

## Author Manuscript

**Title:** Iridium-Catalyzed Enantioselective Hydrogenation of Vinylsilanes

**Authors:** Andreas Pfaltz; Ai-E Wang; Maurizio Bernasconi

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record.

**To be cited as:** 10.1002/adsc.201700162

**Link to VoR:** <https://doi.org/10.1002/adsc.201700162>

# Iridium-Catalyzed Enantioselective Hydrogenation of Vinylsilanes

Aie Wang,<sup>a,b,†</sup> Maurizio Bernasconi<sup>b,†</sup> and Andreas Pfaltz<sup>b,\*</sup>

<sup>a</sup> Department of Chemistry, Fujian Provincial Key Laboratory of Chemical Biology, College of Chemistry, Xiamen University, Xiamen, Fujian 361005, P. R. China.

<sup>b</sup> Department of Chemistry, University of Basel, St. Johannis-Ring 19, CH-4056 Basel, Switzerland.  
Fax: (+41) 61- 267-1103; E-mail: andreas.pfaltz@unibas.ch.

<sup>†</sup> These authors contributed equally to this work.

Received: ((will be filled in by the editorial staff))



Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/adsc.201#####>.

**Abstract.** We have screened a diverse array of iridium complexes derived from chiral N,P-ligands as catalysts for the asymmetric hydrogenation of vinylsilanes, a transformation for which generally applicable catalysts were lacking. Several catalysts emerged from this study that enabled highly enantioselective hydrogenation of a wide range of vinylsilanes with trisubstituted or disubstituted terminal C=C bonds bearing aryl, alkyl, carboethoxy, or hydroxymethyl substituents. In addition to trimethylsilyl and dimethyl(phenyl)silyl derivatives, trialkoxysilyl- and silacyclobutyl-substituted alkenes were used as substrates.

**Keywords:** Asymmetric hydrogenation; Iridium; N,P-ligands; Vinylsilanes

Chiral organosilanes are synthetically valuable compounds, which have found use as versatile precursors for selective carbon–carbon bond formation<sup>1</sup> or as chiral catalysts<sup>2</sup> for asymmetric transformations. In addition, C–Si bonds can be converted into C–O bonds in a stereospecific manner by Fleming–Tamao oxidation.<sup>3</sup> Furthermore, due to their low toxicity and favorable metabolic profiles, chiral organosilanes have received increasing attention in medicinal chemistry.<sup>4</sup> Therefore, methods that enable the synthesis of highly enantioenriched chiral organosilicon compounds are of great interest.

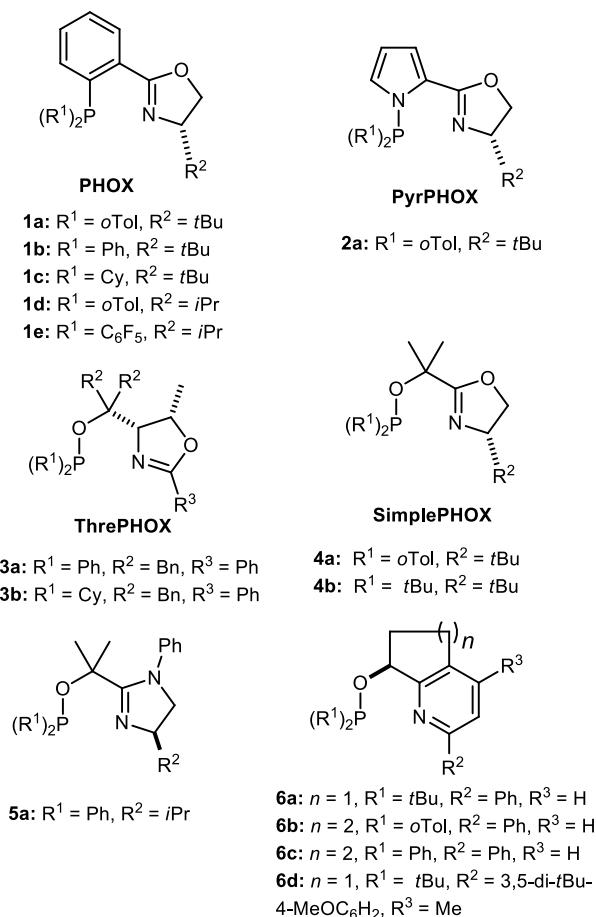
Several enantioselective routes to chiral organosilanes have been described, such as the 1,4-addition of silicon nucleophiles to prochiral  $\alpha,\beta$ -unsaturated carbonyl compounds<sup>5</sup> or the 1,4-addition of carbon<sup>6</sup> or hydrogen<sup>7</sup> nucleophiles to silyl-substituted  $\alpha,\beta$ -unsaturated carbonyl compounds leading to chiral  $\beta$ -silyl carbonyl compounds. Enantioenriched allylsilanes are conveniently accessible by copper-catalyzed enantioselective allylic substitution.<sup>8</sup> The most general and widely used method for the synthesis of chiral silanes is the asymmetric hydrosilylation of alkenes, pioneered by

Hayashi.<sup>9</sup> High enantioselectivities were achieved with monosubstituted or 1,2-disubstituted alkenes, whereas 1,1-disubstituted alkenes usually react with lower enantioselectivity, especially those with terminal dialkyl-substituted C=C bonds. Moreover, regioselectivity is a frequently encountered problem.

