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Formation of Three New Bonds and Two Stereocenters in Acyclic Systems by Zinc-Mediated Enantioselective Alkynylation of Acylsilanes, Brook Rearrangement, and Ene-Allene Carbocyclization Reactions

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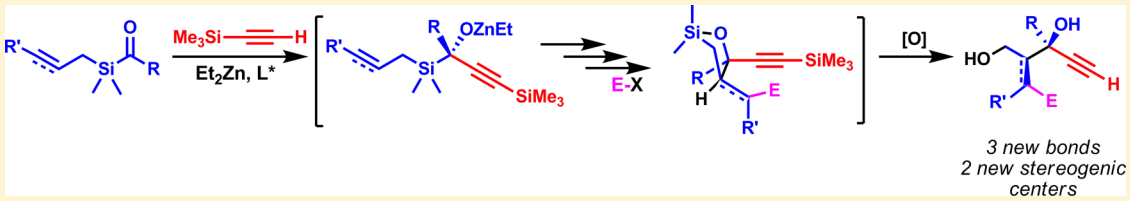
Supporting Information



ABSTRACT: Diastereoisomerically pure (*dr* > 99:1) and enantiomerically enriched (*er* up to 98:2) substituted propargyl diols possessing a tertiary hydroxyl group were synthesized in a single-pot operation from simple acylsilanes through a combined catalytic enantioselective alkynylation of acylsilanes, followed by an allenyl-Zn-Brook rearrangement and Zn-ene-allene (or Zn-yne-allene) cyclization reaction. Two remarkable features of these reactions are the near complete transfer of chirality in the allenyl-Zn-Brook rearrangement and the highly organized six-membered transition state of the Zn-ene-allene carbocyclization found by DFT calculations. In this process, *three new bonds and two new stereogenic centers are created in a single-pot operation in excellent diastereo- and enantiomeric ratios*. DFT calculations show that the allenyl-Zn-Brook rearrangement occurs in preference to the classic [1,2]-Zn-Brook rearrangement owing to its significantly lower activation barrier.

INTRODUCTION

In 1966, Nozaki, Noyori, and co-workers published their pioneering work on enantioselective organometallic catalysis.[1] Since then, a variety of widely used transformations have become possible using enantioselective catalysis, which plays a crucial role in synthetic organic chemistry.[2] Much effort has been devoted to the development of catalytic reactions, but for the synthesis of acyclic products, these highly valued transformations usually combine only two components in the critical step and a single carbon−carbon bond formation occurs. The development of enantioselective catalytic reactions in which more than only one carbon−carbon bond is created in a single-pot operation would tremendously improve the efficiency of catalytic processes.[3] In this context, recent years have witnessed an important change in approach in synthesis, and new directions, such as domino and cascade reactions, leading to multiple carbon−carbon bonds and stereocenters with high chemo- and stereoselectivity are playing a more dominant role.[4] However, only a few methods maintain their efficiency when the structural complexity of the target adducts increases. One element that invariably increases the difficulty of a chemical synthesis is the stereocontrol in acyclic systems.

The challenging goal of step economy in acyclic systems can be attained by using reactions that allow a great increase in complexity or through one-pot operations that unify multiple steps, thereby collectively achieving a high increase in complexity.[5] In this context, we have recently developed different approaches to create several carbon−carbon bonds in single-pot operations that proceed with excellent stereochemical control,[6] including the creation of challenging quaternary carbon stereogenic centers in acyclic systems (Scheme 1).[7] These methodologies can produce sophisticated molecular frameworks while remaining synthetically efficient. However, in these previous cases, selectivity control was usually induced by chiral auxiliaries.

Combining enantioselective catalysis with multiple carbon−carbon bond formation in acyclic systems in a single-pot operation would pave the way to new approaches in synthesis.[3] One potential interesting solution for the formation of several C−C bonds in a single chemical reaction could be the preparation of multifunctional reactive intermediates such as metalated α-hydroxysilanes.

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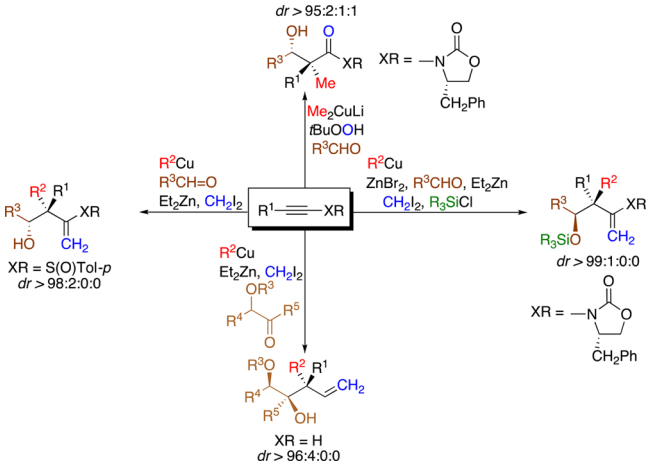
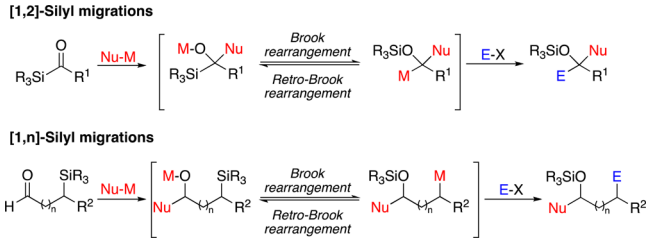
Scheme 1. One-Pot Preparation of Quaternary Carbon Stereocenters from Alkynes



RESULTS AND DISCUSSION

Intramolecular 1,2-anionic migrations of silyl groups from carbon to oxygen atoms were originally recognized and studied by Brook (Scheme 2).[8] These rearrangements, extended to

Scheme 2. [1,2]- and [1,*n*]-Brook Rearrangements



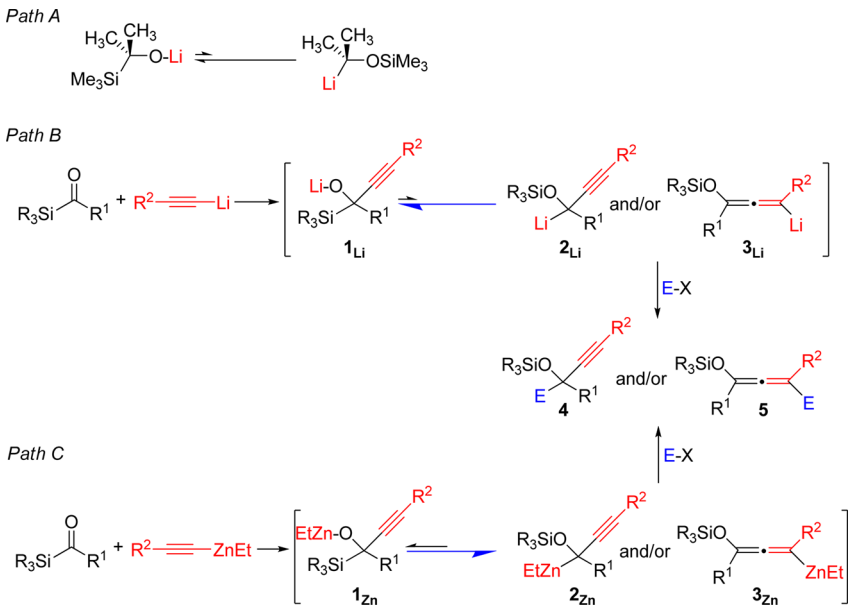
[1,*n*]-silyl migrations and commonly referred to as [1,*n*]-Brook rearrangements (Scheme 2), formally have the potential of creating two carbon−carbon bonds while a new organometallic species is formed after the migration. Such rearrangements have found extensive applications in synthesis, including the synthesis of the first stable silene.[9] It should be mentioned that any approach leading to the creation of an enantiomerically enriched α- or γ-metalated silyl ether, following a [1,2]- or [1,3]-Brook rearrangement, respectively, would be an important tool for the preparation of chiral organometallic species.[10]

However, in the presence of a stoichiometric amount of base, the Brook rearrangement does not proceed easily and the equilibrium can only be shifted toward the end products through either the addition of an electrophile or an elimination reaction (Scheme 3, Path A). Similarly, the lithium salt of α-silylpropargylic alcohol $\mathbf{1}_{Li}$, generated by the addition of lithium acetylide to acylsilane, does not lead experimentally to the Brook rearrangement product $\mathbf{2}_{Li}$ (or $\mathbf{3}_{Li}$ after metallotropic equilibrium, Scheme 3, Path B) since none of the adducts **4** and/or **5** are obtained after hydrolysis. Only when an excess of the starting alkyne is used (2 equiv of an alkyne for 1 equiv of alkynyl lithium), the reaction can be shifted to the products **4** and/or **5** through protonation of $\mathbf{2}_{Li}$ or $\mathbf{3}_{Li}$ by the acidic acetylenic hydrogen atom (E-X = R^2CC-H, Scheme 3, Path B).[11]

The fact that the Brook rearrangement products are obtained only when electrophiles are added indicates that the corresponding organolithium species $\mathbf{2}_{Li}$ or $\mathbf{3}_{Li}$ are not formed in a significant concentration. However, as the presence of the electrophile drives the reaction to completion, such transformations found numerous applications in organic synthesis.[12] When a catalytic amount of base is utilized, the Brook rearrangement typically proceeds efficiently through a rapid and essentially irreversible protonation of the carbanion (i.e., $\mathbf{2}_{Li}/\mathbf{3}_{Li}$) by the starting 2-trimethylsilyl propan-2-ol.

