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Review

# Stereoselective accesses to enantioenriched allyl-, allenyl-, and propargyl-silanes via Si–Si bond activation by palladium–isocyanide catalysts

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**Abstract**

Stereoselective synthesis of allyl-, allenyl-, and propargyl-silanes via palladium-catalyzed intramolecular bis-silylation (IBS) is described. IBS of disilanyl ethers of propargylic and allylic alcohols produced bis-silylation products stereoselectively in good yields via formation of 1,2-oxasiletanes as primary products. From the bis-silylation products, allyl-, allenyl-, and propargyl-silanes were synthesized via Peterson-type elimination or acid-catalyzed 1,2-silyl migration. The IBS/elimination as well as the IBS/migration sequences were carried out in one reaction vessel, providing ready access to those synthetically useful organosilicon compounds. Highly enantioenriched allyl-, allenyl-, and propargyl-silanes including polymer-supported derivatives were stereoselectively synthesized by the new methods. Synthetic application of the highly enantioenriched allenyl- and allyl-silanes is also described.


*Keywords:* Silylation; Isocyanide; Addition; Elimination; Rearrangement; Oxasiletane

## 1. Introduction

The silicon–silicon σ-bond has attracted much attention due to its unique chemical and physical properties, which arise from its high-lying HOMO and low-lying LUMO. In terms of the HOMO–LUMO orbital energies, the Si–Si bond is better compared with the C=C bond rather than the C–C bond despite of the difference in their bond orders. In line with the characteristic orbital energies, the Si–Si bond often exhibits properties that are similar to the C=C bond.

In the mid of 1970s, Kumada's and Sakurai's groups independently reported the catalytic addition of disilanes to alkynes in the presence of palladium complexes (Scheme 1) [1–3]. These reactions were supposed to involve bis(silyl)palladium(II) complexes as a key intermediate, which may be formed through interaction of the Si–Si bond with a palladium(0) complex. The interaction of the Si–Si bond with Pd(0) can be compared to that of C=C bond, which is represented by the Chatt–Dewar–Duncanson model. During that initial decade, much effort was devoted to expanding the scope of the new catalytic reactions [4–9].

The efforts made in this initial decade resulted in transition-metal catalyzed bis-silylation of alkynes, 1,3-dienes, allenes, and some activated alkenes [10]. Most bis-silylation reactions were carried out in the presence of palladium–phosphine catalysts, requiring the use of 'activated disilane', i.e. disilanes bearing electron-withdrawing substituents and strained cyclic disilanes. This requirement may have strongly hampered the synthetic application of the bis-silylation reactions. In the initial period, interest was rather focused on the mechanistic issue as well as on regio- and stereo-chemical outcome of the bis-silylations.

Our contribution to this area began in the late 1980s, when the palladium-catalyzed insertion reaction of isocyanides into the Si–Si bond was being studied in

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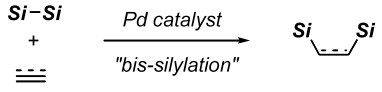



(*Si* denotes a triorganosilyl group)

Scheme 1.

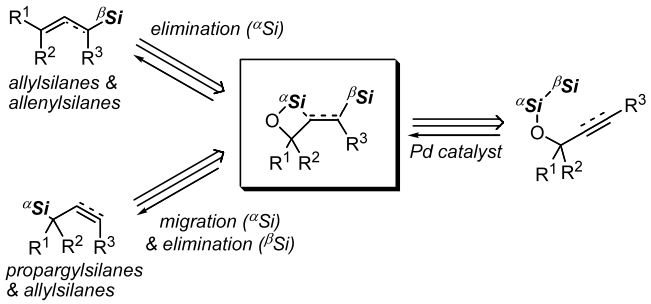
detail [11,12]. We became aware of the ability of isocyanides to facilitate the palladium-catalyzed insertion reaction and found that *t*-alkyl isocyanide served as highly efficient spectator ligands in the bis-silylation reactions [13]. Important applications of this catalyst system involve the intramolecular bis-silylation (IBS) of alkynes and alkenes, whose characteristic regio- and stereo-selectivity, as well as high reaction efficiency, has found wide utility in organic synthesis. It is worth mentioning that IBS of alkenes was achieved by this catalyst system and applied to the stereoselective synthesis of triols and polyols [14–16].

In this paper, we focus on the IBS reactions of allylic and propargylic alcohols. These provide new access to allyl-, allenyl-, and propargyl-silanes, which are highly valuable synthetic reagents in organic synthesis. We put special emphasis on the synthesis of highly enantioenriched derivatives. As shown in Scheme 2, two major pathways to the synthetically useful organosilicon compounds have been demonstrated. In both pathways, four-membered silyl ethers, i.e. 1,2-oxasiletanes, which are produced by IBS reactions, are involved as common intermediates, from which allyl-, allenyl-, and propargyl-silanes are derived via either Peterson-type elimination or acid-catalyzed 1,2-silyl migration. The IBS reaction and the subsequent reactions will be discussed separately in each section.

## 2. Intramolecular bis-silylation

### 2.1. Palladium–isocyanide catalyst

The catalyst we employed for bis-silylation is a palladium complex bearing *tert*-alkyl isocyanides as spectator ligands. The effectiveness of the catalyst system was originally established in the intermolecular



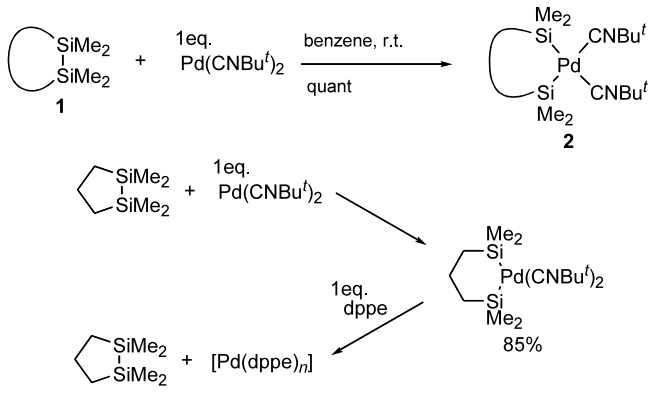

Scheme 2.

bis-silylation of terminal alkynes with hexamethyldisilane [13]. Whereas the conventional palladium–phosphine complexes exhibit only low catalytic activity in bis-silylation reactions using hexaalkyldisilanes [17], the palladium–isocyanide complexes serve as highly effective catalysts for the bis-silylation reactions.

