture was added diethanolamine (6.5 g, 74.3 mmol), and the reaction mixture was stirred at rt for 16 h. After addition of Et_2O, the mixture was filtrated, and the filtrate was dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/AcOEt=100/1, then 50/1) to give (*R*)-**6** (2.5 g, 82%) as pale yellow oil: $[\alpha]_D^{17}$+77.7 (*c* 1.02, $CHCl_3$, >95% ee).

4.1.4. (*R,Z*)-1-*t*-Butyldimethylsilyl-2-buten-1-ol {(*R,Z*)-8}. A suspension of (*R*)-**6** (200 mg, 1.08 mmol) and Lindlar catalyst (10 mg, 0.11 mmol) in AcOEt (10 mL) was stirred under H_2 at rt for 3 h. The mixture was filtrated, and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=35/1) to give (*R,Z*)-**8** (190 mg, 95%) as colorless oil: $[\alpha]_D^{15}$=+49.3 (*c* 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.56 (ddq, *J*=10.6, 10.6, 1.7 Hz, 1H), 5.45 (dqd, *J*=10.6, 6.9, 1.2 Hz, 1H), 4.47 (d, *J*=10.5 Hz, 1H), 1.63 (dd, *J*=6.8, 1.7 Hz, 3H), 1.57 (br s, 1H, exchangeable with D_2O), 0.96 (s, 9H), 0.36 (s, 3H), −0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.0, 123.1, 65.7, 26.8, 17.8, 17.0, −7.8, −8.3; IR (neat) 3370, 2930, 2859, 1722, 1523, 1464, 1351, 1251, 1168, 959, 841 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{10}H_{22}OSi$ $(M)^+$ 186.1440, found 186.1444.

4.1.5. (1*R*,1′*R*,2′*S*)-2′-Methylcyclopropyl *t*-butyldimethylsilyl methanol {(1*R*,1′*R*,2′*S*)-*syn*-9}. To a solution of (*R,Z*)-**8** (1.64 g, 8.82 mmol) in CH_2Cl_2 (50 mL) were added $ZnEt_2$ (56.7 mL, 56.7 mmol) and CH_2I_2 (4.6 mL, 56.7 mmol) at −10°C under an argon atmosphere. After stirring for 3 h, the reaction was quenched by saturated NH_4Cl. The mixture was extracted with Et_2O, and organic layer was washed with brine, dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=50/1) to give (1*R*,1′*R*,2′*S*)-*syn*-**9** (1.32 g, 75%) as pale yellow oil: $[\alpha]_D^{17}$=+29.4 (*c* 1.43, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.05 (d, *J*=11.3 Hz, 1H), 1.58 (br, 1H), 1.07 (d, *J*=5.1 Hz, 3H), 1.03 (m, 1H), 0.97 (s, 9H), 0.87 (m, 1H), 0.73 (m, 1H), 0.07 (s, 3H), 0.03 (s, 3H), 0.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.5, 26.9, 21.7, 16.8, 14.3, 12.4, 11.2, −7.2, −9.0; IR (neat) 3456, 2956, 2936, 2888, 2860, 1464, 1392, 1364, 1250, 1027, 1010, 984, 940, 838, 802, 774 cm^{-1}; HRMS (FAB) *m/z* calcd for $C_{11}H_{23}OSi$ $(M-H)^+$ 199.1518, found 199.1529.

4.1.6. (1*R*,2*S*)-2-Methylcyclopropyl *t*-butyldimethylsilyl ketone (10). To a solution of (1*R*,1′*R*,2′*S*)-*syn*-**9** (3.6 g, 18.1 mmol) in CH_2Cl_2 (20 mL) were added PDC (6.8 g, 18.1 mmol) at rt for 30 min. The mixture was filtrated and the solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=40/1) to give **10** (2.6 g, 72%) as yellow oil: $[\alpha]_D^{14}$=+11.3 (*c* 1.19, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 2.60 (ddd, *J*=8.8, 7.6, 5.6 Hz, 1H), 1.49 (m, 1H), 1.16 (ddd, *J*=7.1, 5.4, 3.7 Hz, 1H), 0.97 (d, *J*=6.1 Hz, 3H), 0.93 (s, 9H), 0.86 (ddd, *J*=15.5, 7.9, 4.9 Hz, 1H), 0.19 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 246.2, 32.4, 26.5, 21.2, 16.8, 15.1, 11.8, −7.1, −7.3; IR (neat) 2964, 2936, 2864, 1732, 1616, 1460, 1368, 1250, 1214 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{11}H_{22}OSi$ $(M)^+$ 198.1440, found 198.1423.