Nevertheless, to have a specific carbanionic species in hand for subsequent reactions, such as **2** or **3**, the presence of an electrophile in the reaction mixture should be avoided. In other words, the equilibrium $\mathbf{1}_{Li} \rightleftharpoons \mathbf{2}_{Li}/\mathbf{3}_{Li}$ should be shifted toward the formation of carbanion **2** or **3** without the addition of an electrophile. Considering that the Brook rearrangement should proceed only if the formed carbanion has a similar or higher thermodynamic stability (i.e., lower energy) than that of the

Scheme 3. Li- vs Zn-Brook Rearrangement



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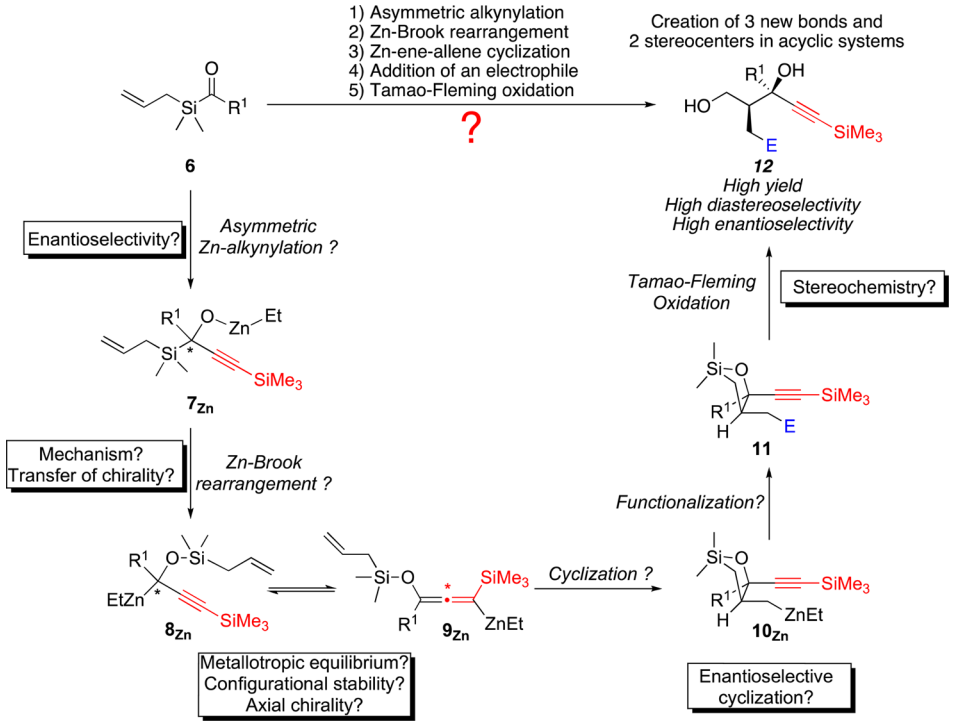
Scheme 4. Proposed Research



initial alkoxide, we have postulated in previous work that a rearranged organozinc species should afford the required extra stabilization through overlap of the nonbonding electrons of the oxygen atom and the filled d-orbitals of the metal with the antibonding π^*-orbitals of the carbon−carbon bonds.[13] We were pleased to find that indeed Zn-alkoxide $\mathbf{1}_{Zn}$ led to the Brook rearranged products $\mathbf{2}_{Zn}$ or $\mathbf{3}_{Zn}$, which can be further reacted with an electrophile to produce **4** and **5** (Scheme 3, Path C).[13,14]

On the basis of these initial findings on Zn-promoted Brook rearrangement, we designed a new approach in which a catalytic enantioselective alkynylation of acylsilane **6**, in the presence of chiral zinc species derived from Et_2Zn and chiral Lewis bases, would give the corresponding enantiomerically enriched zinc α-hydroxypropargyl silane $\mathbf{7}_{Zn}$ (Scheme 4). The intermediate $\mathbf{7}_{Zn}$ would then undergo a Zn-Brook rearrangement to give the stabilized organozinc species $\mathbf{8}_{Zn}$ (or $\mathbf{9}_{Zn}$ after metallotropic equilibrium). Intramolecular carbometalation reaction (Zn-ene cyclization) of $\mathbf{8}_{Zn}$ (or $\mathbf{9}_{Zn}$) would give the corresponding cyclic product $\mathbf{10}_{Zn}$ that would finally react with an electrophile to give functionalized oxysilane **11**. A simple Tamao−Fleming oxidation would then lead to the required acyclic adduct **12** in which three new bonds with two new stereogenic centers in an acyclic system are created in a single-pot operation from an initial acylsilane **6** (Scheme 4). This proposed scheme is extremely appealing, but obtaining a high chemical yield and high diastereomeric and enantiomeric ratios requires a complete control of all the elementary steps and such control can only be achieved if all the important questions summarized below are adequately addressed (see also Scheme 4):

(1) Would the Zn-alkynylation of acylsilanes **6** → $\mathbf{7}_{Zn}$ be highly enantioselective?
(2) Would the zinc-promoted Brook rearrangement $\mathbf{7}_{Zn}$ → $\mathbf{8}_{Zn}$ still proceed in the presence of a chiral ligand on the zinc, and would it proceed with transfer of the stereochemical information?
(3) Would the resulting organometallic species be configurationally stable?
(4) Would the carbocyclization $\mathbf{9}_{Zn}$ → $\mathbf{10}_{Zn}$ be enantioselective?
(5) Would the organozinc species $\mathbf{10}_{Zn}$ be functionalized at the end of the sequence?

The success of this challenging single-pot strategy, in which an enantioselective catalytic reaction initiates a cascade of diastereo- and enantioselective events, requires positive answers to all the questions raised above.[15]

Our initial challenge was the alkynylation of **6** through enantioselective catalysis. The addition of alkynes to carbonyl and imine compounds has been the subject of a large number of studies and reviews;[16] in contrast, the use of acylsilanes as substrates has been much less developed. Johnson, Scheidt, and co-workers have performed the pioneering work for either a tandem alkynylation of silyl glyoxylate by using a chiral amino alcohol[17] or the enantioselective alkyne addition to acylsilanes with tridentate Schiff base ligands.[18] More recently, Zn-salen ligands were also developed for such enantioselective additions.[19] We initially investigated the addition of trimethylsilylacetylene to standard acylsilanes **6**, in the presence of diethylzinc and a catalytic amount of chiral ligands L_{1-7}. The expected chiral propargyl alcohols **7** were obtained in high yields and variable enantioselectivity, as summarized in Scheme 5 and Table 1.[15]

Initially, we used chiral ligand L_1 developed by Scheidt and co-workers for the alkynylation of acylsilane **6**.[18] However, despite the high reactivity and chemical yields, the enantioselectivities were not satisfying (Table 1, entries 1−3). On the other hand, we were delighted that ProPhenol ligand L_2, introduced by Trost et al. for the alkynylation of aldehydes and ketones,[20] showed excellent enantioselectivities for the addition of trimethylsilylacetylene to acylsilane **6a**, albeit with reduced reactivity. The catalyst loading could be reduced to 5 and even 2.5 mol % without affecting the enantiomeric ratio drastically (Table 1, entries 6 and 7, respectively). The best conditions for

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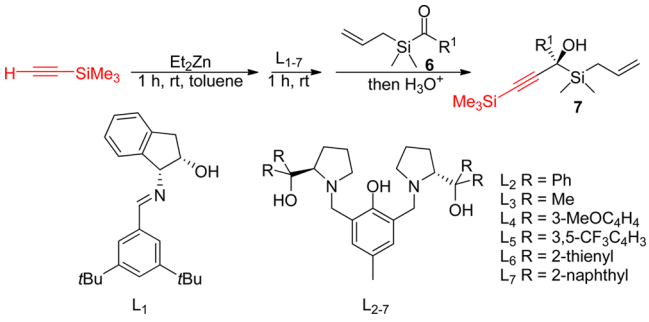
Scheme 5. Enantioselective Alkynylation of Acylsilanes



this reaction involved the use of 5 mol % of L_2 while performing the reaction at temperatures below 15 °C for 48 h (Table 1, entry 8). Two other acylsilanes (R^1 = Bu **6b**, $(CH_2)_2$Ph **6c**) were treated under the same experimental conditions, and similar yields and enantiomeric ratios were obtained (Table 1, entries 9 and 10). The absolute configuration was established by chemical correlations.[13] Several other ProPhenol-type ligands, such as L_{3-7}, were tested, but none could lead to the same balance of yields and enantiomeric ratios (Table 1, entries 11−16).

Interestingly, when the alkynylation reaction was performed on benzoyl(allyldimethyl)silane (R^1 = Ph, not described in Table 1), the only product obtained was the reduced adduct.

Having established a straightforward access to enantiomerically enriched zinc propargyl silanol derivatives **7a−c**, we started to investigate the following steps, namely, the Zn-Brook rearrangeme and subsequent cyclization. Therefore, Et_2Zn was added to racemic **7a−c** in THF and heated at 45 °C for 24 h (Scheme 6). We were pleased to see that the Zn-Brook rearrangement proceeded well for all propargyl silanols and that these adducts cyclized, leading to adducts **11a−c** as single diastereoisomers with conversions higher than 90% (Scheme 6, Path A).[21]

To examine the scope of the reaction, several other zinc propargyl silanol derivatives with different substitutions at the alkynyl position were tested in our combined Zn-Brook rearrangement/cyclization reaction. When R^2 = Ph and Bu, the allenes were quantitatively obtained after hydrolysis without any traces of the cyclization reaction (Scheme 6, Path B; yields could not be determined after purification because these alkoxyallenes are unstable).

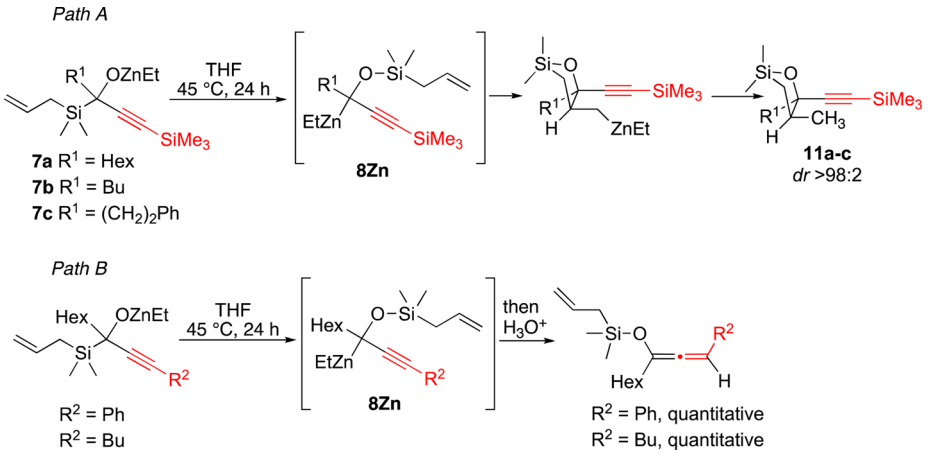
With a smooth procedure for the tandem Zn-Brook rearrangement/cyclization of **7a−c** in hand, we turned our