The palladium–isocyanide catalysts are generated from stable palladium(II) precursors with *tert*-alkyl isocyanides simply by mixing them under an inert atmosphere. For liquid isocyanides, it is recommended that the isocyanides be added to palladium precursors without solvents. The color of the neat mixture thus prepared immediately turns to dark red, indicating successful formation of the active catalyst. Solid isocyanides are added with solvent, whose amount should be kept to the minimum necessary to dissolve the isocyanides. It should be noted here that the reduction of the Pd(II) precursors by aryl isocyanides may not take place at room temperature, thus requiring brief heating in solvents at ca. 100 °C for several minutes, although the aryl isocyanide-palladium complexes are not suitable for most bis-silylation reactions [18,19].

As palladium precursors, $Pd(OAc)_2$, $Pd(acac)_2$, and PdCp(π-allyl) have been successfully used. Among these precursors, the third, which is not commercially available, is used only for special purposes, in which the Pd/ligand ratio needs to be strictly controlled. In the preparation of palladium–isocyanide catalysts from $Pd(OAc)_2$ and $Pd(acac)_2$, part of the added isocyanide may be consumed for the Pd(II)–Pd(0) reduction. The loss of isocyanide, however, can be compensated by using a slight excess of isocyanide. Typically, 4–15 equivalents (to Pd) of isocyanide were employed, and the excess isocyanide usually do not interfere with the bis-slylation reaction [20].

The active species in the catalyst system is believed to be '$(RNC)_nPd(0)$', where the coordination number ($n$) may vary from 2 to 4. Bis(*tert*-butyl isocyanide)palladium(0), which may exist as a trimer, is isolable, despite being thermally unstable [21]. The bis-silylations were effectively catalyzed by the isolated $(t\text{-BuNC})_2Pd(0)$ with an additional amount of *tert*-butyl isocyanide, which may be essential to stabilize the palladium(0) species. The involvement of the palladium(0) species as an active catalyst in the system is also supported by stoichiometric reactions of cyclic disilanes with isolated $(t\text{-BuNC})_2Pd(0)$. Several four- to seven-membered cyclic disilanes **1** undergo oxidative additions to the palladium(0) complex, producing cyclic bis(*tert*-butyl isocyanide)bis(silyl)palladium(II) complexes **2** in high yields (Scheme 3) [22,23]. Interestingly, attempted substitution of the isocyanide ligand by phosphine ligand resulted in reductive elimination of the cyclic disilanes [22]. This observation indicates that, in the equilibrium between disilanes and bis(silyl)palladium complexes, the isocyanide ligand makes the formation of bis(silyl)pal-




Scheme 3.

ladium more favorable than do the phosphine ligands. Furthermore, the other steps involving the migratory insertion step may also be facilitated by the isocyanide ligand, although this has not been proved so far.

The advantages of the isocyanide ligands over ordinary phosphine ligands may be attributed to two major reasons. Single-crystal X-ray analyses revealed that the isocyanide ligands are much less sterically demanding on the palladium center than ordinary phosphines (Fig. 1) [23]. The tertiary alkyl group of the isocyanide is separated from the palladium center by two atoms, i.e. the CN group, in contrast to the phosphine ligand, in which the palladium center is directly bound to the tertiary phosphorus group. This unusual steric environment for the isocyanide-palladium complexes allows effective oxidative addition of the Si–Si bond, by which two sterically bulky organosilyl groups are located on the palladium center. There seems to be another reason that is related to the electronic nature of the isocyanide ligand. Although the formal oxidation state is two, bis(silyl)palladium complexes are characterized by their high electron density on the palladium center, which may be comparable to palladium(0). Stronger π-acidity of the isocyanide ligand may favor the formation of the bis(silyl)palladium(II) complex. Furthermore, the electron-accepting nature of isocyanide may play an important role in facilitating coordination of reacting unsaturated organic molecules to the palladium center.

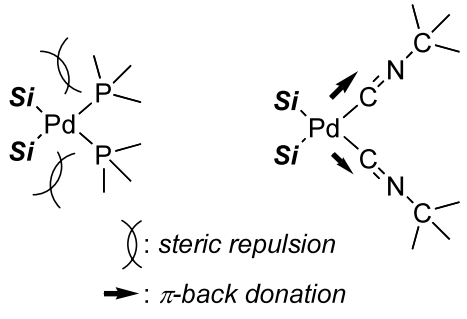
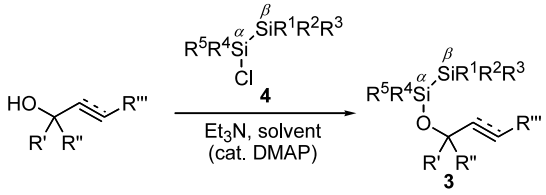
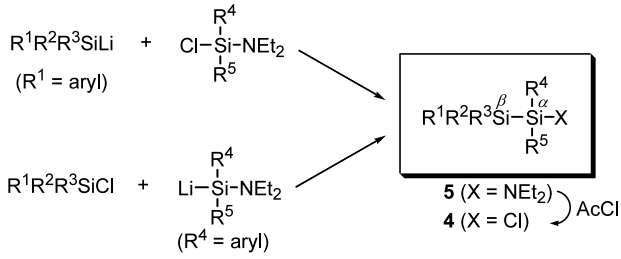



Fig. 1.




Scheme 4.

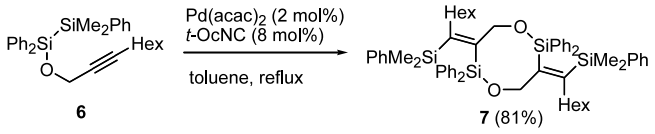



Scheme 5.

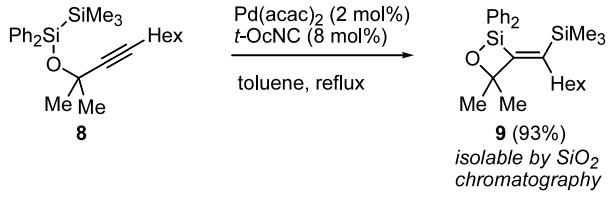
## 2.2. Disilanyl ethers

Prior to the palladium-catalyzed IBS cyclization, the starting disilanyl ethers **3** are readily prepared from alcohols and chlorodisilanes **4** (1 equivalent) in the presence of triethylamine (1.5 equivalent) in a manner similar to that for ordinary alcohol protection by a variety of silyl groups. A catalytic amount of 4-dimethylaminopyridine may be used to facilitate the formation of the disilanyl ether of sterically demanding alcohols. The resultant disilanyl ethers are easily purified either by distillation or silica gel chromatography (Scheme 4).