In this respect, asymmetric hydrogenation of vinylsilanes provides a potentially attractive alternative. However, examples of this approach to chiral silanes are scarce. In 2006, Andersson and coworkers reported the first enantioselective hydrogenation of vinylsilanes by iridium catalysts derived from chiral phosphino-thiazoline or phosphino-oxazoline ligands.<sup>10a</sup> However, only in one case, using (*E*)-trimethyl(2-phenylprop-1-en-1-yl)silane as substrate (structure **7c** in Table 1), high enantiomeric excesses of up to 98% were obtained, while other vinylsilanes reacted with moderate to poor enantioselectivities of 28–58% *ee*. In subsequent studies additional Ir N,P-ligand complexes were tested, although solely in the hydrogenation of **7c**.<sup>10b,c</sup> After completion of our work described herein, Li et al. reported a study on the asymmetric hydrogenation of vinylsilanes with an Ir-ThrePHOX catalyst (ligand **3b** in Fig. 1).<sup>10d</sup> They obtained high enantioselectivities in several cases but the range of substrates investigated was limited to vinylsilanes with a terminal C=C bond. Therefore, the availability of other catalysts that enhance the substrate scope of this transformation is clearly desirable.

As part of our long-term studies of Ir-catalyzed asymmetric hydrogenation,<sup>11–24</sup> we explored the potential of various classes of chiral Ir N,P-ligand complexes for the enantioselective hydrogenation of vinylsilanes. Ir complexes of this type have considerably enhanced the scope of asymmetric hydrogenation of olefins because they do not require the assistance of a coordinating group in vicinity of the C=C bond like Rh and Ru diphosphine complexes. The range of substrates that have been successfully

hydrogenated with these catalysts comprises a wide variety functionalized and unfunctionalized olefins.<sup>11, 19-24</sup> Even purely alkyl-substituted alkenes were found to react with excellent enantioselectivities and high turnover numbers. Therefore, we thought that alkenes bearing a silyl instead of an alkyl group should be feasible substrates as well. Here we report the results of a systematic hydrogenation study of a diverse range of vinylsilanes using Ir complexes derived from N,P-ligands **1-6** as catalysts (see Figure 1).



**Fig. 1** Chiral N,P-ligands used in this study.

For our studies we selected representative examples of Ir catalysts derived from oxazoline-based N,P-ligands PHOX,<sup>13</sup> PyrPHOX,<sup>14</sup> ThrePHOX,<sup>15</sup> and SimplePHOX,<sup>16</sup> an imidazoline analog of SimplePHOX **5a**,<sup>17</sup> and a series of pyridine-based N,P ligands **6a-d**<sup>18</sup> (Fig. 1), which we had successfully applied in previous studies. For an initial screening, we chose (*E*)-trimethyl(2-phenylbut-1-en-1-yl)silane (**7a**) as substrate. Using 0.5 mol% catalyst under 50 bar of hydrogen gas, all catalysts tested gave full conversion to the saturated silane **8a** within 2h at room temperature (entries 1-7, Table 1). In general, complexes with phosphinite based N,P-ligands gave higher enantioselectivities (86-98% *ee*) than PHOX or PyrPHOX ligands (Table 1, entries 3-7 vs entries 1-2). The best enantioselectivity (98% *ee*)

was achieved with the bicyclic pyridine-phosphinite ligand **6b**.

In the hydrogenation of (*E*)-(2-cyclohexylbut-1-en-1-yl)trimethylsilane (**7b**) lacking an aromatic substituent, most catalysts that had given high enantioselectivities for **7a** performed poorly (entries 10-12), with the exception of complexes derived from pyridine-based ligands **6a** and **6b** (entries 13-14). The latter clearly performed best, affording the desired product **8b** with full conversion and 96% *ee*.