Table 1. Diethyl Zinc Mediated Alkynylation of Acylsilanes 6 with Trimethylsilylacetylene To Give Propargyl Alcohols 7 (As Represented in Scheme 5)

entry	R^1	alkyne (equiv)	Et_2Zn (equiv)	ligand	T [°C]	time [h]	yield	er^a
1	Hex (**6a**)	1.1	2.2	L_1, 20%	rt	4.5	96 (**7a**)	39:61
2	Bu (**6b**)	2	2	L_1, 20%	rt	16	89 (**7b**)	35:65
3	Hex (**6a**)	1.1	2.2	L_1, 20%	0	21	94 (**7a**)	34:66
4	Hex (**6a**)	2	2		rt	24	79 (**7a**)	50:50
5	Hex (**6a**)	1.2	2.4	L_2, 20%	0−20	42	70 (**7a**)	18:82
6	Hex (**6a**)	1.2	2	L_2, 5%	5−15	22	60 (**7a**)	6:94
7	Hex (**6a**)	1.2	2.4	L_2, 2.5%	5−15	27	85 (**7a**)	7:93
8	Hex (**6a**)	1.2	2.4	L_2, 5%	5−15	48	90 (**7a**)	2:98
9	Bu (**6b**)	1.2	2.4	L_2, 5%	5−15	48	89 (**7b**)	3:97
10	$(CH_2)_2$Ph (**6c**)	1.2	2.4	L_2, 5%	rt	48	70 (**7c**)	8:92
11	Hex (**6a**)	3	3	L_3, 20%	rt	24	57 (**7a**)	20:80
12	Hex (**6a**)	3	3	L_4, 20%	rt	24	22 (**7a**)	10:90
13	Hex (**6a**)	3	3	L_5, 20%	rt	24	50 (**7a**)	27:63
14	Hex (**6a**)	3	3	L_6, 20%	rt	24	15 (**7a**)	44:56
15	Hex (**6a**)	3	3	L_7, 20%	rt	24	35 (**7a**)	2:98
16	Hex (**6a**)	3	3	L_7, 20%	0	24	41 (**7a**)	1:99

[a]The enantiomeric ratio was determined by HPLC using a chiral column.

Scheme 6. Zn-Brook Rearrangement Followed by a Carbocyclization Reaction



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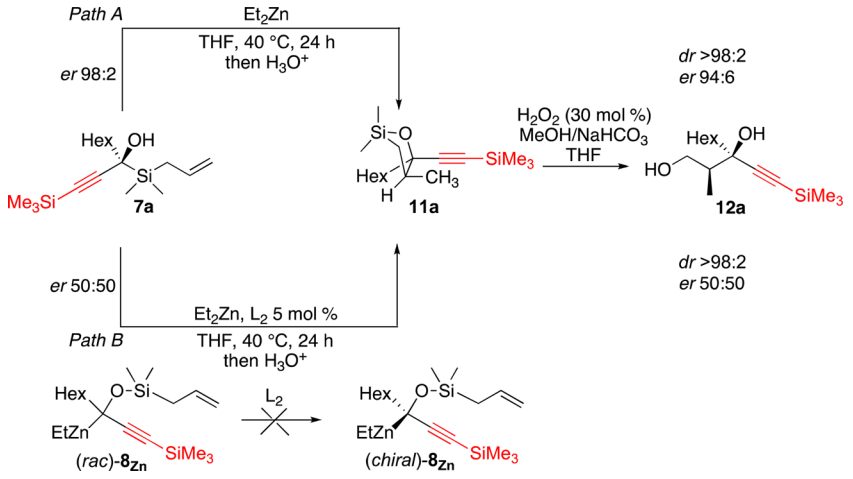
Scheme 7. Stereochemistry of the Zn-Brook Rearrangement and the Following Cyclization Reactions



attention to the stereochemical behavior of enantiomerically enriched **7a** under the same experimental conditions. Indeed, the stereochemical outcome of a silyl migration has been occasionally investigated for organolithium species and occurs with partial inversion of configuration for secondary and tertiary α-silyl benzyl alcohols[22] but with retention (>97%) of configuration for saturated α-silyl alcohols (silyl alkyllithium species are always rapidly and irreversibly intercepted in situ by using a protic source).[23] When a solution of Et_2Zn was added to enantioenriched **7a** (*er* 98:2) in THF and heated at 45 °C for 24 h, the corresponding cyclic product **11a** was obtained, after hydrolysis, as a single diastereomer over the two consecutive steps (Zn-Brook rearrangement/cyclization, Scheme 7, Path A). The enantiomeric ratio could not be determined on the rather sensitive oxysilane **11a**, and therefore, it was determined on the acyclic adduct **12a**, which was obtained easily after a Tamao–Fleming oxidation. In this process, the silyl substituent on the alkyne is also partially removed and yields are determined on the whole sequence after desilylation (see Scheme 7). The absolute configuration of **11a** resulting from this tandem reaction was deduced in analogy with previous studies, and the configuration of **12a** was determined by X-ray analysis.[24] On the other hand, when racemic **7a** was treated with Et_2Zn in the presence of a catalytic amount of chiral ligand L_2, only racemic **11a** was formed, excluding a possible equilibration of racemic propargyl $\mathbf{8_{Zn}}$ (or allenylzinc $\mathbf{9_{Zn}}$) into enantiomerically enriched species through interactions with a chiral ligand (Scheme 6, Path B).

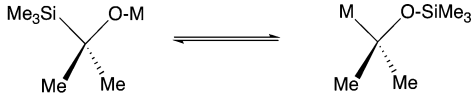
In conclusion, when enantiomerically enriched precursor **7a** is treated with Et_2Zn and heated at 45 °C for 24 h, the tandem Zn-Brook rearrangement, followed by cyclization, leads to diastereomerically pure **11a** with almost the same enantiomeric ratio as that of the starting propargylsilanol **7a**. *Therefore, this tandem reaction proceeds with an almost complete transfer of stereochemical information (er 94:6 vs 98:2).*

Whereas unstabilized sp^3 alkyllithium and magnesium reagents show moderate configurational stability,[25] sp^3 alkylzinc species are usually configurationally stable up to 25 °C.[26] In the particular case of this tandem reaction (Scheme 7), a temperature of 45 °C for 24 h is required to drive the reaction to completion and it was rather surprising that the predicted Zn-Brook rearranged product $\mathbf{8_{Zn}}$ was configurationally stable.

Theoretical Studies. To gain insights into the mechanism of the unusual Zn-Brook rearrangement and of the reactions that follow, we studied by quantum mechanical calculations the transformations in Scheme 4 and also the classic [1,2]-Brook rearrangement in model systems Me_3SiCMe_2OM, M = Li and Zn (eq 1). We used density functional theory (DFT)[27] employing several functionals, i.e., PBE0/6-311G(d,p),[28a,b] B3LYP/6-311G(d,p),[29a–c] and the dispersion corrected functional[29d] B3LYP-D2/6-311G(d,p). The calculations were carried out with the Gaussian 09 suite of programs.[30] All the DFT functionals produced similar results, a fact that lends support to their reliability. Full details of the results of the calculations are given in the Supporting Information material of the current paper and of our preliminary report (ref 15).

The discussion below is based on calculations that use the hybrid PBE0 functional[28a,b] and the 6-311G(d,p) basis set[30] for all atoms except for Zn, which is represented by the Stuttgart/Dresden quasi relativistic effective core potential (ECP 10MWB) and its associated basis set[31] augmented with an f-polarization function.[32] This method is denoted as PBE0/SDD-6-311G(d,p). The solvent (THF) effect was calculated by using the SMD model[33] at the optimized gas phase geometries.[34] $\mathbf{7_{Zn}}$ with R^1 = Et was used for the theoretical analysis of the reactions in Scheme 4.

We first studied the classic [1,2]-Brook rearrangement given in eq 1. The calculated free energy profiles for M = Li and Zn are shown in Figure 1, and a schematic presentation of all the stationary points and their important geometry parameters are shown in Figure 2.



Equation 1. [1,2]-Brook rearrangement

For M = Li, the [1,2]-Brook rearrangement is endothermic by 15 kcal·mol^{-1}. It is a two-step reaction: in the first step, a barrier of 24.5 kcal·mol^{-1} leads to an intermediate (**Int-Li**), which lies in a very shallow minimum relative to **TS1-Li**. In **Int-Li**, the silyl fragment nearly completed its migration from C to O, forming a Si–O bond of 1.68 Å (1.67 Å in the product); simultaneously, the Li approaches C to a distance of 2.01 Å, which is somewhat longer than in the product (1.93 Å). The geometry around C in **Int-Li** is that of an inverted tetrahedron with the Li bridging between C and O (Figure 2). In the second step of the rearrangement, inversion occurs at C and the Li atom completes its migration but remains at a bridging position between C and O. The overall barrier for the rearrangement is 35.7 kcal·mol^{-1}.

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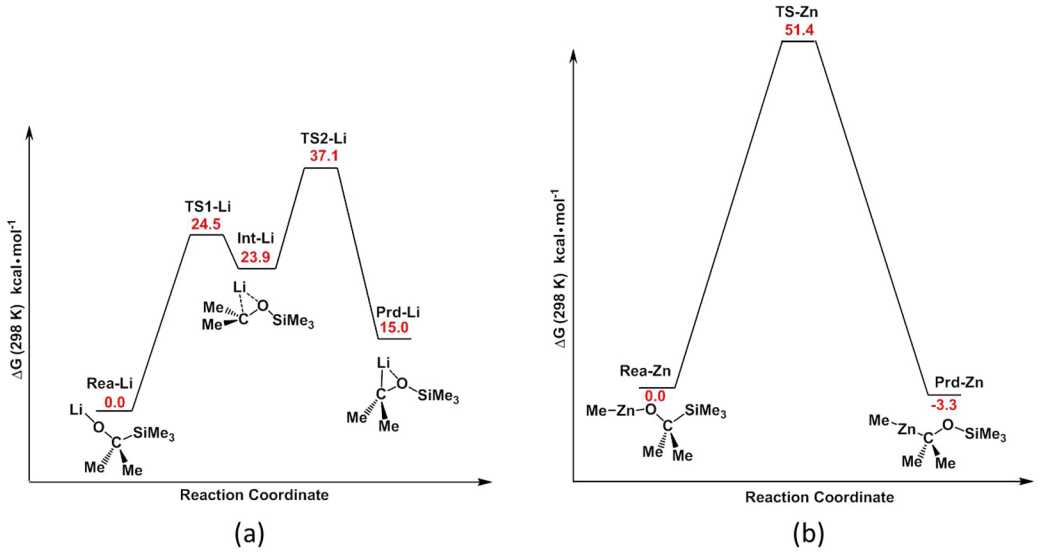

Figure 1. Calculated free energy profiles for the [1,2]-Brook rearrangement (eq 1) in THF: (a) for M = Li, at PBE0/6-311G(d,p)//PBE0/6-311G(d,p) (gase phase geometry), and (b) for M = Zn, at PBE0/SDD-6-311G(d,p)//PBE0/SDD-6-311G(d,p) (gas phase geometry).

