

Chapter 2

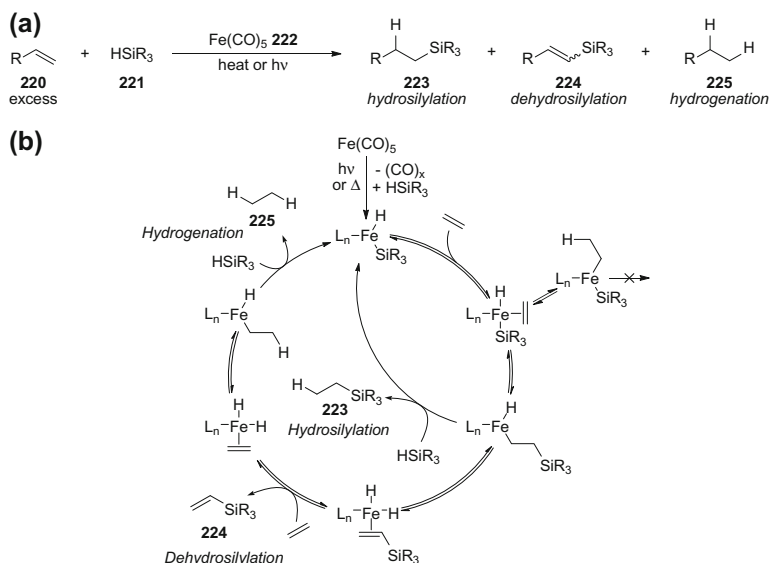
Iron-Catalysed Hydrosilylation of Alkenes and Alkynes

Abstract The hydrosilylation of alkenes represents one of the largest applications of homogeneous catalysis on an industrial scale, and currently uses precious transition-metal catalysts such as platinum. This chapter deals with the development of an iron-catalysed methodology for the hydrosilylation of alkenes and alkynes using a bench-stable iron(II) pre-catalyst, which could be activated in situ. The reaction scope and limitations are presented along with preliminary mechanistic studies, which lead to a discussion of possible reaction mechanisms and future work required to investigate this method further.

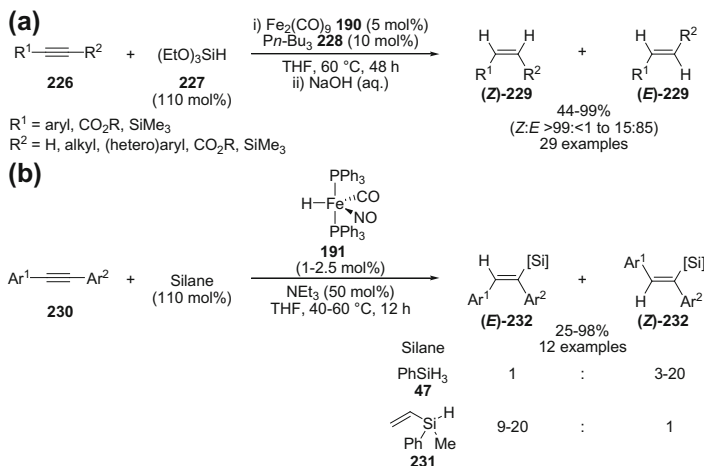
2.1 Introduction

The hydrosilylation of alkenes using iron pentacarbonyl was first reported over 50 years ago. High regioselectivity for linear silane products and good conversions of silane were reported, however excess alkene **220** was required and a mixture of products arising from hydrosilylation **223**, dehydrosilylation **224** and hydrogenation **225** were obtained (Scheme 2.1a) [1]. High temperatures or continual near-UV irradiation was required for pre-catalyst activation and catalyst regeneration following recombination with CO. Although the methodology was not synthetically applicable, Wrighton was intrigued to investigate the mechanism by which dehydrosilylation products were obtained. Based upon work using iron carbonyl complexes, Wrighton was the first to propose and demonstrate the primary catalytic steps of a ‘modified Chalk-Harrod’ mechanism for the hydrosilylation of alkenes [1c]. The significant proposal in this mechanism was alkene insertion into a metal–silicon bond, rather than alkene insertion into a metal–hydride bond (Scheme 2.1b). Following this seminal work, ‘modified Chalk-Harrod’ mechanisms have been proposed for cobalt- [2], rhodium- [3], and iridium-catalysed [4] hydrosilylation reactions.

Although not synthetically useful for the hydrosilylation of alkenes, iron carbonyl pre-catalysts have been used for the hydrosilylation of alkynes to give vinyl silane products. Enthaler reported that in the presence of phosphines, iron carbonyl clusters **190** could be used for the synthesis of (*E*)-vinylsilanes (*syn*-addition of Si-H), which were isolated as (*Z*)-alkenes (**Z**)-**229** following protodesilylation



Scheme 2.1 Iron-catalysed hydrosilylation of alkenes using iron pentacarbonyl as a pre-catalyst. **a** General reaction scheme; **b** ‘Modified Chalk-Harrod’ mechanism proposed by Wrighton



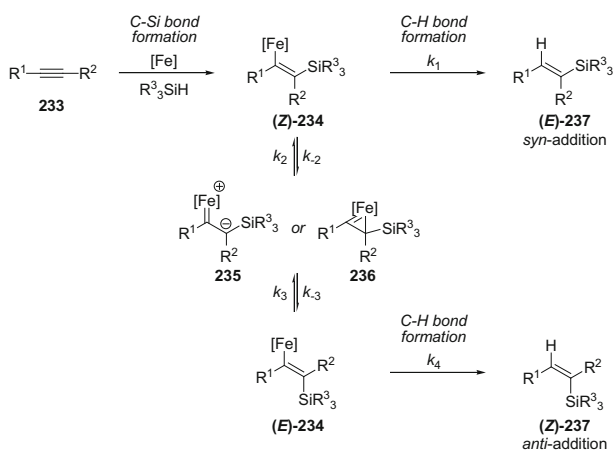
Scheme 2.2 Hydrosilylation of alkynes using iron carbonyl complexes as pre-catalysts. **a** Using a catalyst combination of $\text{Fe}_2(\text{CO})_9$ **190** and tributylphosphine **228**; **b** using (nitroso)iron hydride complex $[\text{FeH}(\text{CO})\text{NO}(\text{PPh}_3)_2]$ **191** as pre-catalyst

(Scheme 2.2a) [5]. A range of electronically-differentiated diarylalkynes **226** were hydrosilylated using triethoxysilane **227**, however the excellent stereoselectivity reported for the hydrosilylation of diphenylacetylene did not prove to be general, and a range of yields and stereoselectivities were reported. The hydrosilylation of

diphenylacetylene was also demonstrated in the presence of reducible functional groups, with aldimines, esters, amides, epoxides and nitriles all tolerated, however aldehydes, ketones and sulfoxides were competitively reduced.

Plietker reported a stereodivergent protocol for the hydrosilylation of alkynes **230** using (nitroso)iron hydride complex $[\text{FeH}(\text{CO})\text{NO}(\text{PPh}_3)_2]$ **191** as a pre-catalyst (Scheme 2.2b) [6]. In this case, the stereochemical outcome of the hydrosilylation of diphenylacetylene could be controlled to give either the (*Z*)-vinylsilane (*Z*)-**232** (*anti*-addition of Si–H) or (*E*)-vinylsilane (*E*)-**232** (*syn*-addition of Si–H) by varying the nature of the silane used. Phenylsilane **47** gave the (*Z*)-vinylsilane (*Z*)-**232**, arising from the formal *anti*-addition of the Si–H bond to the alkyne, whilst more sterically-demanding tertiary silanes **231** gave the (*E*)-vinylsilane (*E*)-**232** (*syn*-addition of Si–H) selectively. Regioselectivity in the hydrosilylation of unsymmetrical alkynes was not reported, as in this case the products were isolated as alkenes following protodesilylation.

The variation in diastereoselectivity in these reactions may be explained by isomerisation of a common intermediate. If a modified Chalk-Harrod mechanism were in operation then a (*Z*)-metallavinylsilane intermediate (*Z*)-**234** would be formed following alkyne insertion into an iron–silicon bond (Scheme 2.3). This metallavinylsilane may then undergo π -bond isomerisation via a zwitterionic carbenoid [3c] **235** or metallocyclopropene [4b, c] **236** intermediate. The hydrosilylation product (*E*)-**237** or (*Z*)-**237** may then be released following carbon–hydrogen bond formation. The diastereoselectivity of hydrosilylation using different catalysts and different silanes may therefore be explained by comparing the thermodynamic stability of metallavinylsilane intermediates (*Z*)-**234** and (*E*)-**234**, and the rate of isomerisation of the initially formed (*Z*)-metallavinylsilane intermediate (*Z*)-**234** relative to the rate of carbon–hydrogen bond formation to give hydrosilylation product (*E*)-**237** ($k_2 + k_3$ vs. k_1). These thermodynamic and kinetic parameters depend upon the electronic and steric properties of the silane, alkyne and ligands

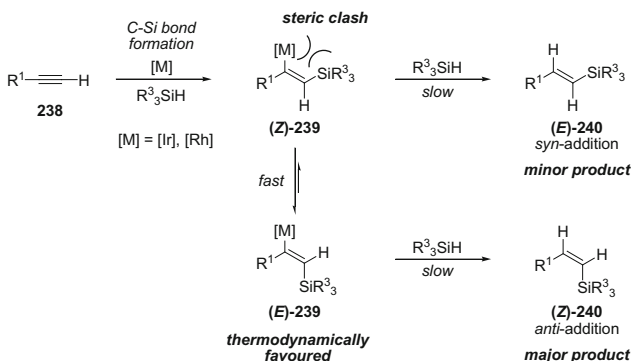


Scheme 2.3 Possible mechanism to explain the stereochemical outcome of iron-catalysed hydrosilylation of alkynes

used in the reaction, and whether carbon–hydrogen bond formation occurs by an intra- or intermolecular reaction.