**Table 1** Asymmetric hydrogenation of vinylsilanes with trisubstituted C=C bonds.

Entry	Substrate	L	Conv. (%) <sup>a</sup>	<i>Ee</i> (%) <sup>b</sup>
1	<b>7a</b>	( <i>S</i> )- <b>1a</b>	>99	8 (-)
2	<b>7a</b>	( <i>S</i> )- <b>2a</b>	>99	31 (-)
3	<b>7a</b>	(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	94 (+)
4	<b>7a</b>	( <i>S</i> )- <b>4a</b>	>99	87 (-)
5	<b>7a</b>	( <i>R</i> )- <b>5a</b>	>99	86 (+)
6	<b>7a</b>	( <i>S</i> )- <b>6a</b>	>99	91 (+)
7	<b>7a</b>	( <i>R</i> )- <b>6b</b>	>99	98 (-)
8	<b>7b</b>	( <i>S</i> )- <b>1a</b>	58	18 (-)
9	<b>7b</b>	( <i>S</i> )- <b>2a</b>	44	8 (-)
10	<b>7b</b>	(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	28 (+)
11	<b>7b</b>	( <i>S</i> )- <b>4a</b>	>99	50 (+)
12	<b>7b</b>	( <i>R</i> )- <b>5a</b>	>99	20 (+)
13	<b>7b</b>	( <i>S</i> )- <b>6a</b>	>99	85 (-)
14	<b>7b</b>	( <i>S</i> )- <b>6b</b>	>99	96 (-)
15	<b>7c</b>	( <i>S</i> )- <b>6a</b>	>99	92 ( <i>R</i> ) <sup>25</sup>
16	<b>7c</b>	( <i>R</i> )- <b>6b</b>	>99	90 ( <i>S</i> )
17	<b>7c</b>	( <i>R</i> )- <b>6c</b>	>99	94 ( <i>S</i> )
18	<b>7d</b>	( <i>S</i> )- <b>6a</b> <sup>c</sup>	>99	92 (-)
19	<b>7d</b>	( <i>R</i> )- <b>6b</b> <sup>c</sup>	>99	91 (+)
20	<b>7d</b>	( <i>R</i> )- <b>6c</b> <sup>c</sup>	>99	95 (+)
21	<b>7e</b>	( <i>S</i> )- <b>4a</b>	>99	83 (-)
22	<b>7e</b>	( <i>R</i> )- <b>5a</b>	>99	80 (+)
23	<b>7e</b>	( <i>S</i> )- <b>6a</b>	>99	77 (+)
24	<b>7e</b>	( <i>S</i> )- <b>6b</b>	>99	80 (+)
25	<b>(Z)-7f</b>	( <i>S</i> )- <b>1a</b> <sup>d</sup>	>99	3 ( <i>R</i> ) <sup>26</sup>
26	<b>(Z)-7f</b>	( <i>S</i> )- <b>2a</b> <sup>d</sup>	>99	23 ( <i>S</i> )
27	<b>(Z)-7f</b>	(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b> <sup>d</sup>	>99	98 ( <i>R</i> )
28	<b>(Z)-7f</b>	( <i>S</i> )- <b>4a</b> <sup>d</sup>	>99	87 ( <i>S</i> )
29	<b>(Z)-7f</b>	( <i>R</i> )- <b>5a</b> <sup>e</sup>	>99	89 ( <i>R</i> )
30	<b>(Z)-7f</b>	( <i>S</i> )- <b>6a</b>	>99	>99 ( <i>R</i> )
31	<b>(Z)-7f</b>	( <i>S</i> )- <b>6b</b>	>99	>99 ( <i>R</i> )
32	<b>(E)-7f</b>	( <i>S</i> )- <b>1a</b>	40	69 ( <i>R</i> )
33	<b>(E)-7f</b>	( <i>S</i> )- <b>2a</b>	88	86 ( <i>R</i> )
34	<b>(E)-7f</b>	( <i>S</i> )- <b>2a</b> <sup>c</sup>	>99	88 ( <i>R</i> )
35	<b>(E)-7f</b>	(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	75	25 ( <i>S</i> )
36	<b>(E)-7f</b>	( <i>S</i> )- <b>4a</b>	42	67 ( <i>R</i> )
37	<b>(E)-7f</b>	( <i>R</i> )- <b>5a</b>	8	63 ( <i>S</i> )

38	( <i>S</i> )- <b>6a</b>	17	62 ( <i>S</i> )
39	( <i>S</i> )- <b>6b</b>	4	75 ( <i>S</i> )

<sup>a</sup> Determined by GC analysis of the reaction mixture after removal of the catalyst. <sup>b</sup> Determined by GC analysis on a chiral stationary phase. Absolute configurations are assigned based on sign of optical rotation reported in the cited references. <sup>c</sup> Reaction time: 4 h. <sup>d</sup> Reaction time: 6 h. <sup>e</sup> Reaction time: 24 h.

The corresponding methyl-substituted vinylsilanes **7c** and **7d** as well gave high enantioselectivities with pyridine-based ligands **6a-c** (entries 15-20). The chloroalkyl-substituted vinylsilane **7e** reacted with lower but still respectable enantioselectivity. In this case oxazoline- and imidazoline-based ligands **4a** and **5a** also performed well, inducing *ee* values of 83% and 80%, respectively, comparable to pyridine-phosphinites **6a** and **6b** (entries 21-24).

Next, we studied the hydrogenation of silane (*Z*)-**7f** with a TMS group at the trisubstituted C atom, which leads to a product with a silyl-substituted stereogenic center. In contrast to Andersson's catalysts,<sup>10</sup> which gave low enantioselectivity (28% *ee*) for this substrate, all of our phosphinite ligands **3a**, **4a**, **5a**, **6a**, and **6b** performed well (entries 27-31). Especially pyridine-based ligands **6a** and **6b** stood out with enantioselectivities of >99% *ee*. Hydrogenation of the isomer (*E*)-**7f** proved to be more challenging (entries 32-39). Most catalysts gave low conversion and only moderate to poor enantioselectivities (entries 33-34). Only the PyrPHOX complex [r(COD)(**2a**)]BAR<sub>F</sub> produced the product with full conversion and an *ee* value of 88% after prolonged reaction time of 4h.

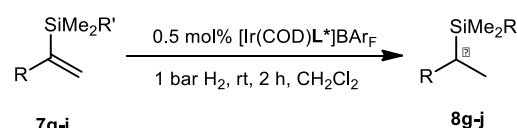
In further studies we focused on hydrogenation of vinylsilanes with terminal C=C bonds. As terminal olefins are known to react with higher enantioselectivity at lower pressure,<sup>30</sup> catalyst screening was performed under 1 bar of hydrogen gas.

