Chiral Silanes

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Catalytic Enantioselective Synthesis of Alkenylhydrosilanes**

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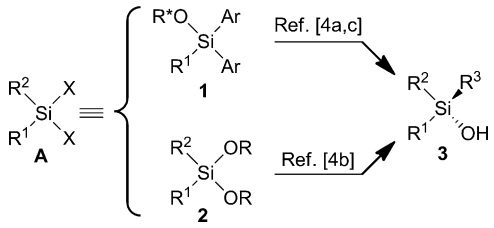
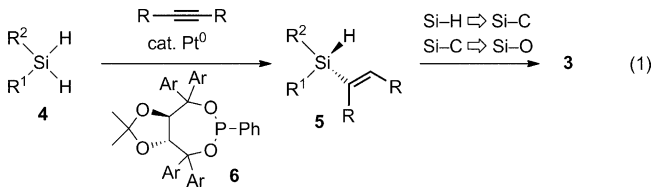
Nonracemic silanes possessing a silicon stereocenter have structural similarity to their carbon congeners, but show substantial differences in their physical and electronic properties. Therefore, nonracemic silanes have attracted attention in the fields of synthetic,[1] material,[2] and bioorganic chemistry.[3] Despite their potential importance, nonracemic silanes are unavailable in nature, and therefore the development of an efficient asymmetric method for their preparation is eagerly awaited.[1] Among the several possible methods for the asymmetric synthesis of chiral silanes, desymmetrization of achiral silanes **A** would be the most rational approach (Scheme 1). Previously, we had developed asymmetric synthetic approaches to chiral silanols **3** from diarylsilanes **1** (X = Ar) and dialkoxysilanes **2** (X = OR) through diastereoselective and enantioselective desymmetrization, respectively.[4] Furthermore, we have demonstrated the synthetic versatility of **3** as a chiral building block for a variety of functionalized nonracemic silanes.[5] However, these approaches require stoichiometric to sub-stoichiometric chiral sources, along with an excess of reagents. Thus, the development of a more efficient catalytic approach to chiral silanes is highly desirable.

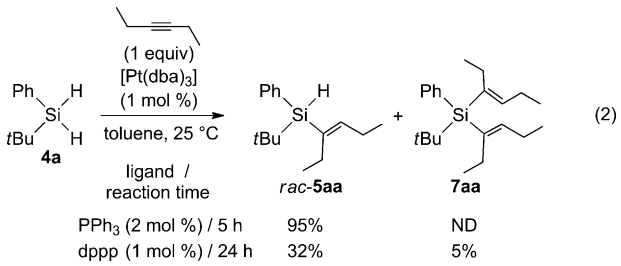


Scheme 1. Our previous approaches to nonracemic silanols.

To this end, we recently examined the asymmetric synthesis of alkenylhydrosilane **5** from dihydrosilane **4** (a variant of **A**, where X = H) by desymmetric hydrosilylation with an alkyne [Eq. (1)].[6–8] As a result, we found that the reaction catalyzed by the complex of phosphonite **6**, which is derived from tetraaryl-1,3-dioxolane-4,5-dimethanol (taddol) and Pt^0, realizes this desymmetrization.[9–13] This new approach allows for the catalytic synthesis of chiral alkenylhydrosilanes **5** in an enantioselective fashion with high atom efficiency. Furthermore, we have achieved the transformation of alkenylhydrosilane **5** into functional chiral silanes such as silanol **3** in enantioenriched form, through the stereoselective conversion of the hydride and/or alkenyl moieties of **5**. Herein, we provide the details of our novel approach and the synthetic value of the resulting chiral silanes.