According to this mechanism the most thermodynamically-favoured metallavinylsilane intermediate will be obtained if the rate of carbon–hydrogen bond formation (k_1) is slower than the rate of metallavinylsilane π -bond isomerisation, $(Z)\text{-234} \rightleftharpoons (E)\text{-234}$, ($k_2 + k_3$) [3c, 4b, c]. There are a number of factors which can increase or decrease the rate of either process. The rate of carbon–hydrogen bond formation can be slow relative to the rate of (intramolecular) π -bond isomerisation if carbon–hydrogen bond occurs by an intermolecular reaction with another equivalent of silane, through either a σ -bond metathesis or oxidative addition–reductive elimination pathway. The rate of carbon–hydrogen bond formation will also be affected by the nature of the catalyst and the structure of the silane used (e.g. silanes bearing electron-withdrawing groups undergo oxidative addition more quickly than those bearing electron-donating groups) [3c]. The rate of π -bond isomerisation between the metallavinylsilane intermediates $[(Z)\text{-234} \rightleftharpoons (E)\text{-234}]$ can be retarded by sterically demanding silanes, alkyne substituents or iron catalysts, in particular if isomerisation occurs through a sterically-congested metallocyclopropene intermediate **236**. In both of the proposed intermediates **235** and **236** there is also significant charge separation, with a build-up of negative charge α - to silicon (and β - to R^2) and a build-up of positive charge β - to silicon (and α - to R^1). Stabilisation of these intermediates by electron-donating or electron-withdrawing substituents on the alkyne (or catalyst), in combination with the ability of silicon groups to stabilise both α -anions and β -cations [7], can be used to help rationalise the relative accessibility of these reaction intermediates.

A classic example in which this mechanism has been used to justify the stereoselectivity of hydrosilylation is in iridium- and rhodium-catalysed hydrosilylation of terminal alkynes **238** [3c, 4b, c]. In both cases the thermodynamically less favoured (*Z*)-vinylsilane product (**Z**)-**240** was obtained selectively (Scheme 2.4). Carbon–hydrogen bond formation was proposed to occur through an intermolecular reaction at a sufficiently slow rate to allow efficient isomerisation between the



Scheme 2.4 Proposed mechanism to explain the stereochemical outcome of iridium- and rhodium-catalysed hydrosilylation of terminal alkynes

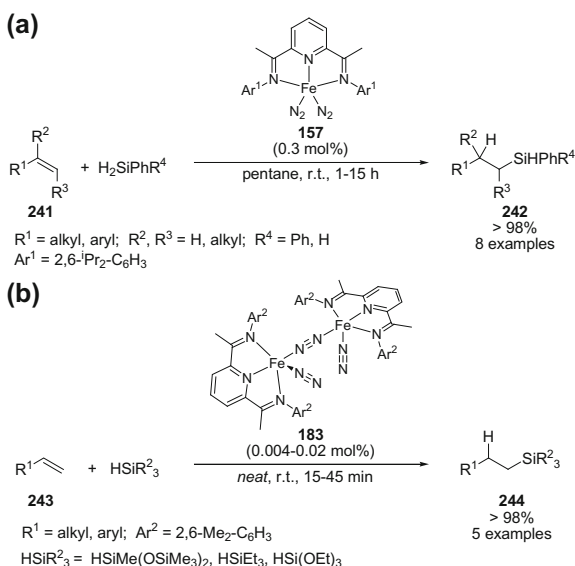
metallavinylsilane intermediates [(*Z*)-**239** $\rightleftharpoons$ (*E*)-**239**]. The initially formed metallavinylsilane intermediate (*Z*)-**239** was proposed to be destabilised by the steric clash between the iridium/rhodium catalyst and silane group. π -Bond isomerisation would relieve this steric clash and give the more thermodynamically-stable (*E*)-metallavinylsilane intermediate (*E*)-**239**. Carbon–hydrogen bond formation from this intermediate then gives the (*Z*)-vinylsilane (**Z**)-**240** as the major product.

In 2004 Chirik reported that bis(imino)pyridine (BIP) iron(0) bis(dinitrogen) complexes **157** were active for the hydrosilylation of alkenes and alkynes (Scheme 2.5a) [8]. The hydrosilylation of terminal alkenes **241** ($R^3 = H$) gave linear silane products **242** ($R^3 = H$) with complete control of regiochemistry, and with no concurrent formation of dehydrosilylation products. Whilst primary alkenes readily underwent hydrosilylation, 1,1- and 1,2-disubstituted alkenes reacted more slowly and tri-substituted alkenes were unreactive, allowing for the chemoselective hydrosilylation of less-substituted alkenes. The hydrosilylation of diphenylacetylene using phenylsilane gave the (*E*)-vinylsilane product stereoselectively (*syn*-addition of Si–H), which is in contrast to the methodologies reported by Enthaler and Plietker, where either low diastereoselectivities or selectivities in favour of the (*Z*)-vinylsilane product (*anti*-addition of Si–H) were observed when using the same substrates. Bis(imino)pyridine ligands (BIP) are known to be redox-active (non-innocent), with the potential to accept up to three electrons [9], and it was shown that the formally iron(0) complex used in these reactions was better described as a resonance hybrid between iron(0) and iron(II) (Scheme 1.22c) [10]. The high activity and selectivity reported by Chirik in this seminal report inspired much of the work in the past decade on iron-catalysed hydrogenation and hydrofunctionalisation reactions using low oxidation-state iron catalysts.

Scheme 2.5 Hydrosilylation of alkenes using bis(imino)pyridine (BIP) iron bis(dinitrogen) complexes.

a Hydrosilylation using first-generation pre-catalyst;

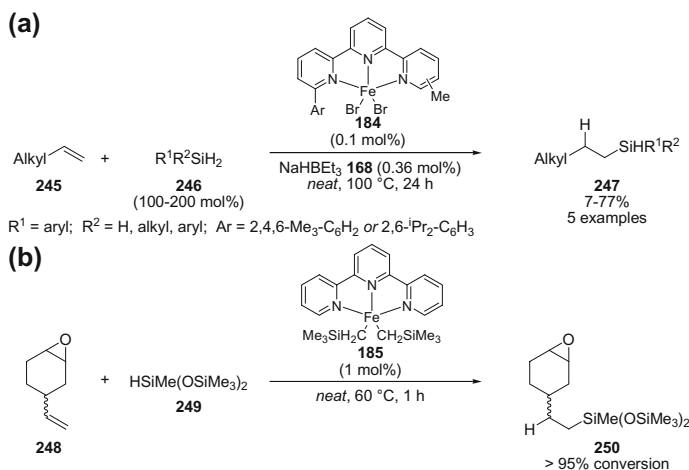
b hydrosilylation using second-generation pre-catalyst



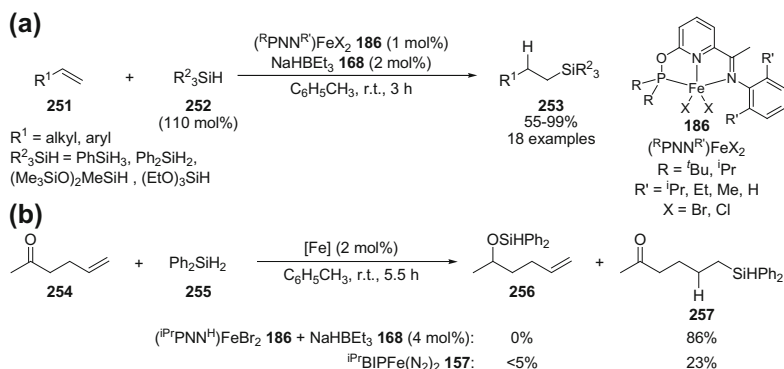
Chirik reported a second generation catalyst **183** following the synthesis and characterisation of a number of bis(imino)pyridine iron bis(dinitrogen) complexes and related low oxidation-state iron complexes [11]. Bis(imino)pyridine (BIP) complexes with less sterically-demanding *N*-aryl substituents gave improved activity for the hydrosilylation of alkenes with tertiary silanes, with catalyst turn-over frequencies of up to 100,000 mol h⁻¹ reported in some examples (Scheme 2.5b) [12]. Silicone polymers prepared using this second generation catalyst were reported to be identical to those prepared using a platinum catalyst, indicating the potential for future industrial applications.