4.1.7. (1*S*,1′*R*,2′*S*)-2′-Methylcyclopropyl *t*-butyldimethylsilyl methanol {(1*S*,1′*R*,2′*S*)-*anti*-9}. To a solution of **10** (450 mg, 2.3 mmol) in CH_2Cl_2 (14 mL) was added DIBAL in *n*-hexane (0.96 mol/l, 2.8 mL) at −78°C under an argon atmosphere. The reaction mixture was stirred at −78°C. After 0.5 h, the reaction was quenched by saturated NH_4Cl. The mixture was extracted with Et_2O, and organic layer was washed with brine, dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=50/1) to give (1*S*,1′*R*,2′*S*)-*anti*-**9** (279 mg, 61%) as pale yellow oil: $[\alpha]_D^{14}$=+18.4 (*c* 0.81, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.11 (d, *J*=11.7 Hz, 1H), 1.29 (br s, 1H, exchangeable with D_2O), 1.18 (d, *J*=6.1 Hz, 3H), 1.08–0.99 (2H), 0.97 (s, 9H), 0.77 (m, 1H), 0.07 (s, 3H), 0.00 (s, 3H), −0.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.5, 27.0, 20.6, 16.8, 12.8, 12.6, 10.3, −7.1, −8.5; IR (neat) 3480, 3064, 2996, 2956, 2932, 2888, 2860, 1466, 1450, 1394, 1364, 1250, 1032, 1018, 982, 836, 778, 656 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{11}H_{24}OSi$ $(M)^+$ 200.1596, found 200.1591.

4.1.8. (*R*)-1-*t*-Butyldimethylsilyl-1-butanol {(*R*)-12}. A solution of (*R*)-**6** (1.00 g, 5.4 mmol) and Wilkinson catalyst (700 mg, 0.76 mmol) in benzene (40 mL) was stirred under H_2 at rt for 1 h. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=30/1) to give (*R*)-**12** (703 mg, 69%) as a colorless oil: $[\alpha]_D^{24}$=−7.89 (*c* 1.47, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.5 (dd, *J*=10.6, 2.6 Hz, 1H), 1.63 (br s, 1H, exchangeable with D_2O), 1.67–1.43 (3H), 1.37–1.28 (m, 1H), 0.95–0.94 (3H), 0.94 (s, 9H), 0.01 (s, 3H), −0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 64.1, 36.5, 27.0, 19.9, 16.8, 13.9, −7.6, −8.7; IR (neat) 3421, 2956, 2929, 2857, 1465, 1362,

1254, 1050, 1006, 953, 806, 774, 655, 572, 419 cm^{-1}; HRMS (FAB) *m/z* calcd for $C_{10}H_{23}OSi$ $(M-H)^+$ 187.1518, found 187.1518.