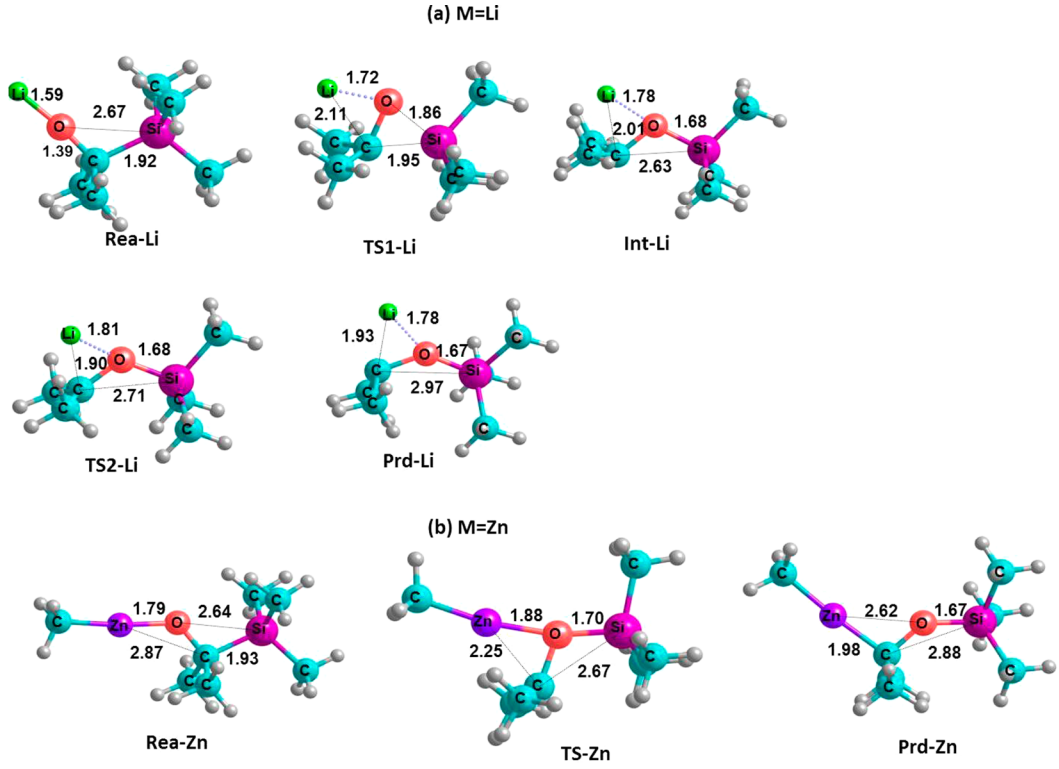

Figure 2. Schematic structures and optimized geometry parameters of stationary points along the [1,2]-Brook rearrangement reaction profiles (a) for M = Li, at PBE0/6-311G(d,p), and (b) for M = Zn, at PBE0/SDD-6-311G(d,p).

The endothermicity of the rearrangement and the relatively high overall reaction barrier suggest that the retro-Brook rearrangement should be the preferred reaction in the absence of electrophiles, as found experimentally by us (Scheme 3) and by others in studies of the retro-Brook rearrangement.[35]

In contrast to the endothermic [1,2]-Li-Brook rearrangement, the [1,2]-Zn-Brook rearrangement is slightly exothermic (ΔG(THF) = −3.3 kcal·mol^{-1}). The difference in the energy of Equation 1 between Li and Zn is consistent with the differences of the formed and broken bond energies[36] during the rearrangement, i.e., Zn−O (64 ± 10)[37] vs Zn−C (66)[38] (kcal·mol^{-1}) relative to Li−O (81)[39] vs Li−C (51) (kcal·mol^{-1}).[40] Interestingly, for M = Zn, a single transition state was located exhibiting a very high reaction barrier of 51.4 kcal·mol^{-1}. The structure of transition state **TS-Zn** (Figure 2) shows that the migration of the silyl group from O to C is nearly complete (r(Si−O) = 1.70 vs 1.67 Å in the product) while the Zn−C bond distance is still significantly longer than in the product (2.25 vs 1.98 Å, respectively). The very high reaction barrier for M = Zn suggests that the [1,2]-Brook rearrangement (or the corresponding retro-Brook rearrangement) will not occur under ambient conditions, and if available, other pathways will be followed.

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Such alternative pathways become available in 7_{Zn} due to the presence of the propargyl substituent.

With this basic information in mind, we calculated the free energy profile of the transformations leading from 7_{Zn}, R^1 = Et to 10_{Zn}, R^1 = Et in THF (ΔG_{sol}),[33,34] as shown in Figure 3 (gas phase values are given in the Supporting Information of ref 15). A schematic presentation of all stationary points located along the reaction path is shown in Figure 4. The overall reaction from 7_{Zn} to the cyclic product 10_{Zn} is calculated to be highly exothermic by 25.9 kcal·mol^{-1} (24.6 kcal·mol^{-1}, gas phase), which provides the driving force for the reaction. Importantly, the calculations reveal that the first step of the reaction is ***not*** the expected classical [1,2]-Brook rearrangement of 7_{Zn} to 8_{Zn} (which may eventually be transformed by a metallotropic equilibrium into 9_{Zn}) as proposed in Scheme 4 on the basis of previous assumptions.[21] Instead, the calculations suggest that 7_{Zn} rearranges directly to 9_{Zn} through an interesting allenyl-Brook rearrangement, with a [1,3]-migration of the ZnEt fragment to the allenyl carbon so that the new C−Zn bond is formed *anti* to the C−Si bond that is cleaved upon the silyl group migration to oxygen (Figure 3).

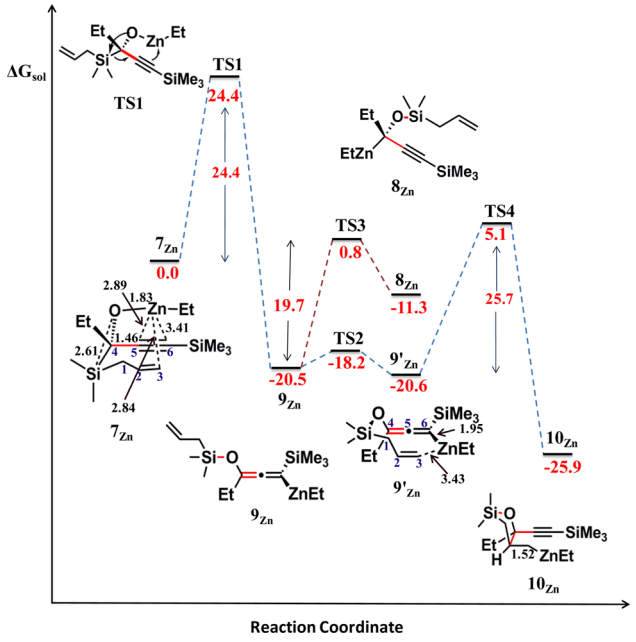

Figure 3. Free energy profile of the transformation of 7_{Zn} to 10_{Zn} in THF (at 298 K) calculated at PBE0/SDD-6-311G(d,p)//PBE(0)/SDD-6-311G(d,p) (gas phase geometry).

A transition state for the classic [1,2]-Brook rearrangement in which the silyl group in 7_{Zn} migrates to the oxygen atom and the ZnEt group coordinates to the central carbon atom (C_4) to form 8_{Zn} could not be located. Furthermore, the calculations show that the allenyl-Brook rearrangement of 7_{Zn} to 9_{Zn} is by 9.2 kcal·mol^{-1} more exothermic than the classical [1,2]-Brook rearrangement of 7_{Zn} to 8_{Zn}. The allenyl-Zn-Brook rearrangement of 7_{Zn} to 9_{Zn} is exothermic by 20.5 kcal·mol^{-1} (in THF), and the free energy barrier for the rearrangement is 24.4 kcal·mol^{-1} (Figure 3). This barrier height is in line with the experimental conditions used to perform the transformations.

A closer examination of the calculated geometries of 7_{Zn} and **TS1** (Figure 4) provides additional insight into the novel allenyl-Zn-Brook rearrangement. The reaction precursor 7_{Zn} exhibits a weak intramolecular chelation of Zn to the C−C triple bond