Despite the high catalytic activities reported, bis(imino)pyridine (BIP) iron bis(dinitrogen) complexes are highly air- and moisture sensitive and challenging to prepare and store. These difficulties, in addition to an absence of published work demonstrating chemoselective alkene hydrosilylation in the presence of other reducible functionalities, has stimulated research in this field from Chirik and others.

Nakazawa and Chirik independently investigated the use of tridentate terpyridine (terpy) ligands for iron-catalysed hydrosilylation of alkenes (Scheme 2.6) [13, 14]. Nakazawa prepared a range of iron(II) chloride and bromide terpyridine complexes **184**, which were reduced in situ to give an active catalyst using sodium triethylborohydride **168** (3.6 equiv. with respect to iron) (Scheme 2.6a) [13]. Primary and secondary silanes **246** reacted with terminal alkenes **245** to give linear hydrosilylation products **247**, without competitive dehydrosilylation. High reaction temperatures and long reaction times were required however, and internal alkenes and tertiary silanes were unreactive.



Scheme 2.6 Hydrosilylation of alkenes using iron(II) terpyridine complexes as pre-catalysts. **a** Using an iron(II) halide complex **184** reduced in situ using NaHBt₃ **168**; **b** using an iron(II) dialkyl complex **185**



Scheme 2.7 Hydrosilylation of alkenes using a phosphinite-iminopyridine (PNN) iron complex as pre-catalyst. **a** General reaction scheme; **b** comparison of chemoselectivity for alkene and ketone hydrosilylation using iron pre-catalysts **186** and **157**

Chirik used an alternative approach to in situ pre-catalyst activation by preparing a range of iron(II) alkyl complexes bearing terpyridine (terpy), bis(imino)pyridine (BIP) and pyridine bis(oxazoline) (Pybox) ligands [14]. Pre-catalyst activation was achieved by heating at 60 °C, and although this represented a simpler approach than the isolation of formally iron(0) complexes, the iron(II) alkyl complexes used were still highly air- and moisture sensitive. Chirik focussed on hydrosilylation using previously challenging tertiary silanes, and found that the iron(II) alkyl complexes bearing terpyridine (terpy) or bis(imino)pyridine ligands bearing small *N*-aryl substituents were effective pre-catalysts, whilst the Pybox iron(II) alkyl complex was inactive. The terpyridine iron(II) dialkyl pre-catalyst **185** was chemoselective for the hydrosilylation of an industrially relevant epoxide-containing alkene substrate, vinylcyclohexene oxide **248** (Scheme 2.6b). In contrast, substantial substrate or catalyst decomposition was observed using either the bis(imino)pyridine (BIP) iron(II) alkyl pre-catalyst or Karstedt's platinum catalyst [15].

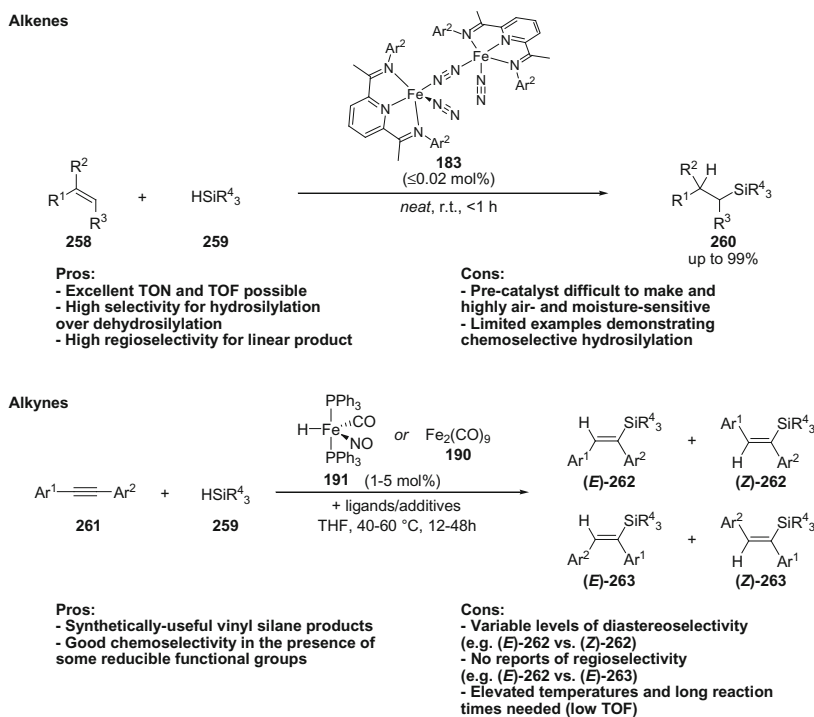
Huang and Walter have reported that phosphinite-iminopyridine (PNN) iron complexes **186** are chemoselective pre-catalysts for the hydrosilylation of alkenes in the presence of carbonyl functionalities (Scheme 2.7) [16]. The iron(II) chloride or bromide pre-catalysts were reduced in situ using sodium triethylborohydride **168** (2 equiv. with respect to iron). The chemoselective hydrosilylation of terminal alkenes **251** was demonstrated in the presence of a number of functional groups, including ethers, tertiary amines, acetals, ketones, esters and amides. Internal alkenes were unreactive however, and substrates containing nitro, nitrile, unprotected alcohol and amine, and heteroaromatic groups were not tolerated. The hydrosilylation of 5-hexan-2-one **254** using PNN iron complex **186** resulted in chemoselective hydrosilylation of the alkene, whilst the bis(imino)pyridine (BIP) iron bis(dinitrogen) complex **157**, gave a combination of alkene and ketone hydrosilylation products **257** and **256** (Scheme 2.7b). The excellent chemoselectivity for alkene

hydrosilylation in the presence of carbonyls was attributed to the electron-donating effect of the PNN ligand, rendering the iron centre less oxophilic relative to bis(imino)pyridine iron complexes.

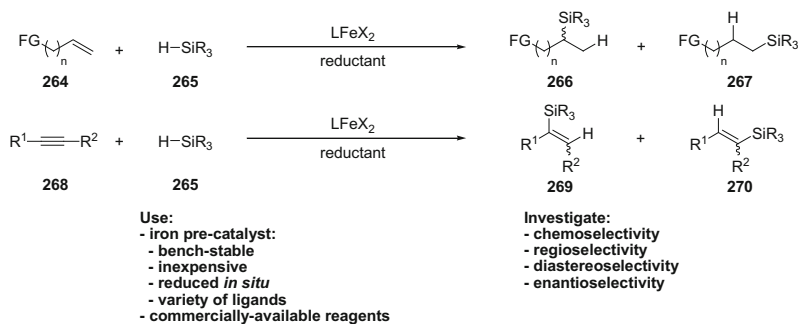
2.2 Results and Discussion

2.2.1 State of the Art at the Outset of the Project

Bis(imino)pyridine (BIP) iron bis(dinitrogen) complexes were the only highly active pre-catalysts reported for the hydrosilylation of alkenes at the outset of this project (Scheme 2.8). Low catalyst loadings and excellent turnover-frequencies had been reported, however the difficult synthesis and isolation of the formally iron(0) bis(nitrogen) complexes not only limits their practical usage, but also limits the diversity of catalyst structures that can be examined. In addition, the chemoselectivity of the reaction had not been investigated. The hydrosilylation of alkynes had been reported using iron carbonyl complexes, however elevated reaction temperatures, long reaction times and variable diastereoselectivity could be seen to affect synthetic utility.



Scheme 2.8 State of the art iron-catalysed hydrosilylation methodologies in early 2012



Scheme 2.9 Proposed development of iron-catalysed hydrosilylation methodology

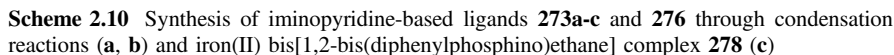
2.2.2 Project Aims

The principal objective of this work was to investigate the possibility of using the *in situ* reduction of an iron pre-catalyst for the hydrosilylation of alkenes (Scheme 2.9). This would allow the use of a bench-stable pre-catalyst and also provide a simple approach to screen a range of different ligands and pre-catalysts. Ideally the pre-catalyst and reducing reagent used should be easy to handle and be commercially-available. The developed methodology would then be applied to the hydrosilylation of a range of alkenes and alkynes focussing on the chemo-, regio- and stereoselectivity of the process.