First, we tested  $\alpha$ -trimethylsilylstyrene (**7g**) as substrate (Table 2). In all cases full conversion was obtained with enantioselectivities ranging from 13% to 88% *ee*. The best catalyst for this substrate was the complex derived from the pyridine-phosphinite ligand **6a** (entry 6). Even better results were obtained with the corresponding cyclohexyl-substituted vinylsilane **7h**. Notably, besides the pyridine-phosphinite **6a**, the oxazoline- and imidazoline-based ligands **4a** and **5a** also performed well with this substrate (entries 11-13). Clearly the highest enantioselectivity (97% *ee*) was induced by ligand **4a**. As observed before for vinylsilanes with trisubstituted C=C bonds (Table 1), replacement of a cyclohexyl substituent by a less sterically demanding *n*-alkyl group resulted in a loss of enantioselectivity (entries 15-17). SimplePHOX **4a** was again the best performing ligand with an *ee* of 69%.

The more sterically hindered dimethylphenylsilyl substituent in substrate **7j** led to a strong decrease in reactivity compared to the TMS analog (entries 18-21). Only 67% conversion was obtained under standard conditions with the catalyst derived from

ligand **6a**, although high levels of enantioselectivity were achieved. To speed up the reaction, the hydrogen pressure was raised to 5 bar. Under these conditions both the SimplePHOX (**4a**) and pyridine-phosphinite (**6a**) complexes produced the product with full conversion and enantioselectivities of 81% and 91% *ee*, respectively, while the complex with the imidazoline-based ligand **5a** showed poor reactivity and selectivity.

**Table 2** Asymmetric hydrogenation of terminal vinylsilanes.



Entry	Substrate	L	Conv. (%) <sup>a</sup>	<i>Ee</i> (%) <sup>b</sup>
1		( <i>S</i> )- <b>1a</b>	>99	30 ( <i>S</i> ) <sup>27</sup>
2		( <i>S</i> )- <b>2a</b>	>99	27 ( <i>S</i> )
3		(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	74 ( <i>S</i> )
4		( <i>S</i> )- <b>4a</b>	>99	20 ( <i>R</i> )
5		( <i>R</i> )- <b>5a</b>	>99	67 ( <i>S</i> )
6		( <i>S</i> )- <b>6a</b>	>99	88 ( <i>S</i> )
7		( <i>S</i> )- <b>6b</b>	>99	13 ( <i>R</i> )
8		( <i>S</i> )- <b>1a</b>	93	20 (+)
9		( <i>S</i> )- <b>2a</b>	>99	36 (+)
10		(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	48 (-)
11		( <i>S</i> )- <b>4a</b>	>99	97 (+)
12		( <i>R</i> )- <b>5a</b>	>99	88 (-)
13		( <i>S</i> )- <b>6a</b>	>99	90 (-)
14		( <i>S</i> )- <b>6b</b>	40	47 (-)
15		( <i>S</i> )- <b>4a</b>	>99	69 ( <i>R</i> ) <sup>28</sup>
16		( <i>R</i> )- <b>5a</b>	>99	65 ( <i>S</i> )
17		( <i>S</i> )- <b>6a</b>	>99	46 ( <i>S</i> )
18		( <i>S</i> )- <b>4a</b> <sup>c</sup>	>99	81 <sup>d</sup> ( <i>R</i> ) <sup>29</sup>
19		( <i>R</i> )- <b>5a</b> <sup>c</sup>	51	50 ( <i>S</i> )
20		( <i>S</i> )- <b>6a</b>	68	91 ( <i>S</i> )
21		( <i>S</i> )- <b>6a</b> <sup>c</sup>	>99	91 ( <i>S</i> )

<sup>a</sup> Determined by GC analysis of the reaction mixture after removal of the catalyst. <sup>b</sup> Determined by GC analysis on a chiral stationary phase. Absolute configurations are assigned based on sign of optical rotation reported in the cited references. <sup>c</sup> Under 5 bar of H<sub>2</sub>. <sup>d</sup> Determined by GC analysis after conversion to its corresponding alcohol.

In view of the promising results obtained with trimethylsilyl- and dimethylphenylsilyl-substituted alkenes, we decided to explore further silane derivatives.

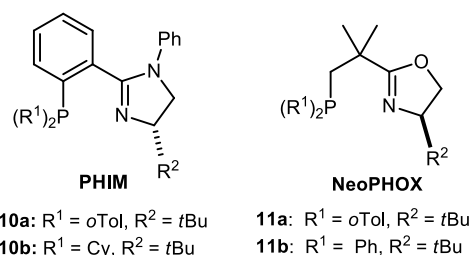
Trialkoxysilyl-substituted alkenes were chosen because the hydrogenation products can be readily transformed to enantioenriched alcohols<sup>3</sup> or trifluorosilanes,<sup>31</sup> the latter being of interest as starting compounds for stereoselective sp<sup>2</sup>-sp<sup>3</sup> Hiyama cross-coupling reactions.<sup>32</sup>

Initial hydrogenations of triethoxy(vinyl)silane **7k** under standard conditions (0.5 mol % catalyst loading, 50 bar H<sub>2</sub>) led to an inseparable mixture of the desired product **8k** and a side product, to which we assigned structure **9** based on MS and NMR data (Table 3, entry 1). As this side product likely results from an acid-promoted<sup>33</sup> condensation, 5 mol% of potassium carbonate was added to the reaction mixture. As hoped, the reaction proceeded smoothly to give the saturated triethoxysilane **8k** as the sole product (entries 2-7). The best enantioselectivity (70% *ee*) was achieved with complexes derived from SimplePHOX ligand **4b** and phosphino-imidazoline (PHIM)<sup>17</sup> **10a**.

