

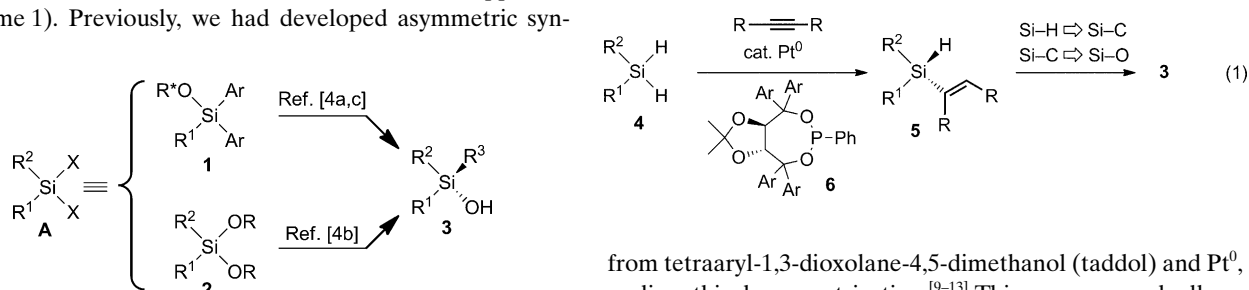
Catalytic Enantioselective Synthesis of Alkenylhydrosilanes**

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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 syn-

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.

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

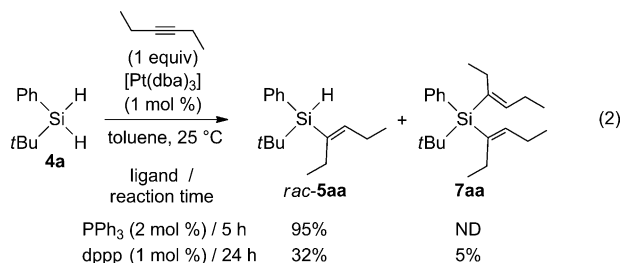


Scheme 1. Our previous approaches to nonracemic silanols.

thetic 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

from tetraaryl-1,3-dioxolane-4,5-dimethanol (taddol) and Pt⁰, 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 Ph₂BuSiH₂ (**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 PPh₃ 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 $[\text{Pt}(\text{dba})_3]$ (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	<i>T</i> [°C]	5aa	
				Yield [%]	ee [%] ^[c,d]
1	6a	Ph	25	74 ^[e]	37 (–) (<i>S</i>)
2	6b	4-MeOC ₆ H ₄	25	69 ^[e]	50 (–) (<i>S</i>)
3	6c	3,5-Me ₂ C ₆ H ₃	25	83 ^[e]	45 (+) (<i>R</i>)
4	6d	3,5-(CF ₃) ₂ C ₆ H ₃	25	96 ^[f]	54 (+) (<i>R</i>)
5 ^[g]	6b	4-MeOC ₆ H ₄	0	72 ^[f] (84) ^[h]	64 (–) (<i>S</i>)
6 ^[j]	6b	4-MeOC ₆ H ₄	–30	47 ^[f] (81) ^[h]	82 (–) (<i>S</i>)

[a] Unless otherwise noted, the reaction was performed with 3-hexyne (1 equiv), $[\text{Pt}(\text{dba})_3]$ (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**. [j] 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-MeOC₆H₄) 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-Me₂C₆H₃) and **6d** (Ar = 3,5-(CF₃)₂C₆H₃) 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

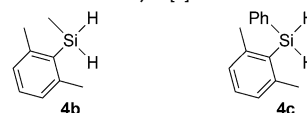
Table 2: Scope and limitation of the asymmetric hydrosilylation of dihydrosilane **4**.^[a]

4

nonracemic-5

Entry	4	Alkyne R	6 ^[b]	<i>T</i> [°C]		5 Yield [%]	<i>ee</i> [%] ^[c,d]
1	4a	Me	6b	25	5ab	63 ^[e]	43 (+) (<i>S</i>)
2 ^[f]	4a	Me	6b	−30	5ab	56 ^[e] (72) ^[g]	72 (+) (<i>S</i>)
3	4a	<i>n</i> Pr	6b	25	5ac	82 ^[e]	46 (−) (<i>S</i>)
4 ^[f]	4a	<i>n</i> Pr	6b	−30	5ac	21 ^[e] (57) ^[g]	78 (−) (<i>S</i>)
5	4a	Me	6d	25	5ab	90 ^[e]	30 (−) (<i>R</i>)
6	4a	<i>n</i> Pr	6d	25	5ac	78 ^[e]	46 (+) (<i>R</i>)
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 (−)

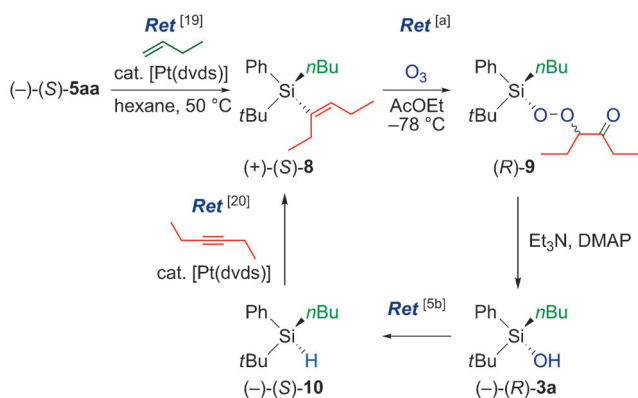
[a] Unless otherwise noted, the reaction was performed with alkyne (1 equiv), $[\text{Pt}(\text{dba})_3]$ (1 mol%), and **6** (2 mol%) in toluene at 25°C for 3 h. [b] Prepared from corresponding (*R,R*)-taddol and PhPCl_2 . [c] Determined by HPLC analysis using a chiral stationary phase. [d] Sign of $[\alpha]_D$ 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** ($\text{R}^1 = 2,6\text{-Me}_2\text{C}_6\text{H}_3$, $\text{R}^2 = \text{Me}$) and **4c** ($\text{R}^1 = 2,6\text{-Me}_2\text{C}_6\text{H}_3$, $\text{R}^2 = \text{Ph}$) 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 $[\text{Pt}(\text{dvds})]$ -catalyzed (dvds = 1,1,3,3-tetramethyl-1,3-divinyl-disiloxane) 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-(dimethylamino)pyridine, dvds = 1,1,3,3,3-tetramethyl-1,3-divinylidisiloxane, 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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