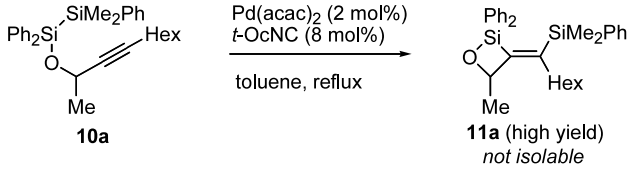
The synthetic utility of the bis-silylation strategy in the synthesis of β,γ-unsaturated organosilicon compounds is increased by ready accessibility to chlorodisilanes **4** possessing a variety of substituents on either silicon atom. Two major synthetic pathways to the chlorodisilanes **4** involving the coupling of silyllithiums with chlorosilanes are shown in Scheme 5. Both Si–Si bond forming steps are followed by the chloro-amino exchange reaction with acyl chloride. Since only silyllithiums possessing at least one aryl group on the silicon atom are readily generated from the corresponding chlorosilanes, each method has certain limitation on the structural variation [24]. Complementary use of these methods enables the synthesis of a variety of chlorodisilanes. Typically, the upper method depicted in Scheme 5 is utilized for the reaction of dimethylphenylsilyllithium with a variety of chloro(diethylamino)diorganosilanes to achieve structural variation at the α-silicon atom. On the other hand, a variety of β-silyl groups including trialkylsilyl groups are conveniently introduced by the lower method in Scheme 5 with use of (diethylamino)diphenylsilyllithium [25].



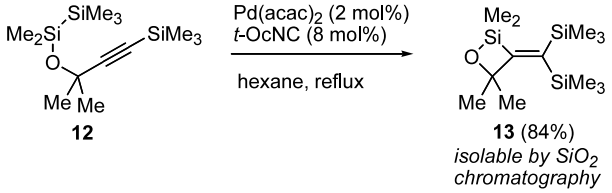

Scheme 6.




Scheme 7.




Scheme 8.




Scheme 9.

### 2.3. IBS of propargyl disilanyl ethers

IBS of propargyl disilanyl ethers was effectively catalyzed by the palladium–isocyanide complexes in a similar manner to that of homopropargylic disilanyl ethers [26]. The only difference between the two cyclizations is the fate of the cyclic silyl ethers that are formed via *exo*-cyclization. In fact, 1,2-oxasiletanes, i.e. four-membered cyclic silyl ethers, are known to be highly unstable not only hydrolytically, but also thermally [27]. As anticipated, the reaction of disilanyl ether **6** of a primary propargylic alcohol yielded the eight-membered ring product **7** in high yield (Scheme 6). This result may be explained by dimerization of an oxasiletane that is formed by IBS. The oxasiletane formed from **6** may easily undergo dimerization, because no trace of oxasiletane was observed on monitoring the reaction course by $^{1}$H-NMR spectroscopy.

To our surprise, however, the oxasiletane product was successfully isolated in the reaction of tertiary propargylic ether **8** (Scheme 7) [28]. Even at the refluxing temperature of toluene, the initially formed oxasiletane **9** does not undergo dimerization, allowing its isolation by column chromatography on silica gel in high yield.

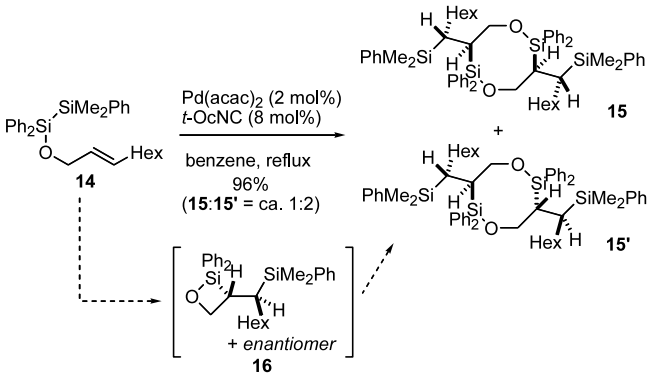
IBS of a secondary propargylic ether **10a** was also tested for comparison with those of the *prim*- and *tert*-propargylic ethers (Scheme 8) [26]. After the reaction under reflux in toluene, exclusive formation of oxasiletane product **11a** was observed, although it decomposed during silica gel column chromatography.

It should be noted that the substituents of the disilanyl groups do not significantly affect the reactivity of disilanyl ethers in the IBS of alkynes. For instance, both the 1,1,3-triphenyldimethyldisilanyl ether **8** and the pentamethyldisilanyl ether **12** undergo clean IBS under *reflux in hexane*, yielding chromatographically stable oxasiletanes **9** and **13**, respectively (Scheme 9) [28]. The permethyl derivative **13**, however, may be less thermally stable than the corresponding oxasiletane **9** with the diphenylsilylene moiety in the four-membered ring, since the reaction of **12** under *reflux in toluene* resulted in the formation of a complex mixture.

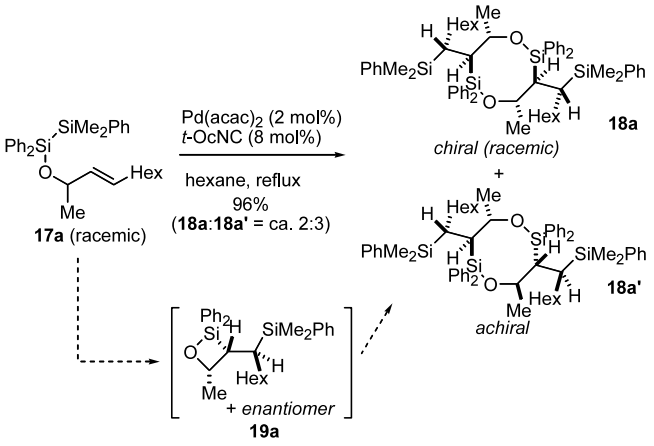
### 2.4. IBS of allyl disilanyl ethers

In general, carbon–carbon double bonds are much more reluctant to undergo bis-silylations. In fact, there have been no reports on the intermolecular bis-silylation of non-conjugated internal alkenes except for norbornene [29]. The IBS also suffers from low reactivity, requiring some modification to the original IBS conditions. It has been established that the efficiency of the IBS of internal alkenes is highly dependent on the substituents on the disilanyl group [30]. Use of aryl-substituted disilane derivatives is more beneficial in attaining a high yield than use of the pentamethyl derivative. In particular, aryl substitution at the α-silicon bound to the ether oxygen is highly favorable. Because of availability and stereochemical simplicity, we usually use 1,1-diphenyldisilanyl derivatives for the IBS of internal alkenes.

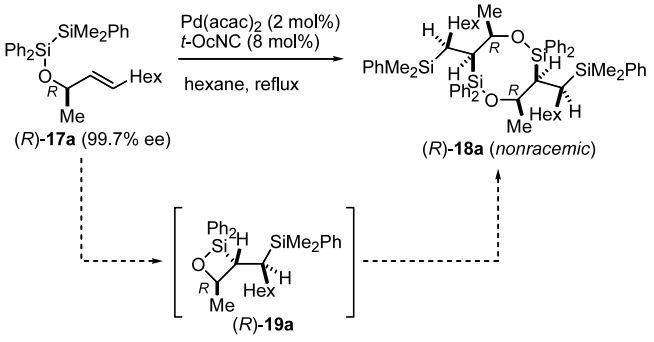
A disilanyl ether **14** of (*E*)-2-nonen-1-ol was subjected to IBS under reflux in benzene (Scheme 10) [31,32]. The reaction went to completion within 2 h, producing eight-membered ring dimeric products **15** and **15′** in high total




Scheme 10.