**Table 3** Asymmetric hydrogenation of trialkoxy(vinyl)silanes

Entry	Substrate	L	Conv. (%) <sup>a</sup>	<i>Ee</i> (%) <sup>b</sup>
1		( <i>S</i> )- <b>4b</b> <sup>c</sup>	53	n.d. <sup>d</sup>
2		(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	64 (-)
3		( <i>S</i> )- <b>4a</b>	>99	44 (+)
4		( <i>S</i> )- <b>4b</b>	>99	70 (+)
5		( <i>S</i> )- <b>6a</b>	>99	20 (+)
6		( <i>R</i> )- <b>6b</b>	>99	16 (-)
7		( <i>S</i> )- <b>10a</b>	>99	70 (+)
8		(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	77 (-)
9		(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b> <sup>e</sup>	>99	80 (-)
10		( <i>S</i> )- <b>4b</b>	>99	51 (+)
11		( <i>S</i> )- <b>10a</b>	90	65 (+)
12		(4 <i>S</i> , 5 <i>S</i> )- <b>3a</b>	>99	44 (+)
13		( <i>S</i> )- <b>4b</b>	>99	88 (-)
14		( <i>S</i> )- <b>10b</b>	>99	79 (-)

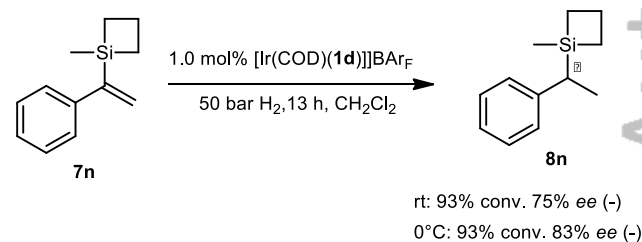
<sup>a</sup> Determined by GC analysis of the reaction mixture after removal of the catalyst. <sup>b</sup> Determined by GC or HPLC analysis on a chiral stationary phase. <sup>c</sup> In the absence of K<sub>2</sub>CO<sub>3</sub>, 16 h. <sup>d</sup> Not determined because of overlapping peaks of one enantiomer and the side product. <sup>e</sup> Under 5 bar of H<sub>2</sub>.



**Fig. 2** ligands **10** and **11**.

The trimethoxysilyl substituted analogue **7l** gave similar results (entries 8-11). However, a different ligand, the ThrePHOX derivative **3a**, performed best in this case. As generally observed for terminal olefins, the enantioselectivity was higher at low hydrogen pressure, however, the difference was small (**3a**: 77% *ee* at 50 bar vs 80% *ee* at 5 bar; entries 8 and 9). Consistent with the results obtained for the TMS analogues **7h** and **7i** (Table 2), better enantioselectivity (88% *ee*) was achieved with the cyclohexyl-substituted vinylsilane **7m** compared to the corresponding *n*-alkyl-substituted substrate **7l**. In this case, the optimal ligand was the SimplePHOX derivative **4b** (entry 13).

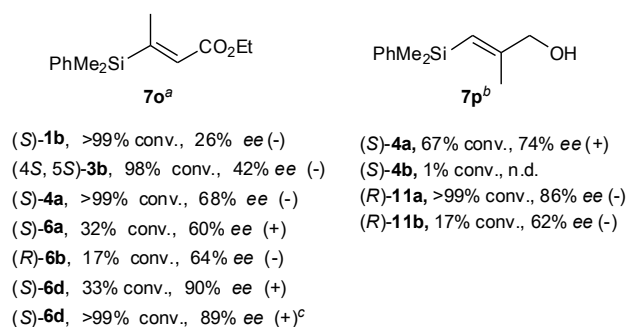
Due to ring strain, siletanes (silacyclobutanes) have unique properties that distinguish them from analogous acyclic alkylsilanes. They have been shown to readily undergo Tamao-Fleming oxidation and therefore can be used as hydroxyl surrogates.<sup>34</sup> Moreover, they can be converted to structurally diverse products by transition metal-catalyzed reactions involving insertion and ring expansion.<sup>35</sup> We therefore decided to study the asymmetric hydrogenation of vinylsiletanes as a possible approach to enantioenriched alkylsiletanes.



**Scheme 1** Asymmetric hydrogenation of vinylsiletanes.

Initial experiments with siletane **7n** were discouraging. With most catalysts complex, mixtures of the desired product **8n** and several unidentified products were formed. Better results were finally obtained with PHOX complexes, especially with [Ir(COD)(**1d**)]BARF, which gave 93% conversion to the hydrogenation product **8n** in 75% *ee* and only minor amounts of an unidentified byproduct (Scheme 1). When the temperature was lowered to 0 °C, the *ee* increased to 83%.

Finally, we investigated the hydrogenation of functionalized vinylsilanes bearing a carboxylic ester or hydroxymethyl group at the C=C bond.



**Figure 3** Asymmetric hydrogenation of  $\alpha,\beta$ -unsaturated ester **7o** and allylic alcohol **7p**. <sup>a</sup> Reaction conditions: 0.5 mol % catalyst loading, 50 bar H<sub>2</sub>, rt, 4 h in CH<sub>2</sub>Cl<sub>2</sub>. <sup>b</sup> Reaction conditions: 1.0 mol % catalyst loading, 50 bar H<sub>2</sub>, rt, 12 h in CH<sub>2</sub>Cl<sub>2</sub>. <sup>c</sup> 1.0 mol % catalyst loading, 12 h.