4.1.9. (*R*,*E*)-1-*t*-Butyldimethylsilyl-2-buten-1-ol {(*R*,*E*)-8}. To a solution of (−)-DIP-Cl (3.79 g, 12.2 mmol) in THF (15 mL) was added a solution of **11** (1.41 g, 7.7 mmol) in THF (15 mL) at −78°C under an argon atmosphere, and the reaction mixture was stirred at rt for 52 h. To the reaction mixture was added diethanolamine (3.04 g, 34.7 mmol), and the reaction mixture was stirred at rt for 14 h. After Et_2O was added the mixture was filtrated, and the filtrate was dried over $MgSO_4$. The solvent was evaporated in vacuo to give a crude residue, which was purified by flash column chromatography on silica gel (*n*-hexane/AcOEt, 80/1) to give (*R*,*E*)-**8** (0.90 g, 4.9 mmol) as pale yellow oil: $[\alpha]_D^{22}$=+33.1 (*c* 1.02, $CHCl_3$, 90% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 5.56 (ddq, *J*=15.6, 7.2, 1.5 Hz, 1H), 5.50 (dqd, *J*=15.0, 6.4, 1.5 Hz, 1H), 4.05 (dt, *J*=7.2, 1.5 Hz, 1H), 1.71 (dt, *J*=6.4, 1.5 Hz, 3H), 1.35 (br, 1H, exchangeable with D_2O), 0.94 (s, 9H), 0.00 (s, 3H), −0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.3, 122.3, 67.0, 27.0, 17.9, 17.0, −7.7, −8.9; IR (neat) 3370, 2932, 2854, 1716, 1635, 1578, 1464, 1365, 1341, 1251, 1224, 1095, 1005, 969, 828, 741 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{10}H_{22}OSi$ $(M)^+$ 186.1440, found 186.1434.

4.2. General procedure for acid-catalyzed rearrangement reaction of α-hydroxysilane with H_2SO_4

To a solution of α-hydroxysilane (1.0 equiv.) in THF was added aqueous 10% H_2SO_4 (20 equiv.) at rt, and the reaction mixture was stirred under the reaction condition. The reaction was quenched by saturated $NaHCO_3$, and the mixture was extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel.

4.3. General procedure for acid-catalyzed rearrangement reaction of α-hydroxysilane with BF_3OEt_2

To a solution of α-hydroxysilane in CH_2Cl_2 was added BF_3OEt at reaction condition. The mixture was stirred under the reaction condition. The reaction was quenched by saturated $NaHCO_3$, and the mixture was extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel.

4.3.1. (*R*,*E*)-5-*t*-Butyldimethylsilyl-4-penten-2-ol {(*R*)-13}. $[\alpha]_D^{11}$=−7.2 (*c* 0.92, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 6.03 (dt, *J*=18.5, 6.4 Hz, 1H), 5.76 (d, *J*=18.4 Hz, 1H), 3.87 (ddq, *J*=6.3, 6.2 Hz, 1H), 2.30 (2H), 1.56 (br, 1H, exchangeable with D_2O), 1.20 (d, *J*=6.2 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 131.7, 66.8, 46.9, 26.4, 22.7, 16.4, −6.1, −6.2; IR (neat) 3740, 3688, 3352, 2956, 2932, 2896, 2856, 1620, 1472, 1466, 1250, 1120, 1078, 992, 828, 812, 780, 656 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{11}H_{24}OSi$ $(M)^+$ 200.1596, found 200.1596.

4.3.2. (1*R*,2*S*,1′*R*)-1-(2-*t*-Butyldimethylsilylcyclopropyl)ethanol (14). $[\alpha]_D^{11}$=+26.9 (*c* 0.98, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.16 (ddd, *J*=13.9, 6.3, 6.3 Hz, 1H), 1.42 (br, 1H, exchangeable with D_2O), 1.28 (d, *J*=6.2 Hz, 3H), 0.93 (s, 9H), 0.81 (m, 1H), 0.49–0.38 (2H), −0.13 (s, 3H), −0.19 (s, 3H), −0.39 (ddd, *J*=10.1, 6.6, 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 74.2, 27.3, 24.1, 23.2, 17.8, 6.9, 0.0, −6.5, −7.2; IR (neat) 3876, 3388, 3060, 2956, 2932, 2884, 2856, 1252, 832, 808, 768 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{11}H_{24}OSi$ $(M)^+$ 200.1596, found 200.1604.