We started our investigations with the readily available Ph*t*BuSiH$_2$ (**4a**) and 3-hexyne as substrates. In this approach, there is concern about the possible overreaction of **5aa** to afford dialkenylsilane **7aa** [Eq. (2); dba = dibenzylideneacetone, dppp = bis(diphenylphosphino)propane, ND = not detected]. To know whether proper choice of the ligand can prevent this overreaction, we performed an achiral version of the reaction using a catalytic amount of [Pt(dba)$_3$] with PPh$_3$ or dppp as a representative monodentate or bidentate ligand,



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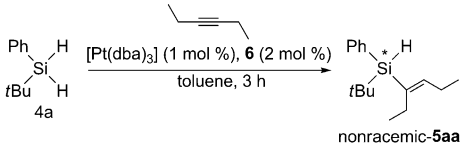
respectively.[14] These reactions showed a sharp contrast: the reaction using PPh_3 afforded the desired **5aa** in excellent yield (95%) in 5 h at 25°C, but the one with dppp afforded **5aa** in low yield (32%) along with the dialkenylsilane **7aa** (5%) and recovered **4a** (48%) after 24 h at the same temperature.

On the basis of these results, we surveyed a number of monodentate chiral phosphorus ligands and found that taddol-derived phosphonites **6** are the ligands of choice. The reaction with $[Pt(dba)_3]$ (1 mol%) and phosphonite **6a** (2 mol%; Ar = Ph) gave **5aa** in 74% yield, in an enantioenriched form (37% *ee*, (−); Table 1, entry 1).[15,16] The absolute stereochemistry of (−)-**5aa** was determined to be the *S* configuration by transforming it into a stereochemically

Table 1: Enantioselective hydrosilylation of dihydrosilane **4a**.[a]



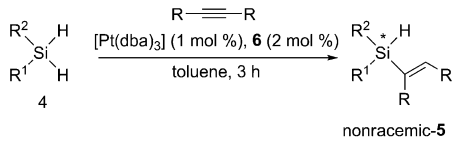
Entry		6[b] Ar	T [°C]	5aa Yield [%]	ee [%][c,d]
1	**6a**	Ph	25	74[e]	37 (−)(*S*)
2	**6b**	4-$MeOC_6H_4$	25	69[e]	50 (−)(*S*)
3	**6c**	3,5-$Me_2C_6H_3$	25	83[e]	45 (+)(*R*)
4	**6d**	3,5-$(CF_3)_2C_6H_3$	25	96[f]	54 (+)(*R*)
5[g]	**6b**	4-$MeOC_6H_4$	0	72[f] (84)[h]	64 (−)(*S*)
6[i]	**6b**	4-$MeOC_6H_4$	−30	47[f] (81)[h]	82 (−)(*S*)

[a] Unless otherwise noted, the reaction was performed with 3-hexyne (1 equiv), $[Pt(dba)_3]$ (1 mol%), and **6** (2 mol%) in toluene at 25°C for 3 h. [b] Prepared from the corresponding (*R*,*R*)-taddol and $PhPCl_2$. [c] Determined by HPLC analysis using a chiral stationary phase. [d] Sign of $[\alpha]_D$ and absolute stereochemistry. [e] Yield of isolated product. [f] Determined by GLC analysis using *n*-tetradecane as an internal standard. [g] The reaction was run for 24 h. [h] Yields based on recovered **4a**. [i] The reaction was run for 7 days.

defined chiral silane (see below). The enantioselectivity was significantly improved to 50% *ee* by the use of **6b** (Ar = 4-$MeOC_6H_4$) as the ligand (entry 2). Furthermore, ligand **6**, which bears a 3,5-disubstituted phenyl moiety, provided the opposite stereoselectivities: the reactions with **6c** (Ar = 3,5-$Me_2C_6H_3$) and **6d** (Ar = 3,5-$(CF_3)_2C_6H_3$) afforded (*R*)-**5aa** in 45% *ee* and 54% *ee*, respectively (entries 3 and 4). After optimization of the reaction conditions, we found that the reactions with **6b** at low temperatures afford high enantioselectivities: 64% *ee* at 0°C and 82% *ee* at −30°C (entries 5 and 6), although the reactions are slow. These results are the first examples of the enantioselective synthesis of an alkenylhydrosilane.