The  $\alpha,\beta$ -unsaturated ester **7o** was first tested under standard conditions (0.5 mol % catalyst loading, 50 bar H<sub>2</sub>, 4h). Most catalysts that we evaluated yielded the desired product **8o** with full conversion, with the exception of Ir complexes derived from pyridine-phosphinite ligands **6a-b** and **6d**, which were poorly active. However, the highest enantioselectivity (90% ee) was achieved with ligand **6d**, which bears a sterically demanding aryl substituent at the pyridine ring (Figure 3). With higher catalyst loading (1 mol%) and over a prolonged reaction time of 12 hours, the reaction went to completion with essentially the same enantioselectivity (89% ee).

Compared to the  $\alpha,\beta$ -unsaturated ester **7o** the allylic alcohol **7p** was less reactive. Using 1.0 mol% of catalyst at 50 bar H<sub>2</sub> at room temperature, most catalysts did not give any conversion after a reaction time of 12 h, except for complexes derived from SimplePHOX<sup>16</sup> and NeoPHOX<sup>36</sup> ligands. The substituents on the phosphorus atom seem to play a crucial role in these catalysts. Ligands **4a** and **11a**, both bearing a bis(ortho-tolyl)phosphine group, showed higher levels of activity and enantioselectivity than their analogues **4b** and **11b**. The best result (>99% conv., 86% ee) was achieved with the catalyst derived from NeoPHOX ligand **11a**.

In conclusion, in this study that included a variety of vinyl silanes with trisubstituted or disubstituted terminal C=C bonds and a diverse array of Ir N,P-ligand complexes as catalysts, we have shown that asymmetric hydrogenation provides efficient access to wide range of chiral organosilanes with high enantioselectivity. Both substrates with or without coordinating groups at the C=C bond were successfully hydrogenated. Depending on the substrate structure, different ligand complexes emerged as the catalysts of choice. The best catalysts identified in our study significantly enhance the substrate scope in the asymmetric hydrogenation of

silyl-substituted C=C bonds, opening up an attractive enantioselective route to chiral organosilanes.

## Experimental Section

A 2 mL glass vial was charged with a cylindrical stirring bar (0.7 cm in length), the relevant iridium catalyst (0.5–1.0 mol%) and the substrate (100  $\mu$ mol). The mixture was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL, 0.2 M) and placed in an autoclave. The autoclave was attached to a high pressure hydrogen line and purged with H<sub>2</sub> three times before being sealed under the appropriate H<sub>2</sub> pressure. The mixture was stirred for the appropriate reaction time at rt. After release of H<sub>2</sub>, the solution was concentrated under a stream of nitrogen. The crude reaction mixture was then dissolved in 0.5 mL of a 4:1 *n*-hexane:MTBE mixture and the catalyst removed by filtration through a plug of SiO<sub>2</sub> in a Pasteur pipette. After washing with ca. 5 mL of a 4:1 *n*-hexane:MTBE mixture, the solvent was concentrated *in vacuo* to yield the hydrogenation product.

Analytical data and determination of enantioselectivities: see supporting information.

## Acknowledgements

Financial support by the Swiss National Science Foundation is gratefully acknowledged.

## References

- [1] (a) C. E. Masse, J. S. Panek, *Chem. Rev.* **1995**, *95*, 1293-1316; (b) L. Chabaud, P. James, Y. Landaïs, *Eur. J. Org. Chem.* **2004**, 3173-3199; (c) M. J. Curtis-Long, Y. Ay, *Chem. Eur. J.* **2009**, *15*, 5402-5416; (d) L.-W. Xu, L. Li, G.-Q. Lai, J.-X. Jiang, *Chem. Soc. Rev.* **2011**, *40*, 1777-1790.
- [2] (a) S. Özçubukçu, F. Schmidt, C. Bolm, *Org. Lett.* **2005**, *7*, 1407-1409; (b) A. G. Schafer, J. M. Wieting, T. J. Fisher, A. E. Mattson, *Angew. Chem.* **2013**, *125*, 11531-11534; *Angew. Chem. Int. Ed.* **2013**, *52*, 11321-11324.
- [3] (a) I. Fleming, R. Henning, H. Plaut, *J. Chem. Soc., Chem. Commun.* **1984**, 29-31; (b) K. Tamao, N. Ishida, T. Tanaka, M. Kumada, *Organometallics* **1983**, *2*, 1694-1696.
- [4] For reviews, see: (a) W. Bains, R. Tacke, *Curr. Opin. Drug Discovery Dev.* **2003**, *6*, 526-543; (b) J. S. Mills, G. A. Showell, *Exp. Opin. Invest. Drugs* **2004**, *13*, 1149-1157; (c) P. K. Pooni, G. A. Showell, *Mini-Rev. Med. Chem.* **2006**, *6*, 1169-1177; (d) S. Gately, R. West, *Drug Dev. Res.* **2007**, *68*, 156-163; (e) A. K. Franz, S. O. Wilson, *J. Med. Chem.* **2013**, *56*, 388-405; for some selected examples, see: (f) M. W. Mutahi, T. Nittoli, L. Guo, S. M. Sieburth, *J. Am. Chem. Soc.* **2002**, *124*, 7363-7375; (g) J. Wang, C. Ma, Y. Wu, R. A. Lamb, L. H. Pinto, W. F. DeGrado, *J. Am. Chem. Soc.* **2011**, *133*, 13844-13847.
- [5] (a) T. Hayashi, Y. Matsumoto, Y. Ito, *J. Am. Chem. Soc.* **1988**, *110*, 5579-5581; (b) C. Walter, G. Auer, M. Oestreich, *Angew. Chem.* **2006**, *118*, 5803-5805; *Angew. Chem. Int. Ed.* **2006**, *45*, 5675-5677; (c) C.