2.2.3 Methodology Development

2.2.3.1 Ligand and Pre-catalyst Synthesis

Bis(imino)pyridine (BIP) ligands **273a-c** bearing sterically-differentiated *N*-aryl substituents were synthesised by condensation of 2,6-diacetylpyridine **271** with two equivalents of an appropriate aniline derivative **272a-c** (Scheme 2.10a) [17]. The reactions were heated at reflux in toluene with *p*-toluenesulfonic acid as a catalyst and with a Dean-Stark apparatus attached [18]. (±)-*N,N'*-Bis(pyridin-2-ylmethylene)cyclohexane-1,2-diamine **276** was synthesised by the condensation of two equivalents of 2-pyridinecarboxaldehyde **274** with (±)-*trans*-diaminocyclohexane **275** [19]. In this case molecular sieves were used to remove water from the reaction. Iron(II) bis [1,2-bis(diphenylphosphino)ethane] complex **278** was prepared according to a literature procedure from iron(II) tetrafluoroborate hexahydrate **277** and 1,2-bis(diphenylphosphino)ethane **154** in acetonitrile (Scheme 2.10c) [20, 21].



Initial studies focussed on the identification of a suitable reducing agent for the in situ activation of a bis(imino)pyridine iron(II) pre-catalyst, and provide a proof of concept (Table 2.1). The hydrosilylation of styrene **53** with phenylsilane **47** in tetrahydrofuran was attempted using a combination of iron(II) chloride **279** and bis(imino)pyridine ligand **273a** (^{iPr}BIP), which were complexed in situ. The use of ethylmagnesium bromide **280** as the in situ reductant was evaluated by systematically varying the quantity of ethylmagnesium bromide **280** used relative to iron pre-catalyst (Table 2.1, entries 1–6). The addition of between two and three equivalents of ethylmagnesium bromide **280** with respect to iron gave the linear hydrosilylation product **281** in quantitative yield within 1 h, without any dehydrosilylation products observed. The use of excess ethylmagnesium bromide **280** resulted in a reduction in catalytic activity, whilst the use of less than two equivalents did not result in any catalytic activity. Similar results were also obtained using *p*-tolylmagnesium bromide **282**, with either two or three equivalents giving an active catalyst (Table 2.1, entries 7–10). Sodium triethylborohydride **168** also produced an active catalyst, however only a moderate yield of hydrosilylation product **281** was obtained in addition to unidentified side-products (Table 2.1, entry 11). The use of *n*-butyllithium **283** resulted in complete conversion of styrene into an unidentified polymeric material, with no hydrosilylation products obtained (Table 2.1, entry 12). Organolithium reagents have been reported to initiate the

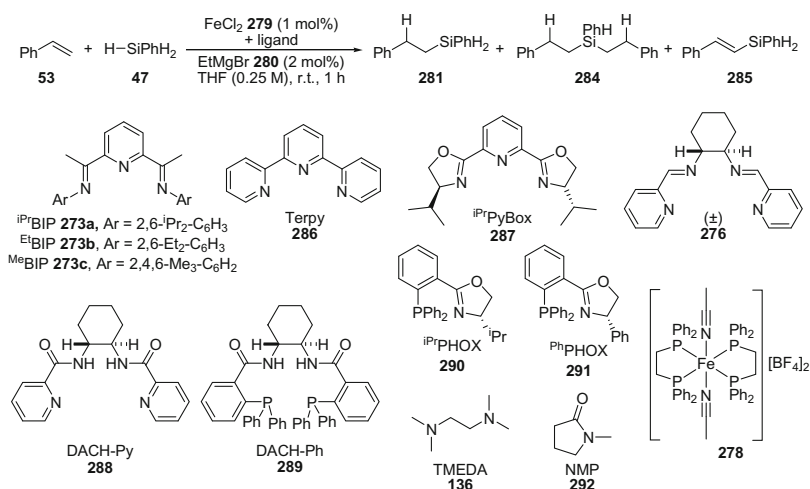
rapid polymerisation of styrene in tetrahydrofuran [22], and therefore we investigated the use of *n*-butyllithium as an activating reagent in toluene and hexane. Unfortunately, bis(imino)pyridine iron(II) dihalide complexes are insoluble in non-polar solvents, and so the same in situ complexation approach could not be used to assess hydrosilylation activity. Reduced bis(imino)pyridine iron complexes are reported to be soluble in non-polar solvents however [8], therefore pre-complexed bis(imino)pyridine iron(II) dibromide **156** was used in the hope that a soluble catalyst would be formed following in situ reduction. Using *n*-butyllithium **283** (3 equivalents with respect to iron) in either toluene or hexane now gave an active catalyst, with quantitative conversion to the linear silane **281** again observed within 1 h (Table 2.1, entries 13–14).

The hydrosilylation of styrene **53** with phenylsilane **47** was then investigated using a combination of iron(II) chloride **279** (1 mol%) and a range of ligands, activated in situ using ethylmagnesium bromide **280** (2 mol%) (Table 2.2). The bis(imino)pyridine class of ligands **279a-c** all gave hydrosilylation products in quantitative yield within 1 h (Table 2.2, entries 1–5). Reducing the size of the 2,6-substituents of the *N*-aryl group from ⁱPrBIP **273a** to ^{Et}BIP **273b** resulted in a

Table 2.1 Identification of iron-catalysed hydrosilylation methodology I: activating agent^a

$ \begin{array}{c} \text{Ph} \\ \diagdown \\ \text{C}=\text{C} \\ \diagup \\ \text{H} \end{array} \quad \text{53} \quad + \quad \text{H}-\text{SiPhH}_2 \quad \text{47} \quad \xrightarrow[\text{Activating agent, solvent, r.t., 1 h}]{\text{FeCl}_2 \text{ 279 (5 mol\%), } ^i\text{PrBIP 273a (5 mol\%)}} \quad \begin{array}{c} \text{H} \\ \\ \text{Ph}-\text{C}-\text{CH}_2-\text{SiPhH}_2 \\ \text{281} \end{array} $			
Entry	Activating agent (mol%)	Solvent	Yield (%) ^b
1	EtMgBr 280 (8)	THF	— ^c
2	EtMgBr 280 (10)	THF	>95
3	EtMgBr 280 (13)	THF	>95
4	EtMgBr 280 (16)	THF	91 ^c
5	EtMgBr 280 (18)	THF	80 ^c
6	EtMgBr 280 (20)	THF	41 ^c
7	<i>p</i> -TolylMgBr 282 (5)	THF	— ^c
8	<i>p</i> -TolylMgBr 282 (10)	THF	>95
9	<i>p</i> -TolylMgBr 282 (15)	THF	>95
10	<i>p</i> -TolylMgBr 282 (20)	THF	21 ^c
11	NaBHEt ₃ 168 (15)	THF	44 ^d
12	<i>n</i> -BuLi 283 (15)	THF	— ^c
13 ^f	<i>n</i> -BuLi 283 (15)	Toluene	>95
14 ^f	<i>n</i> -BuLi 283 (15)	Hexane	>95

^aConditions: styrene **53** (0.7 mmol), FeCl₂ **279** (5 mol%), ⁱPrBIP **273a** (5 mol%), PhSiH₃ **47** (0.7 mmol), activating agent (5–20 mol%), solvent (0.25 M), r.t. 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; ^cRemaining mass balance accounted for by styrene; ^dUnidentified side-products obtained (~25 %); ^e¹H NMR Spectra broad, no starting material or product; ^fPre-complexed ⁱPrBIPFeBr₂ **156** (5 mol%) used in place of FeCl₂ **279** and ⁱPrBIP **273a**

Table 2.2 Identification of iron-catalysed hydrosilylation methodology II: ligands^a

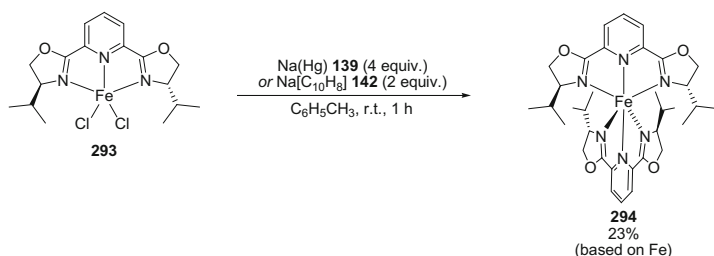
Entry	Ligand/Complex (mol%)	PhSiH ₃ mol%	Yield (%) ^b		
			281	284 ^c	285
1	iPrBIP 273a (1)	100	>95	–	–
2	EtBIP 273b (1)	100	60	40	–
3	EtBIP 273b (1)	110	>95	–	–
4	EtBIP 273b (1)	50	–	>95	–
5 [#]	MeBIP 273c (1)	120	10	90	–
6	None	110	–	–	–
7 ^d	EtBIP 273b (1)	110	–	–	–
8 ^c	EtBIP 273b (1)	110	>95	–	–
9	Terpy 286 (1)	110	<1	–	2
10	iPrPybox 287 (1)	110	1	–	1
11	276 (1)	110	–	–	–
12	DACH-Py 288 (1)	110	–	–	–
13	DACH-Ph 289 (1)	110	–	–	–
14	iPrPHOX 290 (1)	110	<1	–	1
15 ^d	PhPHOX 291 (1)	110	–	–	–
16	TMEDA 136 (4–20)	110	–	–	–
17	NMP 292 (4–20)	110	–	–	–
18	278 (1)	110	–	–	–