Scheme 11.




Scheme 12.

yield. Only two diastereomers were obtained in a ratio of ca. 1:2, suggesting highly stereospecific formation of oxasiletane intermediate **16** via *cis*-addition of the Si–Si bond across the C=C bond, followed by dimerization.

IBS of a racemic secondary allylic alcohol was then tested. Under reflux in hexane, the reaction of **17a** was completed within 2 h to give the corresponding dimers **18a** and **18a′** (Scheme 11). It is interesting to note that only two isomers were detected in the reaction mixture. This result may indicate that the IBS took place in a highly diastereoselective fashion, giving oxasiletane product **19a** as a single isomer.

This interesting stereochemical outcome prompted us to carry out IBS of the highly enantioenriched disilanyl allyl ether (*R*)-**17**. As expected, the eight-membered ring dimer **18a** was obtained as a single diastereomer in high yield (Scheme 12). The excellent diastereoselectivity will be the key to successful application of the bis-silylation to the synthesis of highly enantioenriched allylsilanes.

## 3. Synthesis of highly enantioenriched β,γ-unsaturated organosilicon compounds from the IBS products

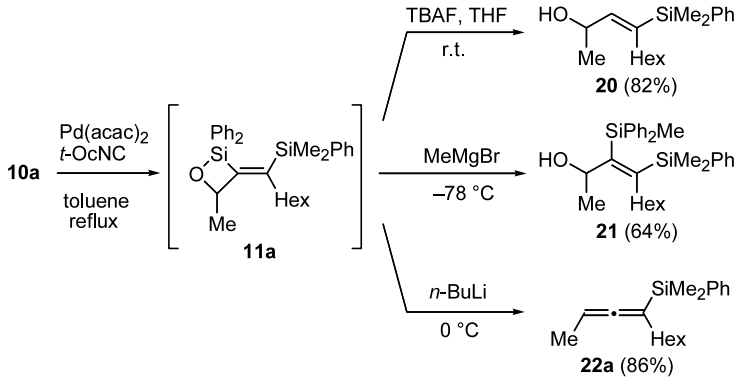
### 3.1. Allenylsilane synthesis via Peterson-type elimination

As mentioned above, IBS of *sec*- and *tert*-propargylic alcohols yields 3-alkylidene-substituted 1,2-oxasiletanes that do not undergo dimerization. We anticipated that treatment of the oxasiletanes with nucleophiles would induce Peterson-type elimination to give allenylsilanes.

A reaction mixture containing oxasiletane **11a** was obtained by IBS of **10a** in toluene and was treated with TBAF, MeMgBr, or *n*-BuLi (Scheme 13) [26]. The use of TBAF only resulted in the formation of γ-silyl allylic alcohol **20** in good yield. In the reaction of **11a** with methyl Grignard reagent, methylation at the silicon atom took place to give **21** and no elimination occurred even at room temperature. Clean Peterson-type elimination was effected by treatment with *n*-BuLi, giving allenylsilane **22a** in 86% yield. It seems to be important to note that, in contrast to the four-membered ring silyl ethers, the eight-membered cyclic dimers, e.g. **7**, scarcely underwent Peterson-type elimination under identical reaction conditions.

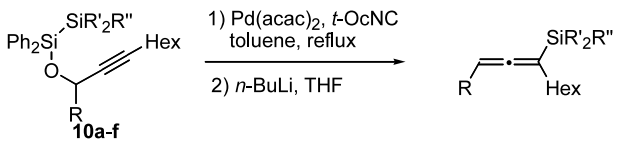
The one-pot bis-silylation–elimination protocol was successfully applied to a series of disilanyl propargylic ethers as shown in Table 1. It was remarkable that this method provides an array of allenylsilanes with a range of silyl groups as well as organic groups at the allenylic moieties.

Highly enantioenriched propargylic ether (*R*)-**10a** was subjected to the IBS–elimination protocol (Scheme 14).

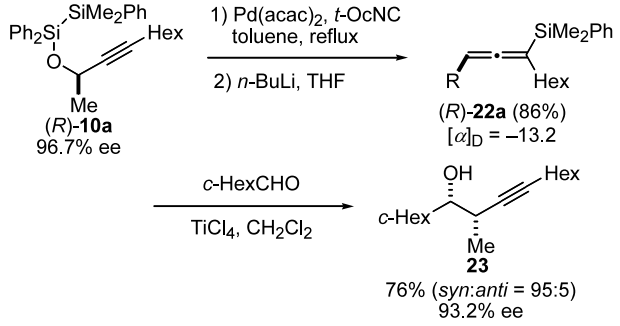



Scheme 13.

Table 1
Synthesis of allenylsilanes via IBS




| Entry | R | $SiR'_2R''$ | Yield (%) |
|---|---|---|---|
| 1 | Me | $SiMe_2Ph$ | 86 |
| 2 | Me | $SiMe_2Bu$-*t* | 95 |
| 3 | Me | $SiMe_3$ | 79 |
| 4 | *c*-Hex | $SiMe_2Ph$ | 81 |
| 5 | *c*-Hex | $SiMe_3$ | 85 |
| 6 | Ph | $SiMe_2Ph$ | 94 |



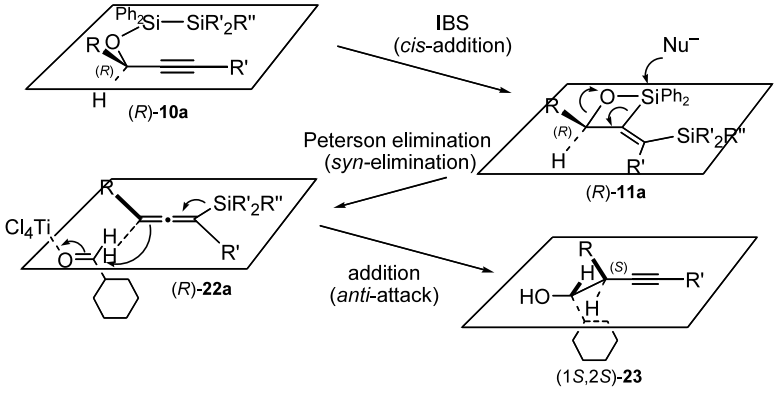

Scheme 14.