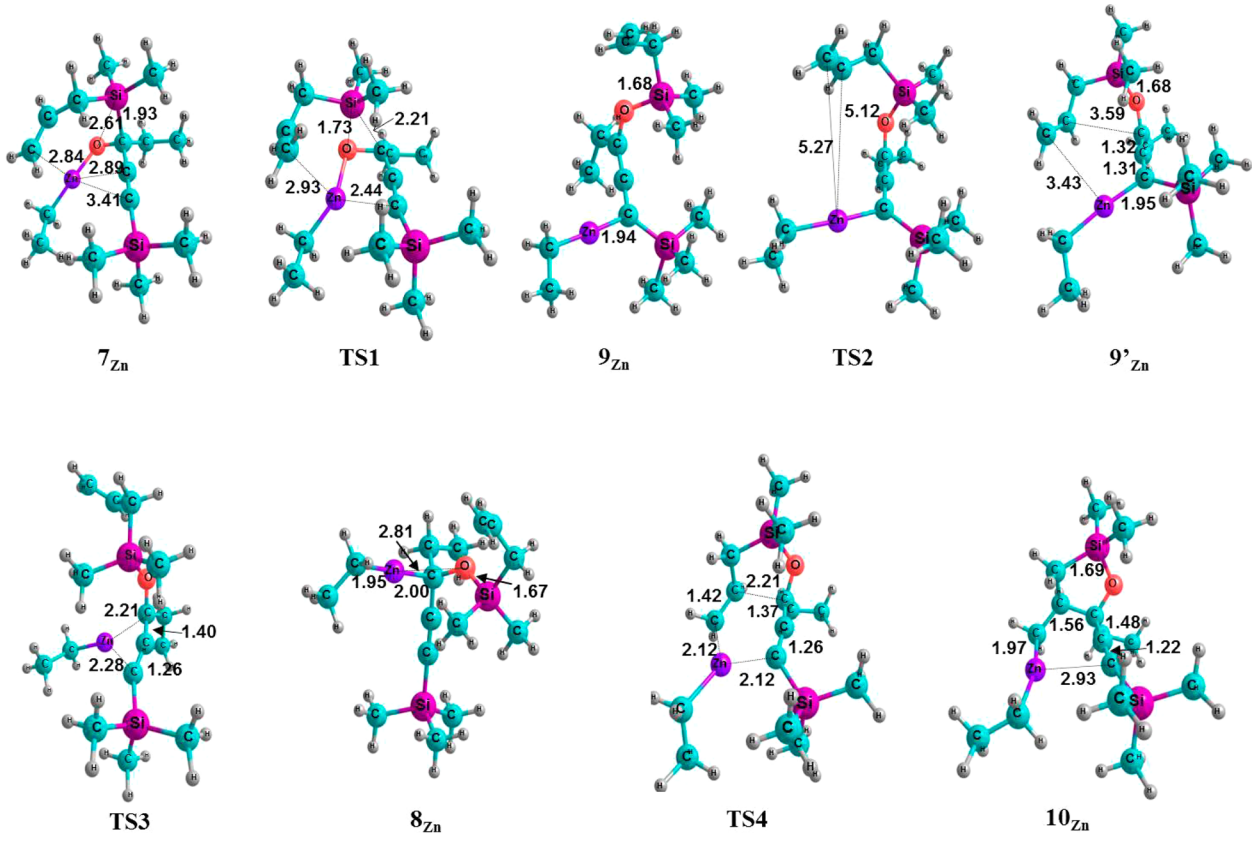

Figure 4. Optimized structures (at PBE(0)/SDD-6-311G(d,p)) of the stationary points on the reaction PES shown in Figure 3.

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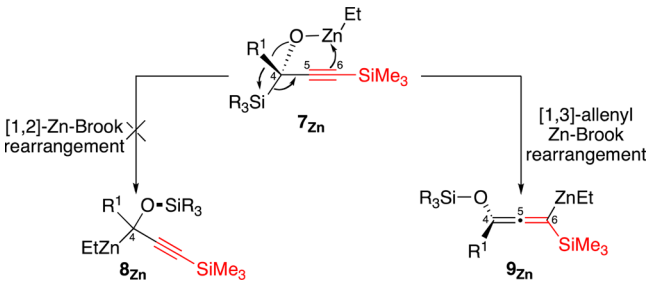
[r(Zn−C_5) = 2.89 Å, r(Zn−C_6) = 3.41 Å]. This weak chelation directs the reaction via **TS1** to yield directly the allenyl intermediate $\mathbf{9}_{Zn}$ (Figure 3). In **TS1**, the C_4−Si bond is stretched from 1.93 to 2.21 Å and the forming silicon−oxygen bond is nearly fully created: r(O−Si) = 1.73 Å (1.68 Å in $\mathbf{9}_{Zn}$); concurrently, the Zn atom approaches the β-propargylic carbon atom (C_6) to a distance of 2.44 Å (1.94 Å in $\mathbf{9}_{Zn}$) and the O−Zn distance is elongated to 2.05 Å from 1.83 Å in $\mathbf{7}_{Zn}$ (Figure 4). Thus, $\mathbf{7}_{Zn}$ undergoes an allenyl-Zn-Brook rearrangement in which the zinc atom is transferred directly to the β-alkynyl carbon atom (C_6) to give the allenyl-zinc intermediate $\mathbf{9}_{Zn}$, bypassing the classical [1,2]-Brook product $\mathbf{8}_{Zn}$. The preference of the allenyl-Zn-Brook rearrangement over the classical [1,2]-Brook rearrangement (M = Zn) is reasonable in view of the calculations reported above for the model [1,2]-Brook rearrangement (eq 1, M = Zn), which revealed an extremely high barrier of 51.4 kcal·mol^{-1} for the latter reaction (Figure 1). Therefore, under the reaction conditions, $\mathbf{7}_{Zn}$ does not rearrange to $\mathbf{8}_{Zn}$. This important finding nicely rationalizes the observation that the rearrangement proceeds without racemization, since allenylzinc species are configurationally stable.[41]

It is important to note that, even if the usual [1,2]-Brook rearrangement occurs and $\mathbf{8}_{Zn}$ is formed, it will, according to the calculations, easily rearrange to $\mathbf{9}_{Zn}$ via **TS3** (Figure 3) with a barrier of only 12.1 kcal·mol^{-1}. This [1,3]-Zn rearrangement occurs via a nearly symmetrical transition state in which the Zn atom is 2.21 and 2.28 Å from the two rearrangement C termini.

In the second step of the reaction sequence in Figure 3, the rotation around the Si−O in $\mathbf{9}_{Zn}$ occurs via **TS2** (with a small energy barrier of 2.3 kcal·mol^{-1}, Figure 3) to $\mathbf{9'}_{Zn}$, which is 0.1 kcal·mol^{-1} lower in energy. This rotation step is followed by cyclization of $\mathbf{9'}_{Zn}$ to yield $\mathbf{10}_{Zn}$, which is by 5.3 kcal·mol^{-1} more stable. The calculated barrier via **TS4** is 25.7 kcal·mol^{-1}. In this cyclization step, the electrophilic zinc atom activates the terminal double bond of $\mathbf{9'}_{Zn}$, leading via a cyclic six-membered transition state (**TS4**), held by zinc chelation (Figure 4), to $\mathbf{10}_{Zn}$. Because of this highly organized cyclic transition state, $\mathbf{10}_{Zn}$ is obtained as a single diastereomer. In this cyclization, the allenylzinc species and the electrophilic double bond play the role of the ene and the enophile moiety, respectively. In analogy to the ene-allene cyclization, this reaction has been named the Zn-ene-allene cyclization.[21] In **TS4**, the Zn atom moves toward the β-vinyl carbon (C_3) so that it is equally distanced (2.12 Å) between C_3 and the allenic C_6 (Figure 4). Concurrently, the α-vinyl carbon (C_2) approaches the π-bond of the α-allenylic carbon (C_4) to a distance of 2.21 Å. The geometry of this cyclic transition state dictates that enantiomerically enriched $\mathbf{9'}_{Zn}$ cyclizes diastereoselectively to enantiomerically enriched $\mathbf{10}_{Zn}$.[21] We note that the free energy barriers for the two critical steps of the overall reaction $\mathbf{7}_{Zn} \rightarrow \mathbf{10}_{Zn}$, i.e., $\mathbf{7}_{Zn} \rightarrow \mathbf{9}_{Zn}$ and $\mathbf{9'}_{Zn} \rightarrow \mathbf{10}_{Zn}$, are nearly the same (~25 kcal·mol^{-1}), and therefore, both steps are important in determining the overall reaction rate. In contrast, when the substituents on C_6 are R^2 = Ph and R^2 = Bu instead of R^2 = $SiMe_3$, the allenes were quantitatively obtained after hydrolysis without any traces of cyclization reaction (Scheme 6, Path B). Calculations (for details, see the Supporting Information) reveal that, for R^2 = Ph, the free energy barrier for the cyclization step is 29.8 kcal·mol^{-1}, higher by 4.1 kcal·mol^{-1} (in THF) than when R^2 = $SiMe_3$, which is a better electron donor, thus supporting the experimental results. We note that a difference of 4.1 kcal·mol^{-1} in activation free energies produces a rate difference of 1000 at 25 °C. However, when R^2 = Me (modeling an alkyl substituent), the barrier is increased by only 0.5 kcal·mol^{-1} to 26.2 kcal·mol^{-1}, which may hint that it is a steric effect of the larger *n*Bu substituent that prevents the carbocyclization.

In conclusion, the quantum mechanical DFT calculations show that $\mathbf{10}_{Zn}$ is obtained from $\mathbf{7}_{Zn}$ by an allenyl-Zn-Brook rearrangement producing first $\mathbf{9}_{Zn}$, bypassing the classic [1,2]-Brook rearrangement (i.e., $\mathbf{7}_{Zn} \rightarrow \mathbf{8}_{Zn}$). The novel allenyl-Zn-Brook rearrangement is responsible for the remarkable experimentally observed transfer of chirality (Scheme 8). As allenylzinc species are generally configurationally stable, the highly organized six-membered transition state of the Zn-ene-allene carbocyclization leads to the cyclic product $\mathbf{10}_{Zn}$ with a complete transfer of diastereoselectivity and nearly the same enantiomeric ratio as that of the starting propargylsilanol **7**. It should be noted that the cyclization of $\mathbf{9}_{Zn}$ to $\mathbf{10}_{Zn}$ is an example of an intramolecular enantioselective carbometalation reaction of an unactivated alkene.[42]

Scheme 8. Allenyl-Zn-Brook versus [1,2]-Zn-Brook Rearrangement.



Extension of the Experimental Studies. Having an easy access to enantiomerically enriched zinc-propargylsilanol $\mathbf{7}_{Zn}$ in hand and understanding the stereochemical outcome as well as the mechanistic pathway of the reaction, we could directly prepare **13** (after desilylation) from acylsilane **6** in a single-pot operation through the unique combination of an enantioselective Zn-alkynylation, followed by an allenyl-Zn-Brook rearrangement and Zn-ene-allene cyclization, as described in Scheme 9.[15] To perform this entire sequence, various acylsilanes **6** were added to trimethylsilyl alkynylzinc species, which were easily obtained by mixing Et_2Zn with trimethylsilylacetylene, in the presence of 5 mol % of ProPhenol ligand L_2 in toluene. Once the enantioselective alkynylation reaction was complete, THF was added and the reaction mixture was heated at 45 °C for 24 h. The addition of electrophiles leads to the cyclic siloxane **11**, which was found to be relatively unstable and was then directly oxidized to **12**. Under these conditions, the trimethylsilyl group on the alkyne was partially cleaved and a complete desilylation reaction could be achieved by a basic aqueous treatment of the crude reaction mixture to give the expected acyclic adduct **13** (Scheme 9).[15] In this one-pot process, acylsilanes were, therefore, transformed into enantiomerically enriched propargylic alcohols **13a−i** in high yields as single diastereomers through the creation of three new bonds and two new stereogenic centers (Scheme 9). Except for **6c** forming **13g−i** (R^1 = $(CH_2)_2Ph$), for which the enantiomeric ratios were slightly lower than that for the initial $\mathbf{7}_{Zn}$ precursor (**7c**, *er* 92:8), the enantiomeric ratios of **12a−f** were very similar to that of $\mathbf{7}_{Zn}$, resulting from the enantioselective alkynylation reaction.