- Walter, M. Oestreich, *Angew. Chem.* **2008**, *120*, 3878-3880; *Angew. Chem. Int. Ed.* **2008**, *47*, 3818-3820; (d) K.-s. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 2898-2890; (e) J. M. O'Brien, A. H. Hoveyda, *J. Am. Chem. Soc.* **2011**, *133*, 7712-7715; (f) K.-s. Lee, H. Wu, F. Haeflner, A. H. Hoveyda, *Organometallics* **2012**, *31*, 7823-7826; (g) V. Pace, J. P. Rae, H. Y. Harb, D. J. Procter, *Chem. Commun.* **2013**, *49*, 5150-5152; (h) V. Pace, J. P. Rae, D. J. Procter, *Org. Lett.* **2014**, *16*, 476-479.
- [6] (a) R. Shintani, K. Okamoto, T. Hayashi, *Org. Lett.* **2005**, *7*, 4757-4759; (b) M. A. Kacprzynski, S. A. Kazane, T. L. May, A. H. Hoveyda, *Org. Lett.* **2007**, *9*, 3187-3190; (c) K. Zhao, T.-P. Loh, *Chem. Eur. J.* **2014**, *20*, 16764-16772.
- [7] B. H. Lipshutz, N. Tanaka, B. R. Taft, C.-T. Lee, *Org. Lett.* **2006**, *8*, 1963-1966.
- [8] (a) M. A. Kacprzynski, T. L. May, S. A. Kazane, A. H. Hoveyda, *Angew. Chem.* **2007**, *119*, 4638-4642; *Angew. Chem. Int. Ed.* **2007**, *46*, 4554-4558; (b) Y. Shido, M. Yoshida, M. Tanabe, H. Ohmiya, M. Sawamura, *J. Am. Chem. Soc.* **2012**, *134*, 18573-18576; (c) L. B. Delvos, D. J. Vyas, M. Oestreich, *Angew. Chem.* **2013**, *125*, 4748-4751; *Angew. Chem. Int. Ed.* **2013**, *52*, 4650-4653; (d) M. Takeda, R. Shintani, T. Hayashi, *J. Org. Chem.* **2013**, *78*, 5007-5017; (e) A. Hensel, M. Oestreich, *Chem. Eur. J.* **2015**, *21*, 9062-9065.
- [9] Reviews: (a) T. Hayashi, K. Yamasaki in *Comprehensive Organometallic Chemistry III, Vol. 10* (Eds: D. Mingos, P. Michael, R. H. Crabtree), Elsevier, Amsterdam, **2007**, pp. 815-838; (b) J. W. Han, T. Hayashi in *Catalytic Asymmetric Synthesis, 3rd edn.* (Ed: I. Ojima), John Wiley & Sons, Hoboken, **2010**, pp. 771-798; (c) J. W. Han, T. Hayashi in *Science of Synthesis, Stereoselective Synthesis, Vol. 1* (Eds: J. G. De Vries, G. A. Molander, P. A. Evans), Georg Thieme Verlag, Stuttgart, **2011**, pp. 923-939; for a selected recent example, see: (d) J. Chen, B. Cheng, M. Cao, Z. Lu, *Angew. Chem.* **2015**, *127*, 4744-4747; *Angew. Chem. Int. Ed.* **2015**, *54*, 4661-4664.
- [10] (a) K. Källström, I. J. Munslow, C. Hedberg, P. G. Andersson, *Adv. Synth. Catal.* **2006**, *348*, 2575-2578; (b) J. Mazuela, A. Paptchikhine, O. Pàmies, P. G. Andersson, M. Dieguez, *Chem. Eur. J.* **2010**, *16*, 4567-4576; (c) J. Mazuela, P.-O. Norrby, P. G. Andersson, O. Pàmies, M. Dieguez, *J. Am. Chem. Soc.* **2011**, *133*, 13634-13645; (d) D.-D. Ma, P. Gu, R. Li, *Tetrahedron Lett.* **2016**, *57*, 5666-5668.
- [11] Reviews: (a) S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402-1411; (b) D. H. Woodmansee, A. Pfaltz, *Chem. Commun.* **2011**, *47*, 7912-7916; (c) D. H. Woodmansee, A. Pfaltz, *Top. Organomet. Chem.* **2011**, *34*, 31-76.
- [12] For contributions of other groups, see: (a) Y. Zhu, K. Burgess, *Acc. Chem. Res.* **2012**, *45*, 1623-1636; (b) Y. Zhu, K. Burgess, *Adv. Synth. Catal.* **2013**, *355*, 107-115; (c) J. J. Verendel, O. Pàmies, M. Dieguez, P. G. Andersson, *Chem. Rev.* **2014**, *114*, 2130-2169; (d) C. Borrás, M. Biosca, O. Pàmies, M. Dieguez, *Organometallics* **2015**, *34*, 5321-5334; (e) B. K. Peters, J. Liu, C. Margarita, W. Rabten, S. Kerdphon, A. Orebom, T. Morsch, P. G. Andersson, *J. Am. Chem. Soc.* **2016**, *138*, 11930-11935, and refs. 10 and 32.
- [13] A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem.* **1998**, *110*, 3047-3050; *Angew. Chem. Int. Ed.* **1998**, *37*, 2897-2899.
- [14] P. G. Cozzi, N. Zimmermann, R. Hilgraf, S. Schaffner, A. Pfaltz, *Adv. Synth. Catal.* **2001**, *343*, 450-454.
- [15] F. Menges, A. Pfaltz, *Adv. Synth. Catal.* **2002**, *344*, 40-44.
- [16] S. P. Smidt, F. Menges, A. Pfaltz, *Org. Lett.* **2004**, *6*, 2023-2026.
- [17] (a) F. Menges, M. Neuburger, A. Pfaltz, *Org. Lett.* **2002**, *4*, 4713-4716; (b) F. Menges, A. Pfaltz, WO 2005021562, **2005**; applicant: Solvias AG, Basel, Switzerland.
- [18] (a) S. Kaiser, S. P. Smidt, A. Pfaltz, *Angew. Chem.* **2006**, *118*, 5318-5321; *Angew. Chem. Int. Ed.* **2006**, *45*, 5194-5197; (b) D. H. Woodmansee, M.-A. Müller, M. Neuburger, A. Pfaltz, *Chem. Sci.* **2010**, *1*, 72-78.
- [19] M. Bernasconi, V. Ramella, P. Tosatti, A. Pfaltz, *Chem. Eur. J.* **2014**, *20*, 2440-2444.
- [20] M. Bernasconi, M.-A. Müller, A. Pfaltz, *Angew. Chem.* **2014**, *126*, 5489-5492; *Angew. Chem. Int. Ed.* **2014**, *53*, 5385-5388.
- [21] M.-A. Müller, A. Pfaltz, *Angew. Chem.* **2014**, *126*, 8812-8815; *Angew. Chem. Int. Ed.* **2014**, *53*, 8668-8671.
- [22] A. Baeza, A. Pfaltz, *Chem. Eur. J.* **2009**, *15*, 2266-2269.
- [23] L. Pauli, R. Tannert, R. Scheil, A. Pfaltz, *Chem. Eur. J.* **2015**, *21*, 1482-1487.
- [24] A. Gani, A. Pfaltz, *Chem. Eur. J.* **2012**, *18*, 6724-6728.
- [25] K. Yamamoto, T. Hayashi, M. Kumada, *J. Am. Chem. Soc.* **1971**, *93*, 5301-5302.
- [26] T. Hayashi, M. Konishi, Y. Okamoto, K. Kabeta, M. Kumada, *J. Org. Chem.* **1986**, *51*, 3772-3781.
- [27] T. Hayashi, K. Tamao, Y. Katsuro, I. Nakae, M. Kumada, *Tetrahedron Lett.* **1980**, *21*, 1871-1874.
- [28] J. P. Gilday, J. C. Gallucci, L. A. Paquette, *J. Org. Chem.* **1989**, *54*, 1399-1408.
- [29] G. Li, G. W. Kabalka, *J. Organomet. Chem.* **1999**, *581*, 66-69.
- [30] S. McIntyre, E. Hörmann, F. Menges, S. P. Smidt, A. Pfaltz, *Adv. Synth. Catal.* **2005**, *347*, 282-288.
- [31] (a) I. A. Kudasheva, R. S. Musarinov, E. P. Nedogrei, R. T. Akhmatdinov, E. A. Kantor, D. L. Rakhmankulov, *Zh. Obshch. Khim.* **1986**, *56*, 617-621; (b) O. Farooq, *J. Chem. Soc., Perkin Trans. 1* **1998**, 661-665.

