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# Iridium-Catalysed Asymmetric Hydrogenation of Vinylsilanes as a Route to Optically Active Silanes

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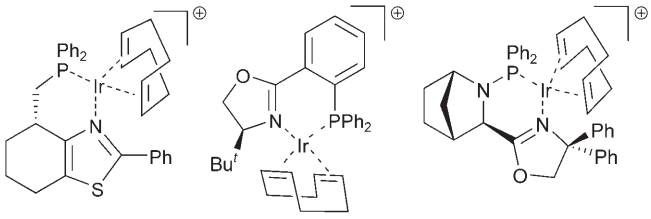
**Abstract:** The first use of vinylsilanes as substrates in the asymmetric iridium-catalysed hydrogenation is reported, providing products with enantioselectivities of up to 98%.

**Keywords:** asymmetric; hydrogenation; iridium; vinylsilanes

The hydrogenation of functionalised olefins is one of the most studied enantioselective catalytic reactions.[1] While the ruthenium- and rhodium-catalysed asymmetric hydrogenations of chelating olefins have a long history, unfunctionalised olefins still represent a challenging class of substrates.[2] During the last few years, Pfaltz[3a–e] and others[4a–i] have used phosphine-oxazoline ligands as chiral mimics of Crabtree's catalyst,[5] which have been used successfully for asymmetric hydrogenations of arylalkenes. Recently, the composition of ligands has expanded to also include oxazoline-carbene ligands[6] and, chiral-at-sulphur, sulphoxide-phosphine ligands.[7] However, iridium-catalysed asymmetric hydrogenation is still highly substrate dependent and the development of new efficient chiral ligands that tolerate a broad range of substrates remains a challenge. With the exception of a few recently reported examples of the asymmetric reduction of some substituted *N*-heteroaromatics,[8,9] further development of new substrate classes has not yet been fully exploited.[2] As part of our ongoing development of Ir-catalysed asymmetric hydrogenation, we have expanded our research to include new substrate classes in parallel with catalyst development.

Organosilanes are important organic intermediates and a number of innovative new organosilicon drugs are in development,[10a–c] in this report we have evaluated the Ir-catalysed reduction of a new class of substrates, vinylsilanes. In order to find a catalyst that can hydrogenate the substrates with both satisfactory rate and enantioselectivity we started with a comparison of three different ligand classes, our newly developed thiazole complex **1**, Pfaltz Ir-PHOX complex **2** and another phosphine-oxazoline complex **3** (Figure 1).[3,11,12]




1 2 3

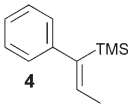
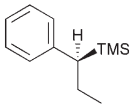
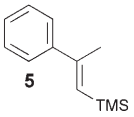
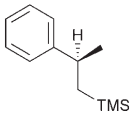
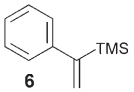
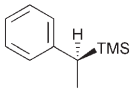
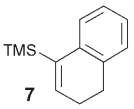
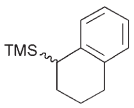
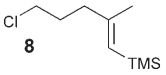
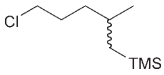
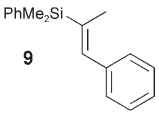
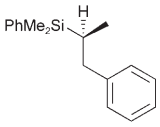
**Figure 1.** Ir complexes used in asymmetric hydrogenation of vinyl silanes. The anion in all cases is $B[3,5\text{-}(CF_3)_2C_6H_3]_4^-$ ($BAr_F$).

All of the catalysts evaluated gave full conversion within 12 h, with complex **1** proving the most selective catalyst for the evaluated substrates (Entries 1 and 2, Table 1). Complexes **2** and **3** hydrogenated substrate **4** (Entry 1) with slightly lower selectivities 25% and 26% *ee*, respectively, when compared to complex **1**, 28% *ee*. When the trimethylsilyl (TMS) group was moved into the non-prochiral position (Entry 2) complex **1** still proved to be the most selective catalyst, although surprisingly complex **2** resulted in a racemic product, whereas complex **3** gave a slightly lower *ee* (96%). Complex **1** was therefore evaluated with a range of vinylsilane substrates, which were readily prepared according to published procedures.[13–15] Catalyst **1** can be prepared according to our previously published procedure,[11] these complexes have the advantage over, e.g., Rh complexes, of being air- and moisture-stable; they can be stored for months in the freezer without any detectable decomposition.