The enantioselective construction of quaternary carbon stereocenters through enantioselective catalysis is one of the most difficult targets to reach. This is particularly challenging in acyclic systems

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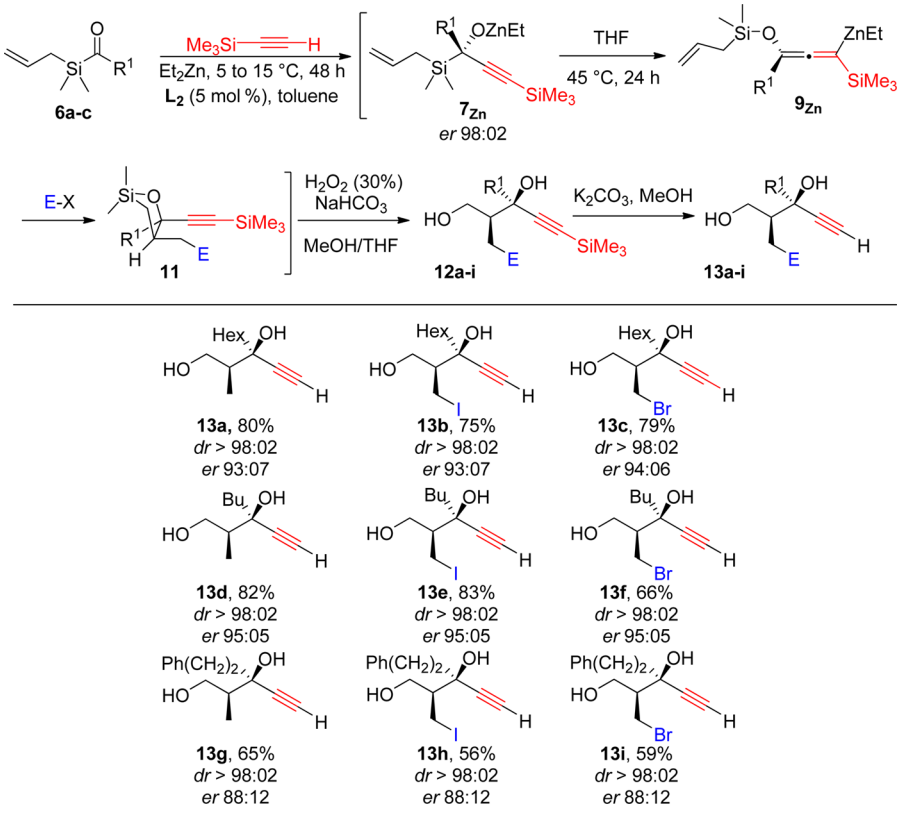
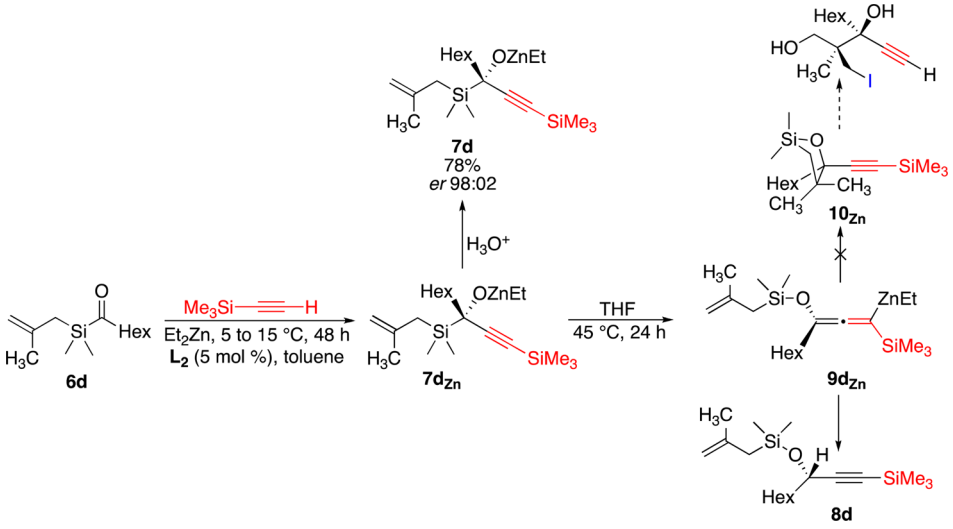
Scheme 9. Combined Zn-Mediated Alkynylation Reaction−Allenyl-Brook Rearrangement−Ene-Allene Cyclization Reaction Sequences



Scheme 10. Attempts to Create Quaternary Carbon Stereocenters



due to the large number of degrees of freedom associated with these structures.[7] The impediment to synthesis presented by such centers arises from the steric congestion imposed by the four attached carbon atoms. Therefore, we were interested to investigate if our one-pot sequence could be successfully used for the formation of this challenging framework. Although propargylsilanol **7d** was easily prepared by the addition of a trimethylsilyl alkynylzinc species to acylsilane **6d**, the addition of THF, followed by heating at 45 °C for a few days, led only to the allenyl-Brook rearrangement product $\mathbf{9d}_{Zn}$ without any traces of the Zn-ene-allene cyclization product $\mathbf{10}_{Zn}$ (Scheme 10), as determined by the unique formation of the propargyl ether product **8d** after hydrolysis (S_E2' reaction of the allenylzinc $\mathbf{9d}_{Zn}$ with H^+). Calculations (details in the Supporting Information) have shown that the barrier for carbocyclization increases by only 1.5 kcal·mol^{-1} for the model compound $\mathbf{7d}_{Zn}$ (with a methyl substituent on C_2, Scheme 10) as compared to the classical case described in Scheme 9, suggesting that the lack of cyclization is not largely due to steric interactions between the two alkyl substituents (Me and Hexyl) in the carbocyclization transition state. The reasons for the fact that **7a−7c** cyclize while **7d** does not remain unexplained.

Finally, we turned our interest to the combined Zn-catalyzed enantioselective alkynylation−allenyl-Brook rearrangement−yne-allene cyclization, as described in Scheme 11. The initial

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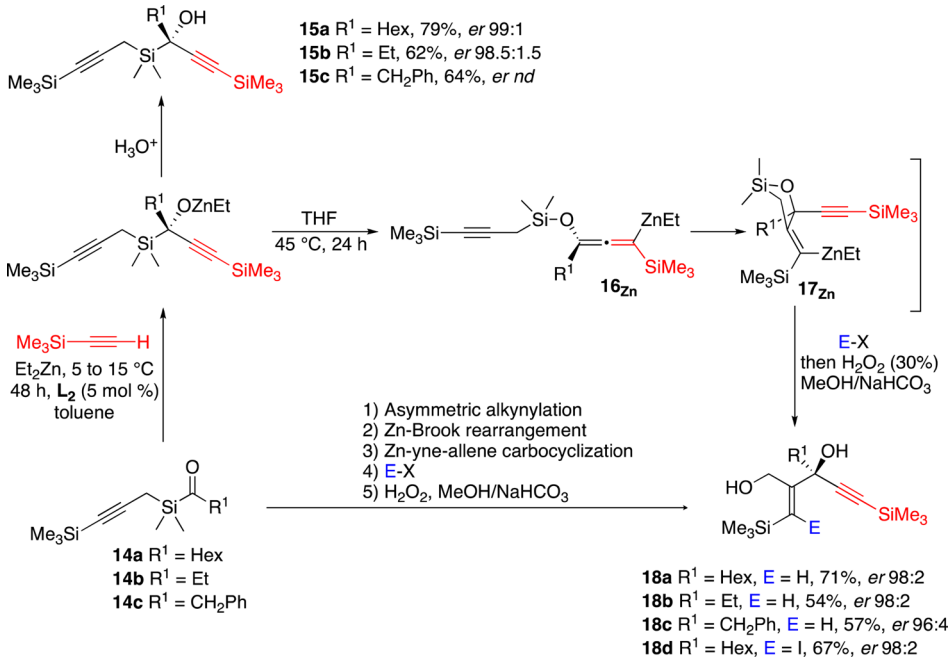
Scheme 11. Combined Zn-Mediated Alkynylation Reaction−Brook Rearrangement−Yne-Allene Cyclization Reaction



Zn-catalyzed enantioselective addition of trimethylsilylacetylene to the new acylsilanes **14a−c** possessing an electrophilic alkynylsilane moiety led to the corresponding propargylsilanol **15a−c** in good yields with excellent enantiomeric ratios (99:1) after acidic hydrolysis (for **15c**, the separation of the two enantiomers by HPLC using a chiral column remained unsatisfactory). By adding THF and heating the reaction mixture at 45 °C for 24 h before the addition of electrophiles, the cyclic products $\mathbf{17_{Zn}}$, resulting from the allenyl-Zn-Brook rearrangement, followed by the Zn-yne-allene carbocyclization, were obtained similarly. After Tamao−Fleming oxidation, the linear propargyl alcohols **18** were obtained as unique geometrical isomers with an almost complete transfer of chirality (Scheme 11).

To our delight, this combined reaction proceeds similarly when the unsaturated electrophiles are an alkyne, and various enyne diols **18a−d** were accessible in high enantiomeric ratios from simple acylsilanes **14a−c**.

CONCLUSION

In summary, we have developed a catalytic enantioselective alkynylation of acylsilanes leading to various α-hydroxypropargyl silanes in high enantiomeric ratios. These substrates can easily be transformed into propargyl alcohols through a combined allenyl-Zn-Brook rearrangement−Zn-ene-allene or Zn-yne-allene cyclization, followed by electrophile addition, all in a single-pot operation, and finally an oxidation reaction. Two remarkable features of these reactions are the almost complete transfer of chirality in the allenyl-Zn-Brook rearrangement and the highly organized six-membered transition state for the Zn-ene-allene carbocyclization. In this process, *three new bonds and two new stereogenic centers are created in a single-pot operation in excellent diastereo- and enantiomeric ratios*. Finally, quantum mechanical calculations revealed an energetic preference of the allenyl-Zn-Brook rearrangement over the classic [1,2]-Brook rearrangement, explaining why the latter reaction does not occur.