The corresponding allenylsilane **22a** was obtained in 86% yield. The allenylsilane exhibited a specific rotation of −13.2, although its enantiopurity could not be determined at this stage. The optically active allenylsilane was reacted with cycohexanecarboxaldehyde in the presence of $TiCl_4$. We found that *syn*-homopropargylic alcohol **23** was formed selectively in good yield. The enantiopurity of the alcohol was determined to be 93.2% ee by HPLC analysis. The first synthesis of a highly enantioenriched allenylsilane was achieved by Buckle and Fleming via an Sn2′ reaction of enantiopure 4-trimethylsilyl-3-butyn-2-yl camphorsulfonate with a MeMgBr/CuBr/LiBr reagent [33,34]. Our protocol offers a complementary way to the highly enantioenriched allenylsilanes via silicon-carbon bond formation [35].

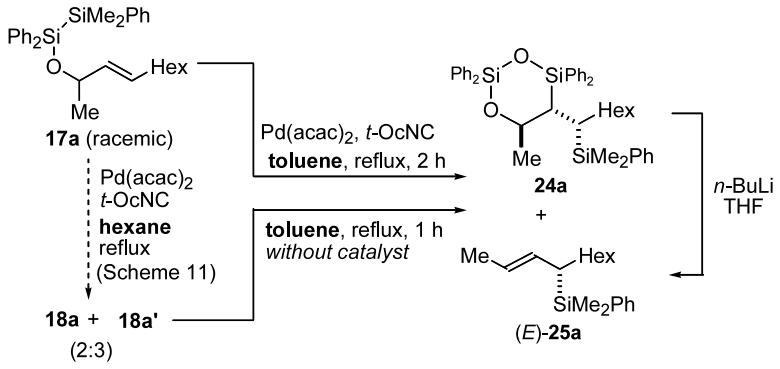
The stereochemical relay in the transformation of enantioenriched disilanyl propargyl ether (*R*)-**10a** to *syn*-homoallylic alcohol **23** may be illustrated as follows (Scheme 15). The formation of the optically active allenylsilane may be ascribed to the highly stereoselective *cis*-addition of the Si–Si bond across the carbon–carbon triple bond and the highly stereospecific *syn*-elimination of the Si–O moiety [36]. The two stereoselective/specific reactions provide the corresponding allenylsilanes with highly effective conversion of the point chirality to the axial chirality. The following reaction with aldehyde may proceed at the π-face anti to the silyl group (*anti* attack) to provide enantioenriched homoallylic alcohol [35]. The overall transformation from the propargylic ether to the homoallylic alcohol proceeds with inversion of the stereochemistry at the propargylic stereogenic center.

### 3.2. Allylsilane synthesis via Peterson-type elimination

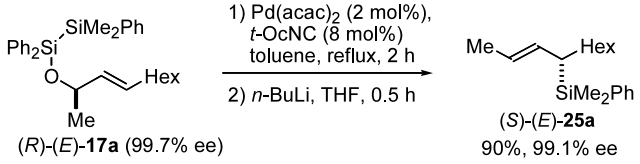
The attempted Peterson-type elimination of dimeric eight-membered ring product **18** derived from bissilylation of allylic substrates was not successful. As observed for eight-membered ring silyl ethers derived from the propargylic substrate, the eight-membered ring products **18** were stable and scarcely underwent the elimination reaction with several nucleophilic reagents, including *n*-BuLi. Fortuitously, we found that the eight-membered ring underwent a thermal ring contraction reaction upon heating the solution under reflux in toluene (Scheme 16) [32]. For instance, a diastereomeric mixture of the dimeric product **18a** and **18a′** obtained from racemic secondary allyl ether **17a** yielded six-membered ring disiladioxane **24a** as a single diastereomer along with (*E*)-allylsilane **25a** in high total yield. The high diastereomeric purity of both products indicated that the ring contraction reaction proceeded




Scheme 15.




Scheme 16.




Scheme 17.

stereospecifically. Furthermore, the six-membered ring product cleanly underwent Peterson-type elimination on treatment with *n*-BuLi, giving the (*E*)-allylsilane in high yield.

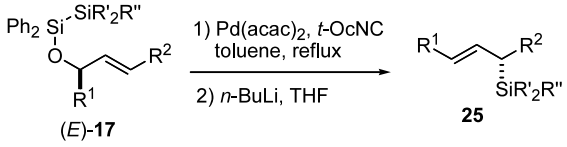
These results prompted us to carry out the IBS reaction at the refluxing temperature of toluene instead of hexane, which was originally used for obtaining dimeric products. As expected, the reaction under reflux in toluene provided a 1:1 mixture of disiladioxane and (*E*)-allylsilane directly in high total yield (Scheme 16) [31]. The higher reaction temperature did not have a negative impact on the stereoselectivity at all. Subsequently, the reaction mixture containing allylsilane and the disiladioxane was treated with *n*-BuLi, leading to clean formation of (*E*)-allylsilane in high isolated yield.

Application of this one-pot protocol to the synthesis of highly enantioenriched allylsilane turned out to be quite successful. Thus, the disilanyl ether prepared from enantiopure *sec*-allylic alcohol (99.7% ee (*R*)) was subjected to IBS at 110 °C and then treated with *n*-BuLi at 0 °C (Scheme 17) [37]. The resultant allylsilane was found to be configurationally (>99% *E*) and enantiomerically pure (99.1% ee). The high degree of stereochemical conservation (>99.4%) indicates that highly efficient chirality transfer is realized throughout the three elementary steps, i.e. IBS, thermal ring contraction, and Peterson-type elimination.

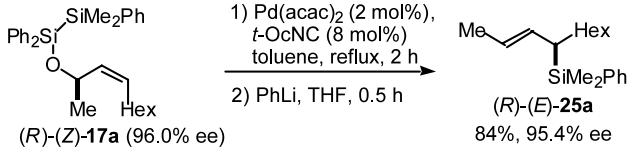
The one-pot protocol was successfully applied to the synthesis of a variety of (*E*)-allylsilanes with high enantiopurity (Table 2). Allylsilanes having a wide range of organic as well as silyl substituents are covered by this protocol. In addition to the structural variation, a high degree of stereochemical conservation was realized in every allylsilane synthesis. These features are particularly important for application of the enantioenriched allylsilanes to asymmetric synthesis.