^aConditions: styrene **53** (0.7 mmol), FeCl₂ **279** (1 mol%), ligand (0.007–0.14 mmol), PhSiH₃ **47** (0.35–0.84 mmol), EtMgBr **280** (2 mol%), tetrahydrofuran (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; ^cYield of bis (hydrosilylation) product **284** based upon silane; ^dNo iron(II) chloride **279** added; ^eHigh purity iron(II) chloride **279** (99.99 %) used [23]; # = Result obtained by Dominik Frank

mixture of two hydrosilylation products (Table 2.2, entry 2). The new hydrosilylation product had formed through the reaction of the secondary silane product **281** with another equivalent of styrene to give a tertiary silane (bis-silylation product) **284**. The mono-silylation product **281** could be obtained exclusively by using 1.1 equivalents of phenylsilane **47**, whilst the bis-silylation product **284** was quantitatively formed by using 0.5 equivalents of phenylsilane **47** (Table 2.2, entries 3–4). Further reduction in the size of the 2,6-substituents of the *N*-aryl group to ^{Me}BIP **273c** gave a highly active catalyst, however a mixture of mono- and bis-silylation products **281** and **284** were obtained, even when using excess phenylsilane (Table 2.2, entry 5). This suggests that under the developed conditions, bis(imino)pyridine ligands with smaller *N*-aryl substituents form more active iron catalysts for hydrosilylation. This is in keeping with the work of Chirik using isolated bis(imino)pyridine iron bis(dinitrogen) complexes [12a]. No hydrosilylation activity was observed in the absence of either iron(II) chloride **279** or ligand (Table 2.2, entries 6–7), and the use of high purity iron(II) chloride **279** (99.99%) [23] in combination with bis(imino)pyridine ligand **273b** (^{Et}BIP) gave the hydrosilylation product **281** in quantitative yield, attesting to the catalytic activity of iron (Table 2.2, entry 8).

A selection of commercially-available, or easily prepared, bi-, tri- and tetradentate nitrogen- and phosphorous-based ligands were applied in the reaction (Table 2.2, entries 9–17). Iron(II) halide salts do not readily form complexes with phosphine ligands, and therefore the pre-formed iron(II) bis[1,2-bis(diphenylphosphino)ethane] complex **278** was used (Table 2.2, entry 18). None of the ligands or complexes tested were effective for the hydrosilylation of styrene, with only very low yields obtained in some examples. Small quantities of the dehydrosilylation product **285** were also observed. In each example the majority of the mass balance was accounted for by unreacted starting material.

The low activity observed using 2,2';6',2''-terpyridine **286** (Table 2.2, entry 9) is in keeping with the results of Nakazawa, who attempted in situ activation of 2,2';6',2''-terpyridine iron(II) halide complexes using sodium triethylborohydride for the hydrosilylation of 1-octene using phenylsilane **47** [13]. Nakazawa attributed the lack of hydrosilylation activity to the formation of catalytically inactive bis(terpyridine) iron(II) complexes, [Fe(terpy)₂][FeX₄]₂ [24]. The low reactivity using the iso-propyl-substituted pyridine bis(oxazoline) ligand (^{iPr}Pybox) **287** (Table 2.2, entry 10) is also comparable to the work of Chirik, who reported that ^{iPr}Pybox iron(II) dialkyl complexes were ineffective pre-catalysts for the hydrosilylation of 1-octene using tertiary silanes [14]. Chirik has also reported that the sodium amalgam **139** or sodium naphthalenide **142** reduction of ^{iPr}Pybox iron(II) chloride complex **293** gives a catalytically inactive (^{iPr}Pybox)₂iron(0) complex **294** (Scheme 2.11) [25]. It is therefore possible that a similar (^{iPr}Pybox)₂iron(0) complex is formed following reduction using ethylmagnesium bromide, and may account for the low catalytic activity observed using ^{iPr}Pybox ligand **287**. It is worthwhile noting that the reduction of bis(imino)pyridine iron(II) chloride complexes bearing less sterically demanding ligands, such as ^{Et}BIP **273b** and ^{Me}BIP **273c**, have also been reported to give catalytically-inactive bis(ligand) iron(0) complexes following reduction with sodium amalgam [26]. Sodium naphthalenide



Scheme 2.11 Reduction of ⁱPrPybox iron(II) chloride complex **293** using sodium amalgam **139** or sodium naphthalide **142** to give catalytically-inactive (ⁱPrPybox)₂Fe(0) complex **294**

reduction of the same bis(imino)pyridine (BIP) iron(II) chloride complexes was shown to give catalytically-active bis(imino)pyridine iron(0) dinitrogen complexes [11], which may indicate that the developed in situ reduction using ethylmagnesium bromide results in reduced iron species more similar to those obtained by sodium naphthalene reduction.

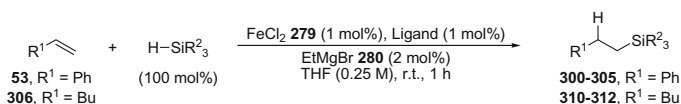
The highest activities for the hydrosilylation of styrene **53** with phenylsilane **47** had been obtained using a combination of iron(II) chloride **279** and a bis(imino)pyridine ligand (^{Et}BIP **273b** or ^{Me}BIP **273c**), reduced in situ using ethylmagnesium bromide **280** (2–3 equivalents with respect to iron). The generality of this procedure was investigated to evaluate the scope and limitations in terms of silane structure, alkene and alkyne substitution, functional group tolerance and regio-, diastereo- and enantioselectivity.

2.2.4 Silane Scope and Limitations

Using a combination of iron(II) chloride **279** (1 mol%) and bis(imino)pyridine ligand **273b** (^{Et}BIP) (1 mol%), the hydrosilylation of styrene **53** using secondary silanes gave linear hydrosilylation products in quantitative yield within 1 h (Table 2.3, entries 1–2). Tertiary silanes proved to be much less reactive, giving only poor to moderate yields of the hydrosilylation product, albeit still with complete control of regioselectivity (Table 2.3, entries 3–5). Bis(imino)pyridine ligand **273c** (^{Me}BIP) had shown high activity for the hydrosilylation of styrene using secondary silanes (Table 2.2, entry 5) and therefore this ligand was tested in the hydrosilylation of styrene using the tertiary silane dimethylphenylsilane **299**. Unfortunately no hydrosilylation product was obtained in this case (Table 2.3, entry 6).

As altering the catalyst structure had not proved effective, the alkene substrate was changed from styrene **53** to 1-hexene **306**, in the hope that the reduced steric effects would improve the efficiency of hydrosilylation. In addition, the significant difference in electronics between styrene **53** and 1-hexene **306** could also have an effect. Using a combination of iron(II) chloride **279** (1 mol%) and bis(imino)pyridine ligand **273b** (^{Et}BIP) (1 mol%), the hydrosilylation of 1-hexene **306** using

Table 2.3 Hydrosilylation of alkenes using different silanes: scope and limitations^a



Entry	R ^I	Ligand	Silane	Yield (%) ^b
1	Ph	^{Et} BIP 273b	Ph ₂ SiH ₂ 255	>95
2		^{Et} BIP 273b	Et ₂ SiH ₂ 296	>95
3 [#]		^{Et} BIP 273b	Me ₂ PhSiH 297	14
4 [#]		^{Et} BIP 273b	BnMe ₂ SiH 298	38
5 [#]		^{Et} BIP 273b	(Me ₃ SiO) ₂ MeSiH 249	5
6 [#]		^{Me} BIP 273c	Me ₂ PhSiH 299	–
7	Bu	^{Et} BIP 273b	BnMe ₂ SiH 298	78
8		^{Et} BIP 273b	(Me ₃ SiO) ₂ MeSiH 249	85
9		^{Et} BIP 273b	Me ₃ SiOSiMe ₂ H 307	86
10		^{Et} BIP 273b	Cl ₃ SiH 13	–
11		^{Et} BIP 273b	(EtO) ₃ SiH 227	–
12		^{Et} BIP 273b	Et ₃ SiH 308	–
13		^{Et} BIP 273b	^t BuMe ₂ SiH 309	–

^aConditions: alkene (0.7 mmol), FeCl₂ **279** (1 mol%), ligand (1 mol%), silane (0.7 mmol), EtMgBr **280** (2 mol%), tetrahydrofuran (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; # = Result obtained by Dominik Frank

tertiary silanes gave linear hydrosilylation products **310–312** in good to excellent yield within 1 h (Table 2.3, entries 7–9). Once again, the linear hydrosilylation product was obtained with complete control of regiochemistry. The tertiary silanes heptamethyltrisiloxane **249** and pentamethyldisiloxane **307** are structurally representative of the silicon-hydrides present in silicone fluids used for the industrial synthesis of cross-linked silicone polymers. The good hydrosilylation activity observed using these silanes may therefore indicate potential industrial applicability of this catalytic system. The hydrosilylation of 1-hexene using tertiary silanes was found not to be general however, with no hydrosilylation products observed using silanes **13**, **227**, **308** and **309** (Table 2.3, entries 10–13). This lack of reactivity may be attributed to the more varied steric (e.g. ^tBuMe₂SiH **309**) or electronic (e.g. (EtO)₃SiH **227** and Cl₃SiH **13**) properties of these silanes.