EXPERIMENTAL SECTION

Synthesis of Starting Materials. *Synthesis of 1,3-Dithianes.* To a flame-dried three-neck flask equipped with an addition funnel, containing Mg^0 (2.91 g, 120 mmol) and $ZnBr_2$ (2 mol %), a solution of dry Et_2O (120 mL) and 3-bromo-1-(trimethylsilyl)-1-propyne (9.8 mL, 60 mmol) was added dropwise at 0 °C. The reaction was stirred for 4 h at 0 °C and titrated (0.3 M). In a separate flame-dried three-neck flask containing 30 mmol of dithiane **I**, prepared by known methods,[43] in 180 mL of dry THF, 1.6 M *n*BuLi (20.6 mL, 33 mmol) was added at −30 °C. The reaction was stirred for 4 h at −10 °C, before addition at −30 °C of dichlorodimethylsilane (3.98 mL, 33 mmol). After stirring the reaction mixture for 3 h, the freshly prepared Grignard reagent was added, and the reaction was warmed to room temperature and maintained for 18 h. The reaction was quenched with saturated ammonium chloride. The aqueous phase was extracted with ether, and the organic phases were washed with brine, dried over $MgSO_4$, filtered, and evaporated. Separation was performed by silica gel chromatography using Et_2O/hexane (1/90) as eluent to give the following three 1,3-dithianes in good yields.

(2-Hexyl-1,3-dithian-2-yl)dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)silane. Isolated as a yellowish clear oil (8.38 g, 22.5 mmol, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (ddd, J = 14.7, 12.2, 2.9 Hz, 2H), 2.44 (ddd, J = 14.3, 4.6, 3.2 Hz, 2H), 2.18−2.14 (m, 2H), 2.03−2.00 (m, 1H), 1.92−1.85 (m, 1H), 1.85 (s, 2H), 1.48−1.42 (m, 2H), 1.31−1.30 (m, 6H), 0.90−0.87 (m, 3H), 0.29 (s, 6H), 0.11 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 105.2, 84.2, 38.7, 37.7, 31.9, 30.0, 27.8, 25.1, 23.7, 22.8, 14.2, 5.9, 0.4, −4.7. HRMS ($C_{18}H_{36}S_2Si_2$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 373.1875, Found, 373.1887.

(2-Ethyl-1,3-dithian-2-yl)dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)silane. Isolated as a yellowish clear oil (6.93 g, 21.9 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (ddd, J = 14.7, 12.3, 2.9 Hz, 2H), 2.43 (dt, J = 14.2, 4.2 Hz, 2H), 2.25 (q, J = 7.4 Hz, 2H), 2.08−1.96 (m, 1H), 1.93−1.89 (m, 1H), 1.87 (s, 2H), 1.09 (t, J = 7.4 Hz, 3H), 0.31 (s, 6H), 0.13 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 105.2, 84.2, 39.5, 30.2, 25.1, 23.6, 12.5, 5.9, 0.4, −4.7. HRMS ($C_{14}H_{28}S_2Si_2$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 317.1249, Found, 317.1211.

(2-Benzyl-1,3-dithian-2-yl)dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)silane. Isolated as a yellowish oil (10 g, 26.4 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.29−7.24 (m, 3H), 3.41 (s, 2H), 2.63 (ddd, J = 14.7, 12.5, 2.9 Hz, 2H), 2.39−2.30 (m, 2H), 1.94−1.84 (m, 1H), 1.77−1.70 (m, 1H), 1.75 (s, 2H), 0.18 (s, 6H), 0.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 131.2, 128.1, 127.1, 105.4,

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84.2, 45.2, 37.6, 24.3, 5.5, 0.4, −5.5. HRMS ($C_{19}H_{30}S_2Si_2$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 379.1406, Found, 379.146.

To a flame-dried three-neck flask equipped with an addition funnel, containing Mg^0 (4.9 g, 200 mmol), a solution of dry THF (200 mL) and 3-chloro-2-methyl-1-propene (9.72 mL, 100 mmol) was added dropwise at rt. The reaction was stirred for 5 h at rt. In a separate flame-dried three-neck flask containing (6.65 g, 32 mmol) of dithiane in 250 mL of dry THF, 1.6 M *n*BuLi (21.25 mL, 34 mmol) was added at −30 °C. The reaction was stirred for 4 h at −10 °C, before addition at −30 °C of dichlorodimethylsilane (4.6 mL, 38.5 mmol). After stirring the reaction mixture for 4 h at 0 °C, the freshly prepared Grignard reagent was added, and the reaction was warmed to room temperature and maintained for 16 h. The reaction was quenched with saturated ammonium chloride. The aqueous phase was extracted with ether, and the organic phases were washed with brine, dried over $MgSO_4$, filtered, and evaporated. Separation was performed by silica gel chromatography using Et_2O/hexane (1/90) as eluent to give the adduct below in a moderate yield.

(2-Hexyl-1,3-dithian-2-yl)dimethyl(2-methylallyl)silane. Isolated as a yellowish clear oil (6.69 g, 21.1 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (s, 1H), 4.54 (s, 1H), 3.04 (ddd, J = 14.6, 12.5, 2.8 Hz, 2H), 2.44 (dt, J = 14.2, 3.9 Hz, 2H), 2.24−2.14 (m, 2H), 2.10−2.00 (m, 1H), 1.97−1.82 (m, 1H), 1.80 (s, 2H), 1.73 (s, 3H), 1.53−1.44 (m, 2H), 1.38−1.27 (m, 6H), 0.93−0.87 (m, 3H), 0.21 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 109.7, 39.1, 37.7, 31.9, 30.1, 27.9, 25.5, 25.3, 24.7, 23.6, 22.8, 14.2,-4.0. HRMS ($C_{16}H_{32}S_2Si$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 317.1793, Found, 317.1761.

Synthesis of Acylsilanes (6d, 14a, 14b, 14c). A flask containing dithiane (20 mmol), 40 mL of methanol, and 13 mL of H_2O was cooled to −5 °C. Then, chloramine-T (13.6 g, 60 mmol) was added in small portions. The solution was stirred for 1 h. Then, the solution was poured into a separatory funnel containing pentane and extracted with pentane five times; the organic phases were washed with brine, dried over Na_2SO_4, and concentrated under vacuum. The product was purified by silica gel chromatography using EtOAc/hexane as eluent to give the desired acylsilanes in moderate yields.

*1-(Dimethyl(2-methylallyl)silyl)heptan-1-one (**6d**).* Isolated as a yellowish clear oil (2.21 g, 9.8 mmol, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 (s, 1H), 4.49 (s, 1H), 2.57 (t, J = 7.3 Hz, 2H), 1.70 (s, 2H), 1.67 (s, 3H), 1.54−1.47 (m, 2H), 1.28−1.19 (m, 6H), 0.86 (t, J = 6.7 Hz, 3H), 0.21 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 247.74, 142.2, 109.8, 49.3, 31.8, 29.2, 25.2, 22.7, 22.2, 14.2, −4.3. HRMS ($C_{13}H_{26}OSi$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 227.1831, Found, 227.1859.

*1-(Dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)silyl)heptan-1-one (**14a**).* Isolated as a yellowish clear oil (3.56 g, 12.6 mmol, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (t, J = 7.3 Hz, 2H), 1.74 (s, 2H), 1.35−1.50 (m, 2H), 1.31−1.25 (m, 6H), 0.88−0.85 (m, 3H), 0.29 (s, 6H), 0.12 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 245.9, 103.6, 84.8, 49.6, 31.8, 29.1, 22.6, 22.1, 14.2, 6.1, 0.3, −5.1. HRMS ($C_{15}H_{30}OSi_2$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 283.1913, Found, 283.1942.

*1-(Dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)silyl)propan-1-one (**14b**).* Isolated as a yellowish oil (2.99 g, 13.2 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 (t, J = 7.2 Hz, 2H), 1.75 (s, 2H), 0.99 (t, J = 7.2 Hz, 3H), 0.30 (s, 6H), 0.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 245.6, 103.5, 84.8, 42.6, 6.1, 6.1, 0.3, −5.1. HRMS ($C_{11}H_{22}OSi_2$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 227.1287, Found, 227.1284.

*1-(Dimethyl(3-(trimethylsilyl)prop-2-yn-1-yl)silyl)-2-phenylethanone (**14c**).* Isolated as a yellowish oil (2.77 g, 9.6 mmol, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.30 (m, 2H), 7.27−7.23 (m, 1H), 7.14−7.12 (m, 2H), 3.91 (s, 2H), 1.64 (s, 2H), 0.19 (s, 6H), 0.13 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 241.7, 132.9, 130.1, 128.8, 127.2, 103.5, 85.0, 56.3, 6.3, 0.3, −4.8. HRMS ($C_{16}H_{24}OSi_2$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 289.1444, Found, 289.1417.

General Procedure for the Preparation of Racemic Propargylsilanols 7 and 15. To a flame-dried three-neck flask containing trimethylsilylacetylene (0.83 mL, 6 mmol) in toluene (4 mL) was added 1.0 M diethylzinc (6 mL, 6 mmol) at room temperature. The reaction was stirred at room temperature for 1 h before acylsilane **6** or **14** (3 mmol) dissolved in toluene (5 mL) was added dropwise. The mixture was stirred for an additional 48 h at <15 °C and then quenched with a saturated ammonium chloride solution. The aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and evaporated. The products were separated by silica gel chromatography using ethyl acetate/hexane as an eluent.

General Procedure for the Preparation of Enantioenriched Propargylsilanols 7 and 15.[15] To a flame-dried three-neck flask containing trimethylsilylacetylene (0.17 mL, 1.2 mmol) in toluene (2 mL), 1.0 M diethylzinc (2.4 mL, 2.4 mmol) was added at room temperature. The mixture was stirred at room temperature for 1 h, and then 0.032 g (0.05 mmol) of (*R*,*R*)-L_2 dissolved in toluene (2 mL) was added. After an additional hour, the reaction was cooled to 0 °C and acylsilane **6** or **14** (1 mmol) dissolved in toluene (3 mL) was added dropwise to the reaction mixture. Stirring was continued for 48 h while the temperature was maintained below 15 °C. The reaction was quenched with a saturated ammonium chloride solution. The aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The products were separated by silica gel chromatography using ethyl acetate/hexane as an eluent, and the enantiomeric ratio was determined by high-performance liquid chromatography (HPLC).