4.3.3. (1*R*,2*S*,1′*S*)-1-(2-*t*-Butyldimethylsilylcyclopropyl)ethanol (15). $[\alpha]_D^{11}$=+20.3 (*c* 1.19, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.05 (ddd, *J*=12.4, 8.3, 6.3 Hz, 1H), 1.69 (br, 1H, exchangeable with D_2O), 1.28 (d, *J*=6.1 Hz, 3H), 0.91 (s, 9H), 0.80 (m, 1H), 0.52 (ddd, *J*=10.2, 4.2, 4.2 Hz, 1H), 0.42 (ddd, *J*=7.1, 7.1, 3.9 Hz, 1H), −0.16 (s, 3H), −0.19 (s, 3H), −0.50 (ddd, *J*=10.3, 6.6, 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 74.4, 26.7, 23.3, 22.8, 17.1, 7.3, −1.3, −7.3, −7.7; IR (neat) 3912, 3804, 3592, 3368, 3060, 2956, 2932, 2888, 2856, 1472, 1466, 1254, 1104, 960, 826, 766 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{11}H_{24}Osi$ $(M)^+$ 200.1596, found 200.1590.

4.3.4. (*E*)-1,4-Butanediol mono-2-(5-*t*-butyldimethylsilylpent-4-enyl)ether (16). ^1H NMR (300 MHz, $CDCl_3$) δ 6.01 (dd, *J*=18.6, 6.6 Hz, 1H), 5.69 (d, *J*=18.6 Hz, 1H), 3.68–3.58 (m, 2H), 3.56–3.36 (m, 3H), 2.48–2.14 (m, 2H), 1.90 (br, 1H), 1.68–1.48 (m, 6H), 1.14 (d, *J*=6.24 Hz, 3H), 0.86 (s, 9H), 0.00 (s, 6H); HRMS (CI) *m/z* calcd for $C_{15}H_{33}O_2Si$ $(M+H)^+$ 273.2250, found 273.2254.

4.3.5. (1*R,1′*R**,2′*R**)-1-(2′-*n*-Butylcyclopropyl)ethanol (19).** ^1H NMR (300 MHz, $CDCl_3$) δ 3.37 (m, 1H), 1.60 (br s, 1H), 1.54–1.26 (6H), 1.30 (d, *J*=5.9 Hz, 3H), 1.07 (m, 1H), 0.90 (t, *J*=7.1 Hz, 3H), 0.85 (m, 1H), 0.70 (m, 1H), 0.04 (q, *J*=4.7 Hz, 1H).

4.3.6. (*E*)-2-Nonen-5-ol (21). ^1H NMR (500 MHz, $CDCl_3$) δ 5.53 (dqt, *J*=15.1, 6.1, 1.5 Hz, 1H), 5.42 (dtq, *J*=15.1, 7.7, 1.2 Hz, 1H), 3.56 (m, 1H), 2.20 (m, 1H), 2.04 (m, 1H), 1.67 (dd, *J*=6.1, 1.2 Hz, 1H), 1.52 (br s, 1H, exchangeable with D_2O), 1.49–1.25 (4H), 0.89 (t, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.8, 127.2, 71.0, 40.7, 36..5, 27.9, 22.7, 18.0, 14.0.

4.3.7. 4-Nonen-2-ol (22, *E/Z* mixture). ^1H NMR (500 MHz, $CDCl_3$) δ 5.56–5.49 (1H), 5.42–5.34 (1H), 3.80–3.73 (1H), 2.26–2.14 (1H), 2.10–1.99 (3H), 1.56 (br s, 1H, exchangeable with D_2O), 1.36–1.24 (4H), 1.18 (d, *J*=6.3 Hz, 1.02H), 1.16 (d, *J*=6.1 Hz, 1.98H), 0.89–0.86 (3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.7, 133.4, 125.8, 125.0, 67.8, 67.3, 42.6, 37.2, 32.3, 31.9, 31.7, 27.1, 22.8, 22.6, 22.3, 22.2, 13.9, 13.8.