2.2.5 Alkene Scope and Limitations

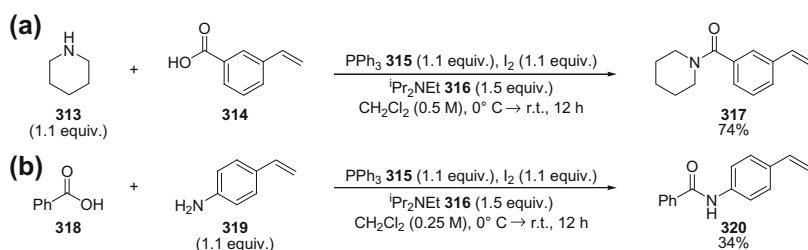
The synthetic utility and chemoselectivity of the developed methodology was investigated using a range of alkenes bearing different substitution patterns and

functional groups. The efficiency of the screening process was maximised by using functionalised substrates which were either commercially-available or could be synthesised in a single step from commercially-available compounds.

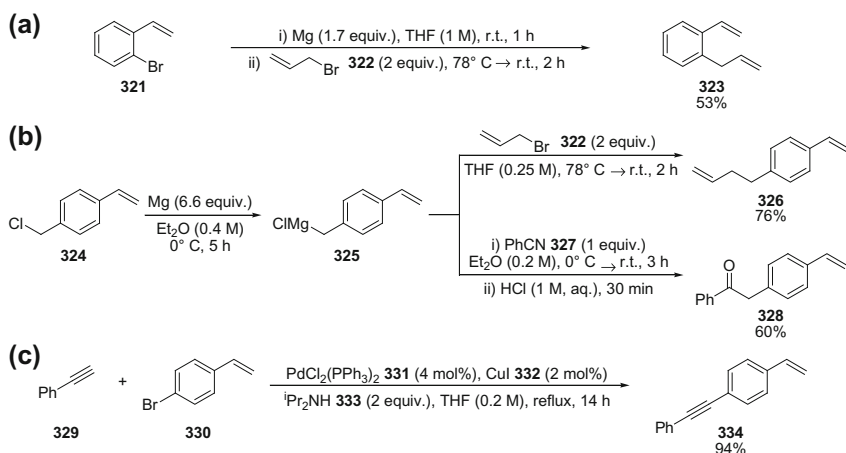
2.2.5.1 Alkene Substrate Synthesis

A wide variety of styrene derivatives are commercially-available and these were used as a starting point for the synthesis of functionalised substrates. The amide-substituted styrene derivatives **317** and **320** were synthesised by the condensation of the appropriate benzoic acids and amines, mediated by a combination of triphenylphosphine **315** and iodine (Scheme 2.12) [27].

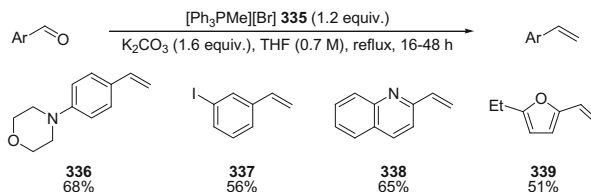
Conversion of 2-bromostyrene **321** and 4-vinylbenzyl chloride **324** into their respective Grignard reagents [28], followed by reaction with either allyl bromide **322** or benzonitrile **327** was used for the synthesis of alkene (**323** and **326**) or keto-functionalised (**328**) derivatives, respectively (Scheme 2.13a, b). A substrate



Scheme 2.12 Synthesis of ester and amide-functionalised styrene derivatives



Scheme 2.13 Synthesis of allyl-, homoallyl-, keto- and alkynyl-substituted styrene derivatives by carbon-halogen bond functionalisation reactions



Scheme 2.14 Synthesis of styrene derivatives and vinyl-substituted heteroaromatic substrates using the Wittig reaction

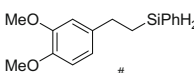
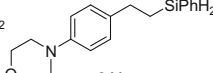
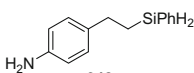
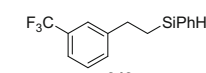
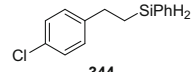
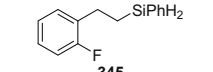
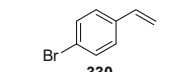
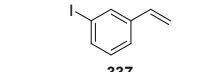
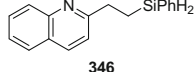
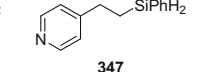
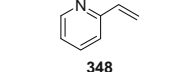
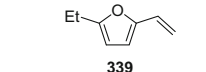
containing both alkene and alkyne functional groups **334** was synthesised by the Sonagashira cross-coupling of phenylacetylene **329** and 4-bromostyrene **330** (Scheme 2.13c) [29].

A range of benzaldehyde derivatives are also commercially-available, and can be conveniently converted to styrene derivatives using the Wittig reaction. Morpholino- and iodo-substituted styrene derivatives **336** and **337**, and vinyl-substituted heteroaromatics **338** and **339** were synthesised using methyltriphenylphosphonium bromide **335** (Scheme 2.14) [30].

2.2.5.2 Hydrosilylation of Alkenes

The hydrosilylation of sterically and electronically-differentiated alkenes and alkynes was evaluated using the optimised conditions of iron(II) chloride **279** (1 mol%), bis(imino)pyridine **273b** (^{Et}BIP) (1 mol%), ethylmagnesium bromide **280** (2 mol%) and phenylsilane **47** (110 mol%). Styrene derivatives bearing a selection of both electron-donating and electron-withdrawing substituents gave hydrosilylation products **340–345** in good to excellent yields, and without a noticeable difference in activity (Table 2.4). In each case the linear silane was obtained with excellent regioselectivity. Primary amines have been reported to poison platinum hydrosilylation catalysts [15], and therefore the efficient hydrosilylation of 4-vinylaniline using this iron catalyst is notable. Chloro- and fluorostyrene derivatives gave the linear silane products **344** and **345**, with conservation of the aryl–halide bond [31]. In contrast, bromo- and iodostyrene derivatives **330** and **337** did not undergo hydrosilylation, with only starting material and small quantities (<5 %) of styrene obtained. The protodehalogenation of these substrates may arise due to cleavage of the carbon–halogen bond by the in situ generated low oxidation-state iron catalyst [32]. Heteroaromatic substrates were tolerated to some extent. 2-Vinylquinoline underwent hydrosilylation to give the linear silane product **346** in excellent yield, however the hydrosilylation of 4-vinylpyridine was accompanied by the formation of a polymeric material, limiting the yield of silane **347** to just 26 %. The attempted hydrosilylation of 2-vinylpyridine **348** gave only polymeric material, with no silane products obtained. The hydrosilylation of 2-vinylfuran **339** was also not successful, however in this case only starting material was recovered. This suggests an inherent lack of reactivity of this alkene towards

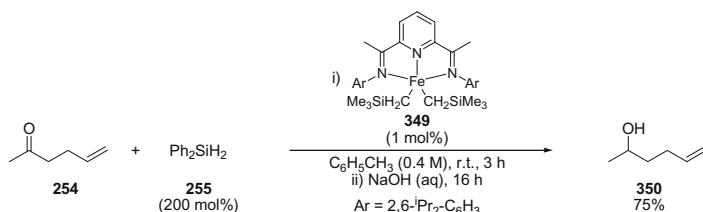
Table 2.4 Hydrosilylation of electronically-differentiated styrene derivatives and heteroaromatic substrates^a

$\text{R}-\text{CH}=\text{CH}_2 + \text{H}-\text{SiPhH}_2 \xrightarrow[\text{(110 mol\%)}]{\text{FeCl}_2 \textbf{279} (1 \text{ mol\%}), \text{Et}^t\text{BIP} \textbf{273b} (1 \text{ mol\%})} \text{R}-\text{CH}_2-\text{CH}_2-\text{SiPhH}_2$		$\xrightarrow[\text{EtMgBr} \textbf{280} (2 \text{ mol\%}), \text{THF} (0.25 \text{ M}), \text{r.t.}, 1 \text{ h}]{\text{Yield}^b \text{ (Isolated yield)}}$	
 340 # >95% (77%)	 341 >95% (90%)	 342 84% (71%)	 343 >95% (92%)
 344 >95% (85%)	 345 >95% (82%)	 330 ~3% styrene obtained	 337 ~5% styrene obtained
 346 >95%	 347 26%	 348 polymerisation	 339 N.R.