Primarily, we were interested in substrates of the type **4** due to the TMS group being located on the

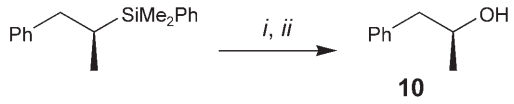
**Table 1.** Asymmetric reduction of vinylsilanes.[a]

| Entry | Substrate | Complex | Conversion [%][b] | *ee* [%] | Product |
|---|---|---|---|---|---|
| 1 |  **4** | **1** | >99 | 28[c] (*S*)[16] |  |
| | | **2** | >99 | 25 (*R*) | |
| | | **3** | >99 | 26 (*R*) | |
| 2 |  **5** | **1** | >99 | 98[c] (*R*)[17] |  |
| | | **2** | >99 | rac. | |
| | | **3** | >99 | 96 (*S*) | |
| 3 |  **6** | **1** | >99 | 58[c] (*S*)[18] |  |
| 4 |  **7** | **1** | >99 | 48[c] (−)[f] |  |
| 5 |  **8** | **1** | >99 | 55[d] (+)[f] |  |
| 6 |  **9** | **1** | >99 | 55[e] (*S*)[19] |  |

[a] *Conditions:* pressure, 30 bar; all reactions were run at room temperature for 12 h in $CH_2Cl_2$; catalyst loading, 0.5 mol%.
[b] Determined by $^1H$ NMR.
[c] GC-MS (G-TA, 60 °C, 30 min, 5 °C min$^{-1}$, 75 °C, 100 kPa).
[d] GC (CP-Chirasil-Dex, 60 °C, 1.5 °C min$^{-1}$, 120 °C).
[e] GC-MS (G-TA, 90 °C, 20 min, 100 kPa). Absolute configurations were determined by optical rotation and comparison with literature data.
[f] Absolute configuration unknown.

prochiral carbon, however, with all the catalysts tested only relatively poor enantioselectivities were obtained. Changing the substitution pattern of the double bond, i.e., exchanging the silyl and methyl groups (substrate **5**), resulted in a product with 98% *ee*, using catalyst **1**. Disappointingly the remaining substrates tested, **6**, **7**, **8** and **9**, only gave rise to moderate *ee*s, 58, 28, 55 and 55%, respectively. Interestingly substrate **8** is one of the few examples of a substrate lacking an aromatic ring being used in asymmetric Ir-catalysed hydrogenations.[20] Substrate **9** is a potentially appealing compound as the resulting reduced vinylsilane can be converted into its corresponding alcohol. Oxidative cleavage of the dimethylphenylsilyl group, using a modified protocol of the original Fleming–Tamao oxidation (Scheme 1),[21a–b] resulted in (*S*)-**10** being isolated in 55% *ee*.

We attempted to rationalise the obtained selectivities using our previously proposed selectivity model.[11] When the substrates are arranged so that the vinylic proton resides in the hindered quadrant and the bulky silyl and phenyl groups occupy the open quadrants (Figure 2), the model correctly predicts the stereochemical outcome for all substrates having known absolute configuration.




*i*: $BF_3{\cdot}Et_2O$, $CH_2Cl_2$, 4 h, r.t.
*ii*: $H_2O_2$, KF, $NaHCO_3$, MeOH/THF 1:1, 50° C, 4 h.

**Scheme 1.** Converting the -$SiMe_2Ph$ moiety into an alcohol function (**10**).

Our previous findings have suggested that substrates possessing a polarised double bond, like α,β-unsaturated esters, introduce an electronic effect into the selectivity of the system.[11] DFT calculations on *trans*-β-methyl cinnamate suggest a strong preference for β-addition of the hydride in the migratory insertion step, whereas for *trans*-α-methyl cinnamate this preference is substantially lower leading to reduced selectivity for this substrate.[11] Since silyl groups are also electron-withdrawing one may also expect to see a similar outcome for the substrates used in this study (substrates **4**, **6**, **7**, **8** and **9**).[22] This may explain why only **5** results with high selectivity, since the other substrates will have a mismatch between sterics and electronics.