4.3.8. (*R*,*E*)-4-*t*-Butyldimethylsilyl-3-buten-2-ol {(*R*)-23}. $[\alpha]_D^{16}$=+4.3 (*c* 1.31, $CHCl_3$, 48% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 6.10 (dd, *J*=18.8, 5.1 Hz, 1H), 5.82 (dd, *J*=18.8, 1.5 Hz, 1H), 4.29 (m, 1H), 1.61 (br s, 1H, exchangeable with D_2O), 1.26 (d, *J*=6.3 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 125.2, 70.6, 26.4, 23.1, 16.4, −6.2; IR (neat) 3341, 2953, 2927, 2883, 2857, 1717, 1619, 1471, 1463, 1362, 1248, 1130, 1060, 990, 939, 830,

777, 662 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{10}H_{22}O_2Si$ $(M)^+$ 186.1440, found 186.1466.

4.3.9. (*Z*)-3-Octen-2-ol (24). ^1H NMR (400 MHz, $CDCl_3$) δ 5.46–5.40 (2H), 4.64 (dq, *J*=6.4, 6.4 Hz, 1H), 2.11–1.99 (2H), 1.69 (br s, 1H, exchangeable with D_2O), 1.39–1.28 (4H), 1.24 (d, *J*=6.4 Hz, 3H), 0.89 (t, *J*=7.0 Hz, 3H).

4.3.10. 1-*t*-Butyldimethylsilyl-1-mesyloxy-2-butyne (26). To a solution of (*R*)-**6** (1.0 g, 5.43 mmol) in CH_2Cl_2 (30 mL) added pyridine (3.1 mL, 38 mmol) at rt for 10 min. To the solution was added MsCl (1.3 mL, 16.3 mmol) at rt. After stirring at rt for 2.5 h, the reaction was quenched by 1N HCl. The mixture was extracted with Et_2O, and organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=30/1) to give 26 (795 mg, 56%) as pale yellow oil: $[\alpha]_D^{27}$=+128.9 (*c* 2.132, $CHCl_3$, >95% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 5.05 (q, *J*=2.44 Hz, 1H), 3.11 (s, 3H), 1.91 (d, *J*=2.44 Hz, 3H), 0.98 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.3, 74.8, 66.3, 39.4, 26.7, 17.0, 3.9, −7.8, −8.3; IR (neat) 2953, 2930, 2860, 1472, 1359, 1252, 1174, 974, 911, 820, 553, 520 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{10}H_{19}O_3SSi$ $(M-Me)^+$ 247.0824, found 247.0818.

4.3.11. 1-*t*-Butyldimethylsilyl-3-mesyloxy-1,2-butadiene (27). $[\alpha]_D^{26}$=−141.0 (*c* 1.68, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 (ddd, *J*=4.15 Hz, 1H), 3.03 (s, 3H), 2.05 (d, *J*=4.15 Hz, 3H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 121.4, 98.6, 37.9, 26.1, 18.5, 16.8, −6.0, −6.1; IR (neat) 2952, 2929, 2885, 2858, 1959, 1471, 1416, 1366, 1251, 1186, 1108, 965, 856, 838, 822, 784, 707, 604, 542, 523 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{10}H_{19}O_3SSi$ $(M-Me)^+$ 247.0824, found 247.0813.

4.3.12. (*E*)-4-*t*-Butyldimethylsilyl-3-buten-2-one (28). ^1H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, *J*=19.27 Hz, 1H), 6.46 (d, *J*=19.27 Hz, 1H), 2.27 (s, 3H), 0.89 (s, 9H), 0.09 (s, 6H); IR (neat) 2927, 2856, 1680, 1464, 1362, 1251, 1219, 997, 830, 530 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{10}H_{21}OSi$ $(M+H)^+$ 185.1362, found 185.1362.

4.3.13. 1-*t*-Butyldimethylsilyl-1-mesyloxy-butane (29). To a solution of *rac*-**12** (1.649 g, 8.76 mmol) in CH_2Cl_2 (40 mL) added pyridine (5 mL, 61.3 mmol) at rt for 10 min. To the solution was added MsCl (1.4 mL, 17.5 mmol) at rt. After stirring at rt for 4 h, the reaction was quenched by 1N HCl. The mixture was extracted with Et_2O, and organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=30/1) to give **29** (1.507 g, 65%) as pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 4.78 (dd, *J*=7.44, 5.00 Hz, 1H), 2.99 (s, 3H), 1.77 (m, 2H), 1.55 (m, 1H), 1.45 (m, 1H), 0.95–0.94 (3H), 0.95 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.9, 39.0, 35.3, 26.8, 20.3, 16.8, 13.9, −7.0, −7.2; IR (neat) 2959, 2932, 2903, 2859, 1466, 1341, 1252, 1172, 971, 915, 879, 838, 824, 809, 778, 522 cm^{-1}; HRMS (EI) *m/z* calcd for $C_7H_{17}O_3SSi$ $(M-t\text{-Bu})^+$ 209.0668, found 209.0669.