Compounds **7a**−**c** have previously been reported.[15]

*(S)-1-Trimethylsilyl-3-(dimethyl(2-methylallyl)silyl)-1-nonyne-3-ol (**7d**).* Isolated as a clear colorless oil (0.75 g, 2.34 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (s, 1H), 4.59 (s, 1H), 1.80−1.61 (m, 4H), 1.75 (s, 3H), 1.58−1.54 (m, 3H), 1.36−1.28 (m, 6H), 0.89−0.87 (m, 3H), 0.16 (s, 12H), 0.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 109.4, 108.9, 92.3, 65.7, 37.4, 31.93, 29.7, 25.4, 24.5, 23.6, 22.8, 14.2, 0.2, −5.3, −5.6. HRMS ($C_{18}H_{36}OSi_2$, ESI$^+$, $[M + Na]^+$) m/z: Calculated, 347.2202, Found, 347.2200.

*(S)-1-Trimethylsilyl-3-((trimethylsilyl)prop-2-yn-1-yl)dimethylsilyl-1-nonyne-3-ol (**15a**).* Isolated as a clear colorless oil (0.3 g, 0.79 mmol, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (s, 1H), 1.79 (d, J = 16.6 Hz, 1H), 1.69 (d, J = 16.6 Hz, 1H), 1.65−1.52 (m, 4H), 1.29−1.24 (m, 6H), 0.90−0.85 (m, 3H), 0.22 (s, 3H), 0.21 (s, 3H), 0.14 (s, 9H), 0.12 (s, 9H). ^{13}C NMR (100 MHz, CDCl3) δ 108.1, 105.4, 92.5, 84.3, 65.5, 37.5, 31.9, 29.7, 23.7, 22.8, 14.2, 5.0, 0.3, 0.2, −6.0, −6.3. HRMS ($C_{20}H_{40}OSi_3$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 381.2465, Found, 381.2477. *er* = 1:99. Enantiomeric ratio was measured by chiral HPLC (Chiralpak IA, 1:99 IPA/heptane, flow of 0.3 mL/min, Rt1 = 14.91, Rt2 = 15.73 min).

*(S)-1-Trimethylsilyl-3-((trimethylsilyl)prop-2-yn-1-yl)dimethylsilyl-1-pentyne-3-ol (**15b**).* Isolated as a clear colorless oil (0.2 g, 0.62 mmol, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 1H), 1.81 (d, J = 16.6 Hz, 1H), 1.69 (d, J = 16.6 Hz, 1H), 1.77−1.63 (m, 2H), 1.07 (t, J = 7.3 Hz, 3H), 0.24 (s, 3H), 0.23 (s, 3H), 0.15 (s, 9H), 0.13 (s, 9H). ^{13}C NMR (100 MHz, CDCl3) δ 107.7, 105.4, 92.5, 84.4, 65.9, 30.5, 8.1, 5.0, 0.3, 0.2, −6.0, −6.3. HRMS ($C_{16}H_{32}OSi_3$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 325.1838, Found, 325.1858. *er* = 1:99. Enantiomeric ratio was measured by chiral HPLC (Chiralpak IA, 1:99 IPA/hexane, flow of 0.3 mL/min, Rt1 = 16.10, Rt2 = 16.62 min).

*(S)-1-Trimethylsilyl-3-((trimethylsilyl)prop-2-yn-1-yl)dimethylsilyl-3-benzyl-1-propyne-3-ol (**15c**).* Isolated as a clear colorless oil (0.24 g, 0.64 mmol, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.27 (m, 5H), 2.98 (d, J = 13.3 Hz, 1H), 2.92 (d, J = 13.3 Hz, 1H), 1.84 (d, J = 16.6 Hz, 1H), 1.80 (s, 1H), 1.77 (d, J = 16.6 Hz, 1H), 0.29 (s, 6H), 0.14 (s, 18H). ^{13}C NMR (100 MHz, CDCl3) δ 135.8, 130.9, 128.1, 127.1, 107.7, 105.2, 93.6, 84.3, 64.7, 43.4, 4.9, 0.4, 0.0−6.2, −6.4. HRMS ($C_{21}H_{34}OSi_3$, ESI$^+$, $[M + H]^+$) m/z: Calculated, 387.1996, Found, 387.1997. Enantiomeric ratio could not be determined by using the available HPLC methods.

General Procedure for the Preparation of Oxasilacyclopentanes (11) from Propargylsilanols (7). To a flame-dried three-neck flask containing propargylsilanol **7** (1 mmol) in THF (3 mL), 1.0 M diethylzinc (1.8 mL, 1.8 mmol) was added at room temperature. The mixture was stirred at room temperature for 30 min and then warmed to 45 °C. After 24 h, the reaction mixture was cooled down to room temperature and quenched with saturated ammonium chloride solution. The aqueous phase was extracted with diethyl ether, and the

combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and evaporated. The oxasilacyclopentanes could not be purified by column chromatography on silica gel and characterized. The crude products were directly subjected to the Tamao−Fleming oxidation reaction.

The general procedure for the preparation of oxasilacyclopentanes **11a**, **11d**, and **11g** from acylsilanes has previously been reported.[15] Compounds **17a−c** were prepared by analogy.

The general procedure for the preparation of oxasilacyclopentanes **11b**,**e**,**f**, followed by treatment with iodine, has previously been reported.[15] Compound **17d** was prepared by analogy using **14a** as starting material.

The general procedure for the preparation of oxasilacyclopentanes **11c**,**f**,**i**, followed by treatment with bromine, has previously been reported.[15]

The general procedure for the Tamao−Fleming oxidation of oxasilacyclopentanes **11** providing **12** has previously been reported.[15] Compounds **18** were prepared from **17** by analogy.

Compounds **12a−i** have previously been reported.[15]

*(R,E)-3-[(Trimethylsilyl)ethynyl]-2-[(trimethylsilyl)methylene]-nonane-1,3-diol (**18a**).* Isolated as a clear colorless oil (0.24 g, 0.71 mmol, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (s, 1H), 4.31 (d, J = 4 Hz, 2H), 2.66 (s, 1H), 2.36 (t, J = 6 Hz, 1H), 1.79−1.75 (m, 2H), 1.47−1.38 (m, 2H), 1.37−1.25 (m, 6H), 0.89−0.87 (m, 3H), 0.18 (s, 9H), 0.17 (s, 9H). ^{13}C NMR (100 MHz, CDCl3) δ 155.9, 130.3, 108.0, 91.1, 76.1, 62.4, 41.8, 31.8, 29.3, 24.6, 22.7, 14.2, 0.3, 0.0. HRMS ($C_{18}H_{36}O_2Si_2$, ESI$^+$, [M]$^+$) m/z: Calculated, 340.2254, Found, 340.2259. *er* = 98:2. Enantiomeric ratio was measured by HPLC using a chiral column (Chiralcel OD, 2:98 IPA/hexane, flow of 0.3 mL/min, Rt1 = 15.40, Rt2 = 16.29 min).

*(R,E)-3-[(Trimethylsilyl)ethynyl]-2-((trimethylsilyl)methylene)-pentane-1,3-diol (**18b**).* Isolated as a clear colorless oil (0.15 g, 0.54 mmol, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (s, 1H), 4.30−4.28 (m, 2H), 2.70 (s, 1H), 2.37 (t, J = 5.8 Hz, 1H), 1.81 (q, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H), 0.17 (s, 9H), 0.16 (s, 9H). ^{13}C NMR (100 MHz, CDCl3) δ 155.4, 130.6, 107.6, 91.2, 76.7, 62.3, 34.8, 9.0, 0.3, 0.0. HRMS ($C_{14}H_{28}O_2Si_2$, ESI$^+$, [M]$^+$) m/z: Calculated, 284.1628, Found, 284.1646. *er* = 98:2. Enantiomeric ratio was measured by HPLC using a chiral column (Chiralcel OD, 2:98 IPA/hexane, flow of 0.3 mL/min, Rt1 = 19.91, Rt2 = 21.07 min).

*(R,E)-3-Benzyl-5-(trimethylsilyl)-2-[(trimethylsilyl)methylene]-pent-4-yne-1,3-diol (**18c**).* Isolated as a clear colorless oil (0.19 g, 0.57 mmol, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 5H), 6.02 (s, 1H), 4.31−4.30 (m, 2H), 3.06 (s, 2H), 2.59 (s, 1H), 2.36 (t, J = 6.2 Hz, 1H), 0.17 (s, 9H), 0.16 (s, 9H). ^{13}C NMR (100 MHz, CDCl3) δ 155.5, 135.7, 131.2, 130.9, 128.0, 127.2, 107.4, 92.3, 75.7, 62.5, 48.8, 0.3, −0.2. HRMS ($C_{19}H_{30}O_2Si_2$, ESI$^+$, [M]$^+$) m/z: Calculated, 346.1784, Found, 346.1765. *er* = 96:4. Enantiomeric ratio was measured by HPLC using a chiral column (Chiralpak IA, 2:98 IPA/hexane, flow of 0.3 mL/min, Rt1 = 33.81, Rt2 = 35.38 min).

*(S,Z)-2-(Iodomethylene)-3-((trimethylsilyl)ethynyl)nonane-1,3-diol (**18d**).* Isolated as a clear colorless oil (0.26 g, 0.67 mmol, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62 (s, 1H), 4.30−4.22 (m, 2H), 3.09 (s, 1H), 2.75 (s, 1H), 2.05−1.97 (m, 2H), 1.58−1.49 (m, 1H), 1.46−1.38 (m, 1H), 1.36−1.23 (m, 6H), 0.90−0.87 (m, 3H), 0.19 (s, 9H). ^{13}C NMR (100 MHz, CDCl3) δ 150.7, 105.1, 91.7, 77.9, 73.9, 67.6, 40.5, 31.8, 29.2, 23.6, 22.7, 14.2, −0.1. HRMS ($C_{15}H_{27}IO_2Si$, ESI$^+$, [M + Na]$^+$) m/z: Calculated, 417.0723, Found, 417.0744.

The general procedures for the cleavage of the silyl group of **12** and compounds **13a−i** have previously been reported.[15]

■ ASSOCIATED CONTENT

Supporting Information

Cartesian coordinates as well as total energies in the gas phase and in THF calculated by using the PBE0 and B3LYP functional are provided for all stationary points located on the PESs of the model [1,2]-Brook rearrangement (M = Li, Zn) and copies of all new NMR and HPLC spectra. This material is available free of charge via the Internet at http://pubs.acs.org. See additional computational details on the stationary points located on the PES shown in Figure 3 in the Supporting Material of ref 15.

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Notes

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■ DEDICATION

Dedicated to Professor Armin de Meijere on the occasion of his 75th birthday.

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