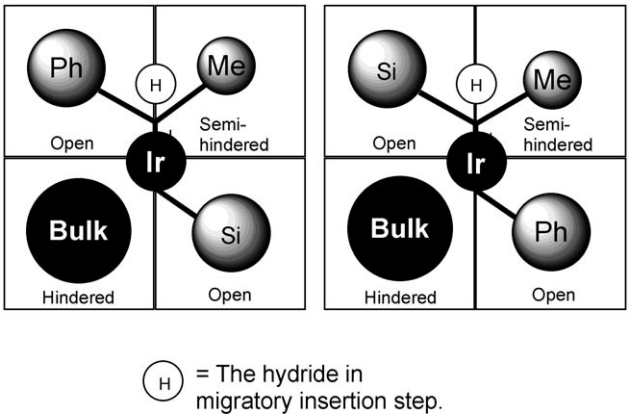



**Figure 2.** Schematic diagram of the selectivity model with substrates **5** (*left*) and **9** (*right*) coordinating onto the catalyst.

In conclusion, we have reported the first successful hydrogenation of a range of vinylsilanes and shown that the reduction of simple olefins need not be restricted to the model substrates that have so far dominated the field of Ir-catalysed asymmetric hydrogenations.

## Experimental Section

### General Methods

All reactions were conducted under argon using dried glassware and magnetic stirring. $CH_2Cl_2$ was freshly distilled under $N_2$ from powdered $CaH_2$ prior to use. NMR samples were dissolved in $CDCl_3$ and run at room temperature; $^1H$ (400 MHz) and $^{13}C$ (100 MHz) NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts for protons are reported using the residual $CHCl_3$ as internal reference ($\delta = 7.26$), carbon spectra were referenced to the shift of the $^{13}C$ signal of $CDCl_3$ ($\delta = 77.0$).

### Materials

The vinylsilanes were all synthesised *via* previously published procedures: **4**,[14] **5**,[13] **6**,[23] **7**,[14] **8**,[24] **9**.[15]

### Typical Hydrogenation Procedure

Catalyst (0.0025 mmol) and substrate (0.5 mmol) were dissolved in $CH_2Cl_2$ (2 mL), the system was purged three times with argon and then pressurised with hydrogen (30 bar), and the reaction was left, with stirring, for 12 h. The solvent was evaporated under vacuum and the conversion measured by $^1H$ NMR. All spectroscopic data were in agreement with previously reported data. The products were dissolved in pentane:$Et_2O$ (1:1) and filtered through a short silica column to remove trace amounts of catalyst prior to *ee* determination. The *ee*s were determined by chiral GC-MS.

### (5-Chloro-2-methylpentyl)trimethylsilane

Compound **8** was hydrogenated *via* the typical protocol After 12 h hydrogen pressure was vented and reaction contents were filtered through a short silica plug, eluting with pentane. Solvent was removed under vacuum, providing pure (5-chloro-2-methylpentyl)trimethylsilane; yield: 96 mg (>99%); $[\alpha]_D^{25}$: +3.30° (*c* 2.0, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 3.53$ (t, $J = 7$ Hz, 2H), 1.74–1.81 (m, 2H), 1.59–1.65 (m, 1H), 1.39–1.45 (m, 1H), 1.29–1.35 (m, 1H), 0.93 (d, $J = 7$ Hz, 3H), 0.64 (dd, $J = 5$, 15 Hz, 1H), 0.43 (dd, $J = 8$, 15 Hz, 1H), 0.02 (s, 9H); $^{13}C$ NMR (400 MHz, $CDCl_3$): $\delta =$ 45.7, 40.0, 30.7, 29.4, 25.3, 23.0, −0.4; IR (neat): $\nu_{max} = 2955.6$ (s), 2894.0, 1248.7 (s), 909.4, 838.0 (s), 735.2 (s), 692.3 $cm^{-1}$; MS (EI): $m/z = 177$ ($M^+$−Me), 135, 114, 95, 93; anal. calcd. for $C_9H_{21}ClSi$: C 56.07, H 10.98; found: C 56.12, H 11.02.

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