4.3.14. (*Z*)-2-*t*-Butyldimethylsilyl-2-butenal (*E*-30). ^1H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.31 (q, *J*=7.15 Hz, 1H), 2.12 (d, *J*=7.15 Hz, 3H), 0.88 (s, 9H), 0.23 (s, 6H); IR (neat) 2955, 2927, 2856, 1250, 836, 668, 419 cm^{-1}.

4.3.15. (*E*)-2-*t*-Butyldimethylsilyl-2-butenal (*E*-30). ^1H NMR (300 MHz, $CDCl_3$) δ 10.34 (s, 1H), 6.92 (q, *J*=7.34 Hz, 1H), 2.18 (d, *J*=7.34 Hz, 3H), 0.85 (s, 9H), 0.11 (s, 6H); IR (neat) 2955, 2927, 2856, 1250, 836, 668, 419 cm^{-1}.

4.3.16. Bis(1-*t*-butyldimethylsilyl-butyl)oxide (31). $[\alpha]_D^{27}$=−9.94 (*c* 3.25, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.06 (dd, *J*=9.64, 2.81 Hz, 2H), 1.61–1.40 (6H), 1.35–1.20 (2H), 0.93–0.89 (6H), 0.91 (s, 18H), −0.04 (s, 6H), −0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 64.1, 36.6, 27.3, 20.0, 16.9, 14.0, −7.2, −7.5; IR (neat) 3198, 2956, 2928, 2857, 2360, 2343, 1464, 1398, 1365, 1308, 1247, 1119, 1076, 1052, 1008, 959, 937, 830, 808, 781, 661, 574 cm^{-1}.

4.3.17. (*S*)-3-Octyn-2-ol {(*S*)-32}. To a solution of *rac*-**32** (2 g, 15.9 mmol) in *n*-hexane was added MS4A and vinyl acetate (4.5 g, 52.4 mmol) and Lipase AK (1 g, 50 wt%) at rt. After stirring at rt for 5 h, the reaction mixture was filtrated. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=40/1) to give (*R*)-2-acetoxy-3-octyne (1.53 g, 58%) and (*S*)-**32** (0.57 g, 29%, >95% ee) as colorless oil: $[\alpha]_D^{27}$=−30.1 (*c* 1.73, $CHCl_3$, >95% ee); ^1H NMR (300 MHz, $CDCl_3$) δ 4.49 (ddq, *J*=2.0, 2.0, 6.6 Hz, 1H), 2.18 (ddd, *J*=1.8, 7.0, 7.0 Hz, 2H), 1.98 (br, 1H), 1.40 (d, *J*=6.4 Hz, 3H), 1.33–1.55 (4H), 0.89 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.58, 82.19, 58.52, 30.67, 24.70, 21.86, 18.27, 13.53; IR (neat) 3400, 2936, 1464, 1372, 1330, 1156, 1078, 1010, 968 cm^{-1}.