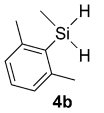
This enantioselective hydrosilylation has a broad substrate scope. The reactions of **4a** with 2-butyne and 4-octyne also afforded nonracemic silanes with moderate to good enantioselectivities: (*S*)-**5ab**, 43% *ee* at 25°C and 72% *ee* at −30°C; (*S*)-**5ac**, 46% *ee* at 25°C, and 78% *ee* at −30°C (Table 2, entries 1–4).[17] Again, a switch in selectivity was observed when the ligand was changed from phosphonite **6b** to **6d** (entries 5 and 6). Furthermore, the reaction was

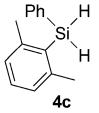
Table 2: Scope and limitation of the asymmetric hydrosilylation of dihydrosilane **4**.[a]



Entry	4	Alkyne R	6[b]	T [°C]	5	Yield [%]	ee [%][c,d]
1	**4a**	Me	**6b**	25	**5ab**	63[e]	43 (+)(*S*)
2[f]	**4a**	Me	**6b**	−30	**5ab**	56[e] (72)[g]	72 (+)(*S*)
3	**4a**	*n*Pr	**6b**	25	**5ac**	82[e]	46 (−)(*S*)
4[f]	**4a**	*n*Pr	**6b**	−30	**5ac**	21[e] (57)[g]	78 (−)(*S*)
5	**4a**	Me	**6d**	25	**5ab**	90[e]	30 (−)(*R*)
6	**4a**	*n*Pr	**6d**	25	**5ac**	78[e]	46 (+)(*R*)
7	**4b**	Et	**6d**	25	**5b**	95[h]	60 (+)
8[i]	**4b**	Et	**6d**	0	**5b**	88[h]	68 (+)
9[j]	**4c**	Et	**6b**	25	**5c**	83[k]	67 (−)
10[f]	**4c**	Et	**6b**	−30	**5c**	28[k] (58)[g]	86 (−)

[a] Unless otherwise noted, the reaction was performed with alkyne (1 equiv), $[Pt(dba)_3]$ (1 mol%), and **6** (2 mol%) in toluene at 25°C for 3 h. [b] Prepared from corresponding (*R*,*R*)-taddol and $PhPCl_2$. [c] Determined by HPLC analysis using a chiral stationary phase. [d] Sign of $[\alpha]_D$ and absolute stereochemistry. [e] Determined by ^1H NMR analysis using anisole as an internal standard. [f] The reaction was run for 7 days. [g] Yields based on recovered **4**. [h] Determined by GLC analysis using *n*-tetradecane as an internal standard. [i] The reaction was run for 24 h. [j] The reaction was run for 2 days. [k] Yield of isolated product.

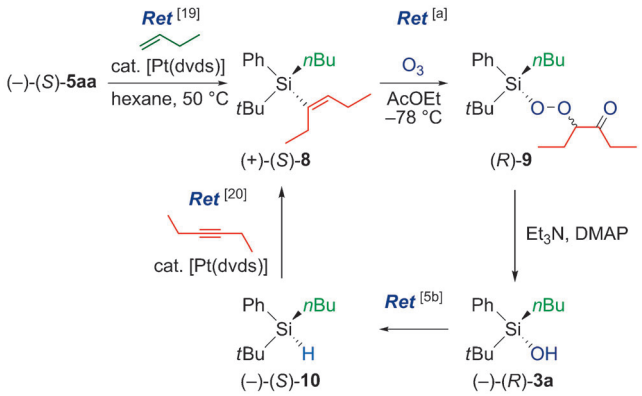




applicable to the hydrosilylation of substrates **4b** (R^1 = 2,6-$Me_2C_6H_3$, R^2 = Me) and **4c** (R^1 = 2,6-$Me_2C_6H_3$, R^2 = Ph) as well (entries 7–10).[18] In particular, the reaction of **4c** with 3-hexyne in the presence of **6b** afforded excellent enantioselectivities: 67% *ee* at 25°C and 86% *ee* at −30°C (entries 9 and 10).