^aConditions: alkene (0.7 mmol), FeCl₂ **279** (1 mol%), Et^tBIP **273b** (1 mol%), PhSiH₃ **47** (0.77 mmol), EtMgBr **280** (2 mol%), tetrahydrofuran (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; # = Result obtained by Dominik Frank

hydrosilylation using this catalyst, however the excellent recovery of starting material indicates the possibility that remote furan functionalities may be tolerated in the reaction.

Numerous iron-catalysed methodologies have been reported for the hydrosilylation of carbon–heteroatom multiple bonds including aldehydes, ketones, imines, esters, amides and nitriles [33]. Significant to this work, Chirik has shown that a bis(imino)pyridine iron(II) dialkyl pre-catalyst **349** is effective for the hydrosilylation of aldehydes and ketones [34]. Chirik found that the hydrosilylation of 5-hexene-2-one **254** gave the secondary alcohol product **350**, with no hydrosilylation, or reduction, or the terminal alkene reported (Scheme 2.15).

**Scheme 2.15** Chemoselective hydrosilylation of the ketone functionality in 5-hexen-2-one **254** using a bis(imino)pyridine iron(II) dialkyl pre-catalyst **349**

The chemoselectivity of the developed methodology was therefore investigated for the hydrosilylation of a range of alkenes bearing functional groups containing carbon–heteroatom multiple bonds (Table 2.5). Ester-substituted alkenes were tolerated in the reaction, with linear silane products **351**, **352** and **353** obtained in quantitative yield and with no hydrosilylation of the ester was observed. Bis(imino)pyridine (BIP) iron bis(nitrogen) complexes have been shown to undergo oxidative addition into carbon–oxygen bonds of esters such as methylbenzoate and phenylacetate to give iron benzoate and phenolate complexes, respectively [35]. These complexes were catalytically inactive in hydrogenation reactions, and thus have been identified as possible decomposition products for bis(imino)pyridine iron-catalysed reactions. Under the developed hydrosilylation conditions however, no carbon–oxygen bond cleavage was observed in methylbenzoate or phenylacetate derivatives **351** and **352**. This may indicate that the rate of alkene hydrosilylation outcompetes the rate of carbon–oxygen bond cleavage, or that the reactions of isolated bis(imino)pyridine iron bis(nitrogen) complexes are not representative of the active iron catalyst formed under the developed reaction conditions.

In contrast, the amide-functionalised alkenes **317**, **320** and **354** were unreactive, with only starting material recovered in each case (Table 2.5). Similarly low activity

Table 2.5 Hydrosilylation of alkene substrates bearing reducible functional groups^a

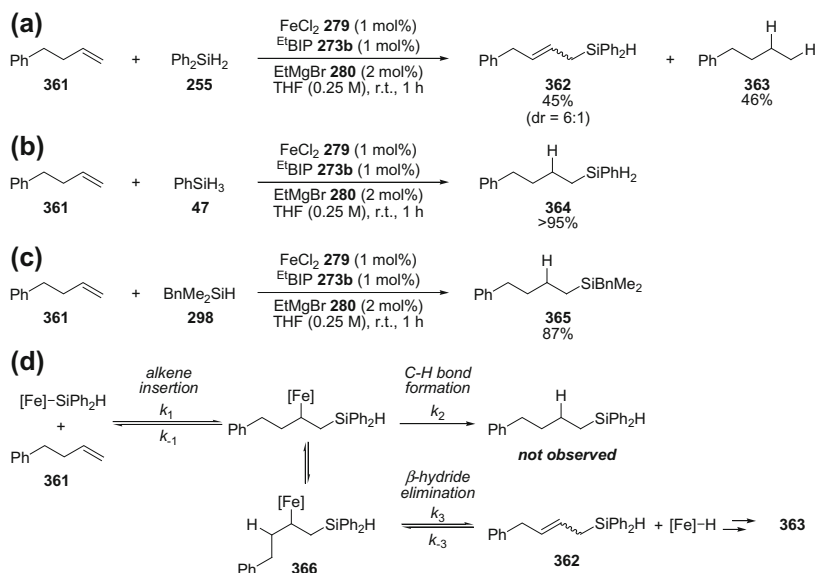
$\text{R}-\text{CH}=\text{CH}_2 + \text{H}-\text{SiPhH}_2 \xrightarrow[\text{EtMgBr } \mathbf{280} \text{ (2 mol\%), THF (0.25 M), r.t., 1 h}]{\text{FeCl}_2 \mathbf{279} \text{ (1 mol\%), } ^{\text{Et}}\text{BIP } \mathbf{273b} \text{ (1 mol\%)}}$		Yield ^b (Isolated yield)
	351 >95% (91%)	
	352 >95% (83%)	
	353 ^{c, #} >95% (67%)	
	317 N.R.	
	320 N.R.	
	354 N.R.	
	355 ^{d, e} >95% (77%)	
	356 ^{c, #} (57%) ^{f, g}	
	357 [#] polymerisation	
	358 ^{d, #} 90%	
	359 ^{c, #} >95% (85%)	
	360 41% (32%)	

^aConditions: alkene (0.7 mmol), FeCl₂ **279** (1 mol%), ^{Et}BIP **273b** (1 mol%), PhSiH₃ **47** (0.77 mmol), EtMgBr **280** (2 mol%), tetrahydrofuran (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; ^cFeCl₂ **279** (3 mol%), ^{Et}BIP **273b** (3 mol%), EtMgBr **280** (6 mol%) used; ^dFeCl₂ **279** (5 mol%), ^{Et}BIP **273b** (5 mol%), EtMgBr **280** (10 mol%) used; ^eOlefin added before the addition of EtMgBr **280**; ^f14 % of alcohol product **350** also isolated; ^gYield using quantitative NMR spectroscopy not determined; # = Result obtained by Dominik Frank

has been reported for the hydrogenation of amide-substituted alkenes using bis(imino)pyridine iron bis(nitrogen) pre-catalysts, and this may reflect strong and inhibitive binding of the amide to the iron catalyst [35b]. Ketones have also been shown to bind strongly to bis(imino)pyridine iron bis(nitrogen) complexes [35b], and it was initially found that the hydrosilylation of 1-phenyl-2-(4-vinylbenzene)-ethanone **328** gave the hydrosilylation product **355** in only low yield. Increasing the pre-catalyst loading to 5 mol% and adding the substrate immediately after pre-catalyst reduction, rather than before, gave the hydrosilylation product **355** in quantitative yield. No reduction of the ketone functionality was observed. The hydrosilylation of 5-hexene-2-one **254** was also chemoselective for alkene hydrosilylation to give the alkyl silane product **356**. In this case the ketone was also reduced at a competitive rate, however a chemoselectivity of 4:1 in favour of alkene hydrosilylation was still achieved. This is in contrast to Chirik's work using bis(imino)pyridine iron(II) dialkyl pre-catalysts (Scheme 2.15) [34], and most likely reflects a difference in the oxidation-states of the active catalysts in each case. Bis(imino)pyridine iron(II) dialkyl complexes have been suggested to give low oxidation-state iron catalysts upon thermally-activated iron-carbon bond homolysis [14], however under the room temperature reaction conditions used for aldehyde and ketone hydrosilylation an iron catalyst in an oxidation-state of +2 is more likely [34]. The attempted hydrosilylation of an aldehyde-functionalised alkene substrate, 4-vinylbenzaldehyde **357**, was unsuccessful, with only polymeric material produced.

Chemoselectivity for the hydrosilylation of alkenes in the presence of carbon-nitrogen multiple bonds was also investigated (Table 2.5). Aldimine and imino ester functionalities were both tolerated giving linear silanes **358** and **359** as the major products, however small quantities of unidentified side-products were also obtained. The hydrosilylation of 4-cyanostyrene gave a mixture of products and polymeric material, resulting in a low mass recovery. The linear silane **360** was isolated as the major product in a modest yield of 41 %. A combined total of approximately 7 % of two aldehyde products were also observed in the crude reaction mixture by ¹H NMR spectroscopy. These may have been produced by competitive hydrosilylation of the nitrile group of the starting material and product to give *N*-silylated aldimine products, which were hydrolysed upon reaction work-up.