4.3.18. 2-Mesyloxy-octane {(*R*)-34}. To a solution of (*R*)-2-octanol ((*R*)-**33**, 556 mg, 4.27 mmol) in CH_2Cl_2 (15 mL) added pyridine (2.4 mL, 29.9 mmol) at rt for 10 min. To the solution was added MsCl (0.7 mL, 8.55 mmol) at rt. After stirring at rt for 2.5 h, the reaction was quenched by 1N HCl. The mixture was extracted with Et_2O, and organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=15/1) to give (*R*)-**34** (890 mg, quant) as pale yellow oil: $[\alpha]_D^{26}$=−9.80 (*c* 1.66, $CHCl_3$, >95% ee); ^1H NMR (300 MHz, $CDCl_3$) δ 4.77 (m, 1H), 2.97 (s, 3H), 1.77–1.52 (2H), 1.40 (d, *J*=6.24 Hz, 3H), 1.37–1.19 (8H), 0.87 (t, *J*=6.79 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.4, 38.6, 36.6, 31.6, 28.9, 25.0, 22.5, 21.1, 14.0; IR (neat) 2933, 2859, 1467, 1353, 1176, 972, 918, 531 cm^{-1}; HRMS (FAB) *m/z* calcd for $C_9H_{21}O_3S$ $(M+H)^+$ 209.1211, found 209.1185.

4.3.19. *t*-Butyldimethylsilyl propyl ketone (35). ^1H NMR (300 MHz, $CDCl_3$) δ 2.57 (t, *J*=7.16 Hz, 2H), 1.53 (qt, *J*=7.43, 7.16 Hz, 2H), 0.92 (s, 9H), 0.87 (t, *J*=7.43 Hz, 3H), 0.17 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 247.7, 52.2, 26.4, 16.4, 15.3, 13.8, −7.0; IR (neat) 2958, 2930, 2859, 1641, 1464, 1363, 1250, 837, 824, 806, 774, 419 cm^{-1}.

4.3.20. (*E*)-1-*t*-Butyldimethylsilyl-3-chloro-1-butene (36). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (dd, J=18.42, 6.96 Hz, 1H), 5.86 (dd, J=18.54, 0.73 Hz, 1H), 4.51 (ddq, J=7.32, 6.83, 0.73 Hz, 1H), 1.59 (d, J=6.59 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.77, 128.19, 59.86, 29.70, 26.34, 24.74, −6.28, −6.30; IR (neat) 2954, 2927, 2856, 1726, 1464, 1362, 1255, 1173, 837, 668 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{10}H_{21}ClSi$ $(M)^+$ 204.1101, found 204.1120.

4.3.21. 2-Chloro-3-octyne (37). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.66 (qd, J=6.79, 2.09 Hz, 1H), 2.23 (td, J=6.97, 2.09 Hz, 2H), 1.72 (d, J=4.22 Hz, 3H), 1.57–1.34 (4H), 0.91 (t, J=7.15 Hz, 3H).

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16. Two alcohols *E*- and *Z*-**22** were inseparable by the column chromatography on silica gel. Their *E*/*Z* ratio was estimated by ^{1}H NMR.
17. The alcohol (*S*,*Z*)-**24** was prepared from α-hydroxyalkynylsilane (*S*)-**32** by hydrogenation using the Lindlar catalyst.
18. The mesylate (*R*)-**26** was prepared from α-hydroxyalkynylsilane (*R*)-**6** {MsCl (3 equiv.), pyridine (7 equiv.), CH_2Cl_2, rt, 2.5 h, 56%} On the other hand, the reaction of α-hydroxyalkenylsilane (*R*,*Z*)-**8** under the same conditions did not give its mesylate but gave the allylic alcohol (*R*)-**23** (26% yield, 56% ee)[8] and the allylic chloride **36** (32%).
19. The absolute configuration of the allene **27** was not determined.
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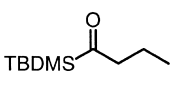
21. (*R*)-2-Octanol (>95% ee) is commercially available from Kawaken Fine Chemicals Co. Ltd.
22. The mesylate (*R*)-**34** {$[\alpha]_D^{26}$=−9.8 (*c* 1.66, $CHCl_3$), >95% ee} was prepared from (*R*)-**33** {MsCl (2 equiv.), pyridine (7 equiv.), CH_2Cl_2, rt, 2.5 h, quant} On the other hand, the reaction of the propargylic alcohol (*S*)-**32** under the same conditions did not give its mesylate but gave the propargylic chloride **37** (68%).



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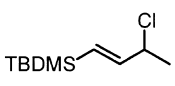

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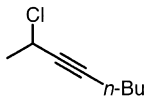

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