- [32] (a) Y. Hatanaka, T. Hiyama, *J. Am. Chem. Soc.* **1990**, *112*, 7793-7794; (b) H. Matsubashi, M. Kuroboshi, Y. Hatanaka, T. Hiyama, *Tetrahedron Lett.* **1994**, *35*, 6507-6510; (c) H. Matsubashi, S. Asai, K. Hirabayashi, Y. Hatanaka, A. Mori, T. Hiyama, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 437-444.
- [33] Burgess et al. have shown that Ir-hydride complexes formed as intermediates in the catalytic cycle are strong Brønsted acids: Y. Zhu, Y. Fan, K. Burgess, *J. Am. Chem. Soc.* **2010**, *132*, 6249-6253.
- [34] J. D. Sunderhaus, H. Lam, G. B. Dudley, *Org. Lett.* **2003**, *5*, 4571-4573.
- [35] (a) H. Sakurai, T. Imai, *Chem. Lett.* **1975**, *4*, 891-894; (b) K. Hirano, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2007**, *129*, 6094-6095; (c) K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2008**, *10*, 2199-2201; (d) R. Shintani, K. Moriya, T. Hayashi, *J. Am. Chem. Soc.* **2011**, *133*, 16440-16443; (e) R. Shintani, K. Moriya, T. Hayashi, *Org. Lett.* **2012**, *14*, 2902-2905.
- [36] M. G. Schrems, A. Pfaltz, *Chem. Commun.* **2009**, 6210-6212.



Iridium-Catalyzed Enantioselective Hydrogenation of Vinylsilanes

*Adv. Synth. Catal.* **Year**, *Volume*, Page – Page

Aie Wang, Maurizio Bernasconi, Andreas Pfaltz\*