A disilanyl ether of enantioenriched (*Z*)-allylic alcohol also provides (*E*)-allylsilane selectively in high yield

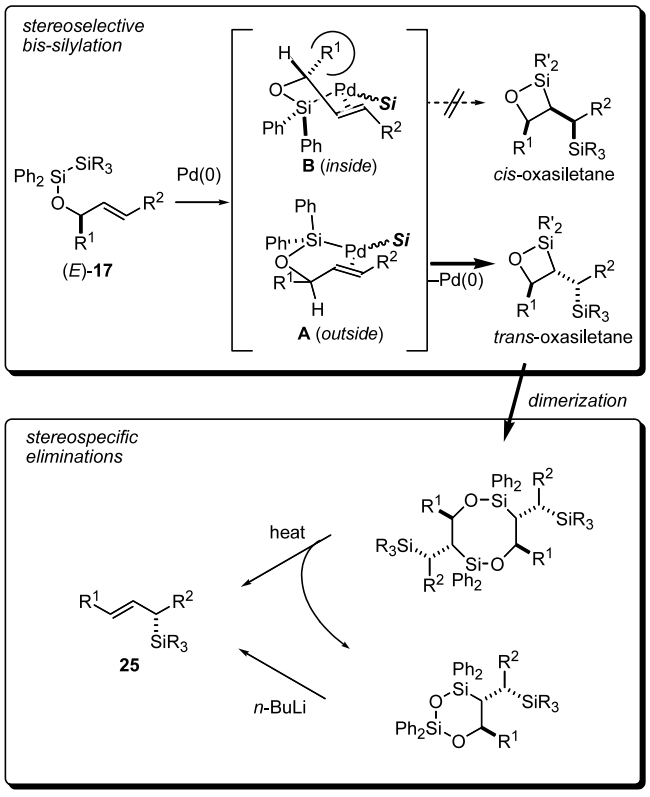
Table 2
Synthesis of enantioenriched allylsilanes via IBS




| Entry | **17** (% ee) | $R^1$ | $R^2$ | $SIR'_2R''$ | Yield (%) | **25** (% ee) |
|---|---|---|---|---|---|---|
| 1 | **a** (99.7) | Me | Hex | $SiMe_2Ph$ | 90 | **a** (99.1) |
| 2 | **b** (>99.0) | Ph | Hex | $SiMe_2Ph$ | 99 | **b** (>98.7) |
| 3 | **c** (99.8) | *c*-Hex | Hex | $SiMe_2Ph$ | 96 | **c** (99.0) |
| 4 | **d** (98.2) | Me | Ph | $SiMe_2Ph$ | 92 | **d** (98.1) |
| 5 | **e** (99.6) | Me | Hex | $SiMe^3$ | 81 | **e** (99.1) |
| 6 | **f** (99.6) | Me | Hex | $SiMe_2Bu$-*t* | 82 | **f** (99.4) |
| 7 | **g** (99.6) | Me | Hex | $SiEt_3$ | 94 | **g** (99.2) |
| 8 | **h** (99.6) | Me | Hex | $Sipr'_3$ | 62 | **h** (98.8) |



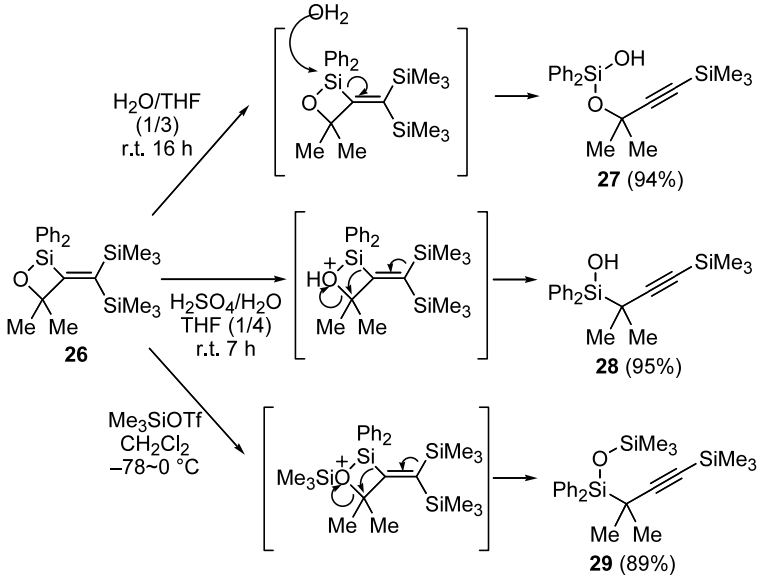

Scheme 18.




Scheme 19.

(Scheme 18). It is noteworthy that, in the reaction of the (*Z*)-allylic ether (*R*)–(*Z*)-**17a**, allylsilane (*E*)-**25a** whose absolute configuration is opposite to that obtained in the reaction of the corresponding (*E*)-allylic ether (*R*)–(*E*)-**17a** was formed stereoselectively, when both the allylic ethers were homochiral. This is particularly important from the synthetic point of view, since both (*E*)- and (*Z*)-allylic alcohols are prepared stereoselectively from the corresponding propargylic alcohols. Thus, starting from a single enantiomer of propargylic alcohol, either the (*R*)- or (*S*)-enantiomer of (*E*)-allylsilane is accessible.

The conversion of the enantioenriched disilanyl allyl ethers to the (*E*)-allylsilanes with efficient 1,3-chirality transfer is summarized in Scheme 19. The overall transformation consists of multiple steps including IBS, dimerization, thermal ring contraction, and Peterson-type elimination. The most important factor that is responsible for the observed 1,3-chirality transfer is high stereoselectivity of the IBS reaction, which exclusively yields a *trans*-oxasiletane as an intermediate. The *trans*-oxasiletane may be formed via bis(silyl)palladium intermediate A, which encounters less steric repulsion in the olefin insertion step than the diastereomeric intermediate B. The enantiomeric purity of the resultant allylsilanes is determined at the IBS step. On the other hand, stereospecificity of the elimination steps affects the geometrical purity of the resulting allylsilanes. It is remarkable that every step proceeds efficiently and stereoselectively to give highly enantioenriched allylsilanes in high yield. From the synthetic point of view, the new method seems to be advantageous over other known methods for enantioenriched allylsilanes due to its wide applicability and operational simplicity.

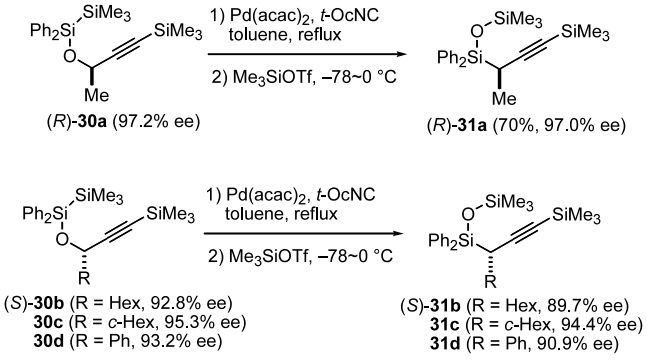



Scheme 20.