The nonracemic hydrosilanes **5** can be converted into a variety of optically active silanes through transformation of the hydride and/or alkene moieties. Regarding the conversion of the hydride moiety, we successfully converted the Si–H bond into a Si–C bond in nonracemic alkenylhydrosilane (−)-**5aa** (53% *ee*) and obtained alkenylsilane (+)-**8** by the [Pt(dvds)]-catalyzed (dvds = 1,1,3,3,-tetramethyl-1,3-divinyldisiloxane) hydrosilylation with 1-butene, without loss of enantiopurity (Scheme 2, 69% yield, 53% *ee*).

The absolute stereochemistry of (−)-**5aa** and (+)-**8** was adequately determined by comparison with the separately synthesized authentic sample, as follows. Initially, we prepared stereochemically defined hydrosilane (*S*)-**10** (59% *ee*) from enantioenriched silanol (*R*)-**3a** by our previously reported procedure.[5b] Pt-catalyzed hydrosilylation of (*S*)-**10** and 3-hexyne gave (+)-**8** in 59% *ee*. Compound (+)-**8** was determined to have an *S* configuration based on the retention of stereochemistry at silicon in the Pt-catalyzed hydrosilylation of nonracemic hydrosilanes with alkenes[19] and alkynes[20] that has been reported by the groups of Sommer and Brook, respectively. Hence, it was revealed that (−)-**5aa** has an *S* configuration.



Scheme 2. Transformation and determination of absolute stereochemistry of alkenylhydrosilane **5aa**. [a] This work. DMAP = 4-(dimethyamino)pyridine, dvds = 1,1,3,3,-tetramethyl-1,3-divinyldisiloxane, Ret = retention of configuration.

Furthermore, we have succeeded in the stereoselective conversion of the alkenyl group in a nonracemic alkenylsilane into an OH group by our previously reported ozone oxidation method.[21] The reaction of alkenylsilane (*S*)-**8** (53% *ee*) with ozone afforded peroxysilane (*R*)-**9** as a diastereomeric mixture, which was then converted into nonracemic silanol (*R*)-**3a** through base-mediated β-elimination, although the enantiopurity was slightly decreased (**3a**; 88% yield over 2 steps, 44% *ee*). From this stereochemical outcome, it was revealed that the Si–C to Si–O transformation by ozone oxidation proceeds predominantly with retention of configuration at the silicon stereocenter. Thus, alkenylhydrosilanes **5** are versatile chiral building blocks for a variety of functionalized nonracemic silanes through stereoselective conversion of the hydride and alkenyl moieties into alkyl or oxy functional groups by Pt^0-catalyzed hydrosilylation or ozone oxidation, respectively.

In summary, we have developed a catalytic desymmetrization of dihydrosilanes based on Pt^0-catalyzed hydrosilylation with taddol-derived phosphonite ligands. This method affords a multifunctionalized nonracemic alkenylhydrosilane, which is a synthetically valuable sila-chiral building block. Further studies toward expanding the present asymmetric method to other functionalized silanes and investigation of their applications are in progress.

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[15] For the results of a similar reaction using other monodentate and bidentate chiral phosphorous ligands, see the Supporting Information.
[16] The catalytic system of $[Pt(dba)_3]$ and phosphonite **6** in a 1:2 molar ratio afforded the highest enantioselectivities in our attempts.
[17] The absolute stereochemistry of **5ab** and **5ac** were determined by a method similar to that described in Scheme 2 for **5aa**, see the Supporting Information for more information.
[18] The absolute stereochemistry of **5b** and **5c** has not yet been determined. Attempts to derivatize these nonracemic alkenylhydrosilanes into crystalline compounds or stereochemically defined authentic samples are in progress.
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