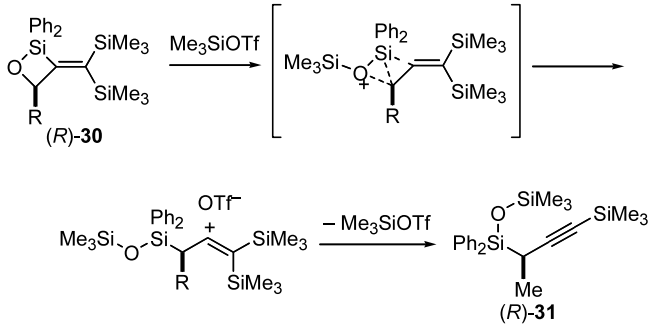
### 3.3. Propargyl- and allyl-silane synthesis via acid-catalyzed [1,2]-silyl shift

In the course of our studies on the reactivity of oxasiletanes derived by IBS of *tert*-propargylic ethers, we found their reactivity in aqueous media to be interesting. While oxasiletane **26** underwent hydrolysis in aqueous THF at room temperature to give **27**, the corresponding reaction in the presence of sulfuric acid yielded propargylsilane **28** in high yield (Scheme 20) [28]. The rearrangement reaction may proceed through the generation of a tertiary carbocation followed by 1,2-silyl migration and subsequent elimination of the TMS group. A similar reaction takes place in aprotic media in the presence of a catalytic amount of TMSOTf, giving **29** in good yield.

The acid-catalyzed rearrangement reaction was tested for related oxasiletanes **30** derived from enantioenriched secondary propargylic alcohols (93.2–97.2% ee) [28]. The oxasiletanes were generated in situ by the IBS reaction, and their solutions were treated with TMSOTf at low temperature. We fortuitously found that the corresponding propargylsilanes **31** were formed and these were isolated in high yields. Interestingly, the enantiopurities of the starting disilanyl ethers were almost completely conserved in the produced propargylsilanes. It is remarkable that even **30d**, whose rearrangement may involve a highly stabilized phenyl-substituted carbocation, gave the corresponding product **31d** with a high degree of stereoconservation (97.5%). Further interest was focused on the stereochemical course of the migration. We could determine that all reactions proceeded with retention of the configuration of the starting propargyl ethers (Scheme 21).



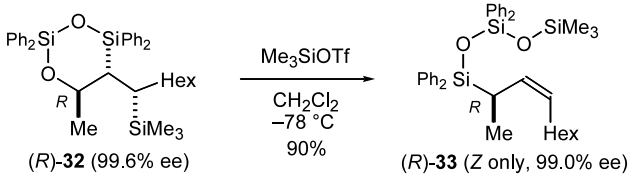

Scheme 21.



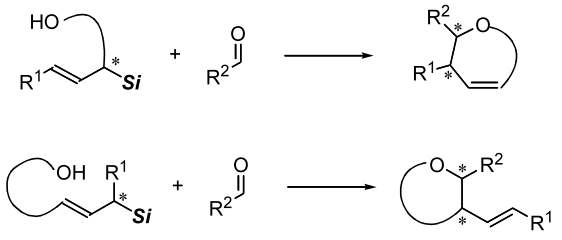

Scheme 22.

From these results, the following reaction mechanism involving a stereospecific 1,2-silyl shift with retention of configuration at the migration termini was proposed (Scheme 22). The stereospecific *syn*-migration of the silyl group may be ascribed to the *syn*-orientation of the leaving oxygen and migrating silicon atoms, which are fixed in the four-membered ring. Although cationic 1,2-migration of silyl groups is known in the literature, *syn*-specificity has never been reported [38]. The reaction may be related to the pinacol rearrangement, in which migration of an organic group instead of a silyl group is involved. In the pinacol-type rearrangement, racemization or inversion of stereochemistry at the migrating termini is commonly accepted [39]. Our results for the first time demonstrate that cationic 1,2-rearrangement of an optically active compound bearing a sole stereogenic center proceeds with retention of stereochemistry at the migrating terminus.

Application of the *syn*-rearrangement reaction to the IBS products derived from allylic alcohols was examined [28]. Although the eight-membered cyclic dimer scarcely reacted under the TMSOTf-catalyzed reaction conditions, the six-membered cyclic disiladioxane (*R*)-**32** obtained by ring contraction of (*R*)-**18** successfully yielded allylsilane (*R*)-**33** in high yield (Scheme 23). The allylsilane was obtained with almost perfect retention of configuration, suggesting a possibility that the *syn*-migration mechanism is generally applicable to oxasilacycles in which the oxygen and silicon atoms are separated by two carbon atoms.




Scheme 23.



Scheme 24.

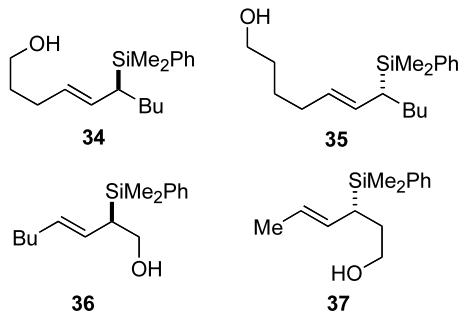
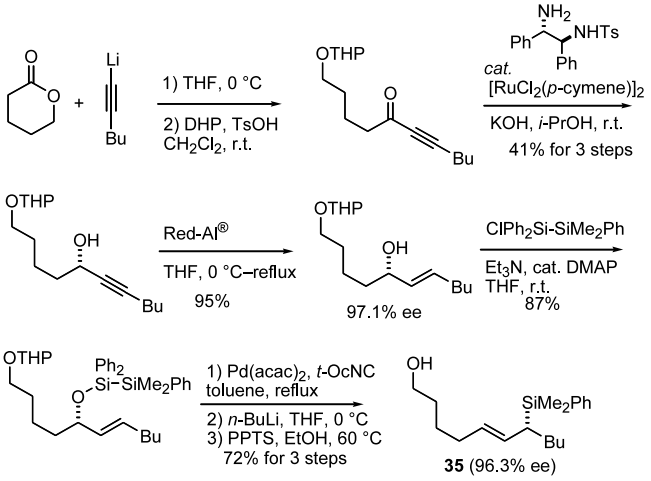



Fig. 2.

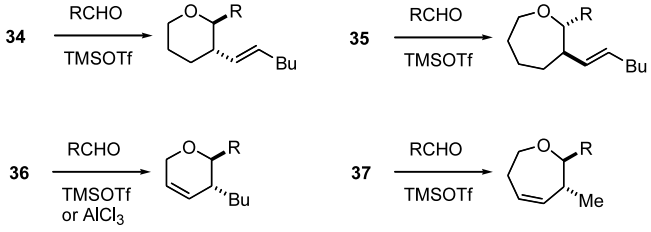



Scheme 25.

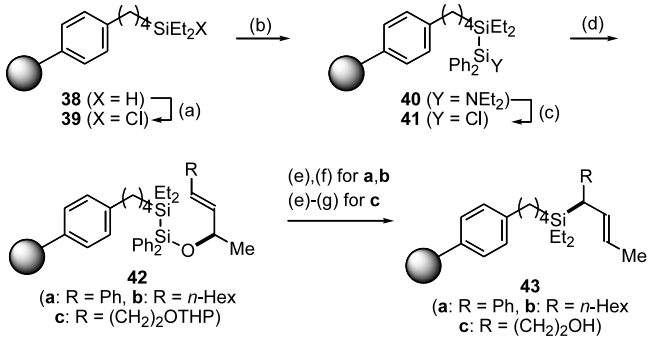
## 4. Synthetic applications

### 4.1. Asymmetric synthesis of cyclic ethers with functionalized enantioenriched allylsilanes

The IBS–elimination protocol is suitable for the synthesis of highly enantioenriched allylsilanes bearing base-tolerant functional groups. In particular, those bearing hydroxy groups or their protected derivatives seem to be synthetically valuable targets in terms of the applicability to organic synthesis, including the Marko-type acetalization–cyclization protocol in the reaction with aldehydes (Scheme 24) [40]. We have so far synthesized a range of enantioenriched (*E*)-allylsilanes such as **34**–**37** bearing hydroxy or protected hydroxy groups as exemplified in Fig. 2 [41–43]. An example of the synthesis of hydroxy-substituted enantioenriched allylsilane **35** is shown in Scheme 25 [42]. Asymmetric hydrogenation of alkynyl ketone by the Noyori procedure and *trans*-selective reduction of the triple bond by the hydroalumination-hydrolysis sequence are generally applicable to the preparation of highly enantioenriched (*E*)-allylsilanes. The THP protection is found to be most




Scheme 26.




Scheme 27.

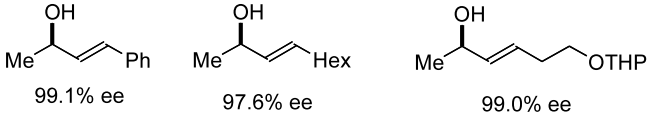



Fig. 3.

effective for the allylsilane synthesis, since it is not only tolerant toward *n*-BuLi treatment after the IBS step but also is selectively removable at the final stage with no undesirable protodesilylation at the allylsilane moiety.

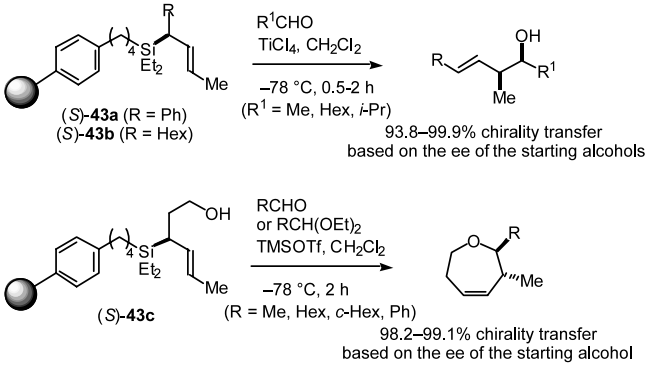
These allylsilanes **34**–**37** reacted with aldehydes in the presence of Lewis acid catalysts, giving medium-sized ring ethers in high yields (Scheme 26). It is remarkable that this protocol was particularly effective for stereoselective construction of seven-membered cyclic ethers, which are not easily accessible by other means. Remarkably, a high degree of chirality transfer was realized in the seven-membered ring formations. Furthermore, six-membered ring formations were successfully carried out by the same protocol.

### 4.2. Solid-phase synthesis of polymer-supported enantioenriched allylsilanes and their synthetic utility

Our attention was then directed to the IBS reaction on the solid phase. It is likely that the IBS–elimination protocol for allylsilane synthesis is especially suitable for the application to solid-phase synthesis, since the IBS step may scarcely be affected by attachment to the polymer-support in terms of stereoselectivity as well as reactivity.

Our strategy involved the use of polymer-supported chlorodisilane, onto which enantioenriched allylic alcohols were introduced for subsequent IBS and elimination reactions. The polymer-supported allylsilanes thus prepared are linked to the polymer-support at the silicon atom, and therefore do not require any additional linking groups on the organic moieties that are incorporated into products. These 'traceless-type' enantioenriched allylsilanes are highly attractive for asymmetric synthesis, although they had never been synthesized, due to the lack of an appropriate method for their preparation. It should be noted here that Panek and Zhu reported polymer-supported allylsilanes, which are prepared by the reaction of polystyrene resin with enantioenriched allylsilanes bearing a hydroxy group on their organic group for the attachment [44].

We prepared polymer-supported chlorodisilane **41** via reaction of the readily available polymer-supported chlorosilane **39** with (diethylamino)diphenylsilyllithium followed by chlorination with acetyl chloride (Scheme 27) [45]. Reactions of the polymer-supported disilanyl chloride **41** with enantioenriched allylic alcohols listed in Fig. 3 proceeded efficiently to give polymer-supported disilanyl allyl ethers **42**. Remarkably, the allyl ether formation did not require excess amounts of allyl alcohols: use of just one equivalent of the alcohols provided the allyl ether product in optimal yield. The resultant disilanyl allyl ethers were then subjected to solid-phase IBS reaction followed by treatment with *n*-BuLi. Although the yield and the degree of 1,3-chirality transfer could not be evaluated at this stage, the formation of enantioenriched allylsilane **43a**, **b** on the polymer-support was unambiguously proven by the formation of highly enantioenriched homoallyl alcohols in the reactions with aldehydes (Scheme 28). The asymmetric acetalization–cyclization protocol was applied to the polymer-supported allylsilane **43c**, resulting in high yield as well as high stereoselectivities. For instance, the reactions yielded highly enantioenriched 2,3-disubstituted oxa-4-cycloheptane with almost perfect chirality transfer.




Scheme 28.

## 5. Conclusion

We summarize our recent findings on the IBS of allylic and propargylic alcohols, which leads to the formation of 1,2-oxasiletanes as primary products. The stability of the oxasiletane products largely depends upon substituents on the four-membered ring. From the IBS products, allyl-, allenyl-, and propargyl-silanes were synthesized via either Peterson-type elimination or cationic 1,2-silyl migration reaction. The most striking features of the transformation are the stereochemical aspects, which are characterized by highly efficient chirality transfer. In particular, these new synthetic protocols have allowed convenient access to highly enantioenriched organosilicon compounds that are otherwise difficult to synthesize. These findings critically rely on the development of a new catalytic system, i.e. the palladium–isocyanide catalysts. The high catalytic activity toward the activation of the Si–Si bond has found further application to the activation of Si–Sn and Si–B bonds [9].

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