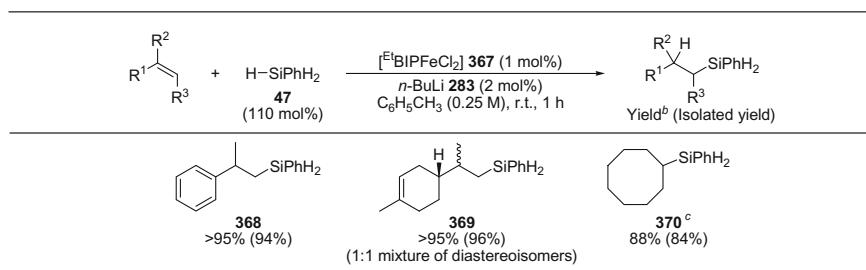
The reaction of terminal alkenes with primary silanes had consistently given hydrosilylation products (Tables 2.1, 2.2, 2.3, 2.4, 2.5), however the reaction of 4-phenylbutene **361** with diphenylsilane **255** unexpectedly gave a mixture of dehydrosilylation and hydrogenation products (Scheme 2.16a). Allylsilane **362** was obtained in close to 50 % yield, with excellent regioselectivity and in a 6:1 mixture of diastereoisomers. The hydrogenation product, butylbenzene **363**, was also obtained in a similar yield. This was in contrast to the hydrosilylation of styrene **53** using diphenylsilane **255** which had been found to give the hydrosilylation product **300** (Table 2.3, entry 1). The selectivity for dehydrosilylation in the reaction between 4-phenylbutene **361** and diphenylsilane **255** also could not be attributed to a property specific to 4-phenylbutene, as reaction with primary and tertiary silanes gave the hydrosilylation products **364** and **365**, with no dehydrosilylation products



Scheme 2.16 Hydrosilylation of 4-phenylbutene **361** using primary, secondary and tertiary silanes

obtained (Scheme 2.16b, c). Although the source of this intriguing selectivity has not been identified, these results suggest that a ‘modified Chalk-Harrod’ mechanism [1c, 2–4] of hydrosilylation may be in operation. The formation of the allylsilane product **362** can be explained by alkene insertion into an iron–silicon bond, followed by β -hydride elimination (Scheme 2.16d). The high selectivity observed for dehydrosilylation can be explained if the rate of β -hydride elimination (k_3) is significantly faster than the rate of carbon–hydrogen bond formation (k_2) to give the hydrosilylation product. The iron–hydride species formed may then react with another equivalent of alkene to give the hydrogenation product **363**. The same product distribution cannot be explained by a mechanism in which alkene insertion into an iron–hydride bond takes place.

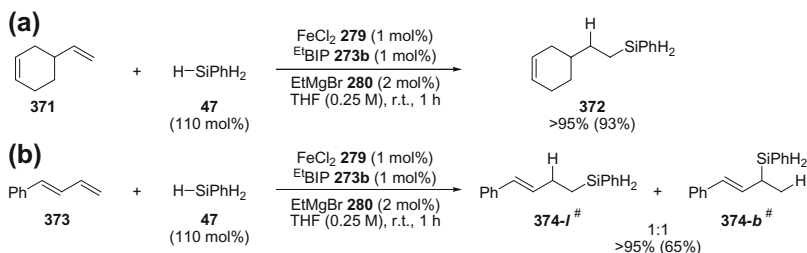
The scope and limitations of the methodology for the hydrosilylation of more highly-substituted alkenes was then investigated. Unfortunately, 1,1- and 1,2-disubstituted alkenes did not undergo hydrosilylation using the developed reaction conditions. It was rationalised that in comparison to primary alkenes these more sterically hindered alkenes may bind less favourably to iron, and thus coordination of the tetrahydrofuran solvent may become competitive with substrate binding. The hydrosilylation of 1,1- and 1,2-disubstituted alkenes was therefore attempted in toluene solution, using pre-complexed bis(imino)pyridine iron(II) chloride pre-catalyst EtBIPFeCl_2 **367** (1 mol%) and *n*-butyllithium **283** as in situ reductant (2 mol%) (Table 2.6). Under the modified conditions, α -methylstyrene

Table 2.6 Hydrosilylation of 1,1- and 1,2-disubstituted alkenes^a

^aConditions: alkene (0.7 mmol), ^{Et}BIPFeCl₂ **367** (1 mol%), PhSiH₃ **47** (0.77 mmol), *n*-BuLi **283** (2 mol%), toluene (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; ^cReaction in neat cyclooctene

and (*R*)-(+)-limonene both underwent hydrosilylation to give linear silanes **368** and **369** in excellent yield, with the latter obtained as a 1:1 mixture of diastereoisomers. Cyclooctene also underwent hydrosilylation, however silane **370** was obtained in only a modest yield of 24 %. Switching from toluene to neat cyclooctene improved hydrosilylation activity further, with the cyclooctyl silane product **370** obtained in an 88 % yield within 1 h.

Due to the low propensity of 1,2-disubstituted alkenes to undergo hydrosilylation in tetrahydrofuran, diene substrates **371** and **373** were used in the hope of chemoselective hydrosilylation of the terminal alkene. 4-Vinylcyclohexene **371** gave the linear silane **372** in excellent yield, with no competitive reduction of the internal alkene observed (Scheme 2.17a). The terminal alkene of *trans*-1-phenyl-1,3-butadiene **373** also underwent chemoselective hydrosilylation, however in this case a 1:1 mixture of regioisomers **374-I** and **374-b** were formed (Scheme 2.17b). This is the only reported example of an iron-catalysed hydrosilylation in which the hydrosilylation of a terminal alkene has given a secondary silane product.



[#] = Result obtained by Dominik Frank

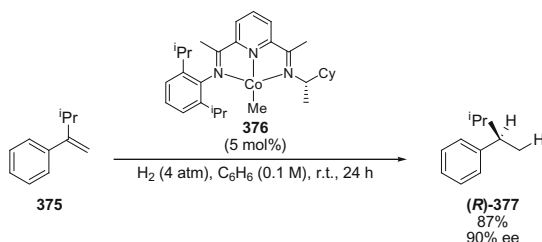
Scheme 2.17 Chemoselective hydrosilylation of the terminal alkene of diene substrates **371** and **373**

Hydrosilylation of 1,1-Disubstituted Alkenes Using Enantiopure Bis(imino)pyridine Iron(II) Pre-catalysts

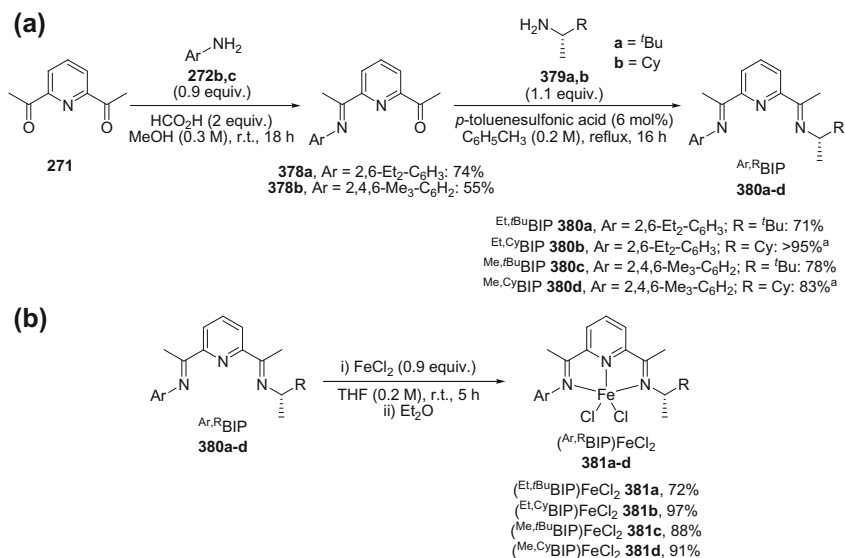
The enantioselective cobalt-catalysed hydrogenation of 1,1-disubstituted aryl alkenes was recently reported by Chirik using an enantiopure cobalt(I) bis(imino)pyridine complex **376** (Scheme 2.18) [36], however the application of these ligands in enantioselective iron-catalysed reactions was not reported. This may indicate that Chirik found only low enantioinduction using the bis(imino)pyridine iron analogues, or that the bis(imino)pyridine iron(0) bis(dinitrogen) pre-catalysts favoured by Chirik were inaccessible. As the developed hydrosilylation methodology had been successfully applied to the hydrosilylation of prochiral 1,1-disubstituted alkenes, the possibility of enantioselective iron-catalysed hydrosilylation using enantiopure bis(imino)pyridine iron complexes was investigated.

A range of enantiopure C_1 -symmetric bis(imino)pyridine ligands **380a-d** were synthesised from the sequential condensation of 2,6-diacetylpyridine **271** with an aniline derivative **272b-c**, followed by condensation with an enantiopure amine **379a-b** (Scheme 2.19a). The first condensation to give the mono(imino)pyridine intermediates **378a-b** was complicated by concurrent formation of the bis(imino)pyridine analogues, even when using substoichiometric quantities of the aniline derivative **272b-c**. The mono- and bis(imino)pyridine derivatives could not be separated by recrystallisation, however the bis(imino)pyridine impurity could be effectively removed by complexation with an equivalent of iron(II) chloride **279**. Condensation of the mono(imino)pyridine intermediates **378a-b** with (*S*)-(+)-3,3-dimethyl-2-butylamine **379a** gave crystalline bis(imino)pyridine derivatives ^{Et}*t*BuBIP **380a** and ^{Me,tBu}BIP **380c**, which could be purified by recrystallisation. In contrast, condensation of the mono(imino)pyridine intermediates **378a-b** with (*S*)-(+)-1-cyclohexylethylamine **379b** gave the bis(imino)pyridine derivatives ^{Et,Cy}BIP **380b** and ^{Me,Cy}BIP **380d** as viscous oils, and were therefore complexed with iron (II) chloride without further purification.

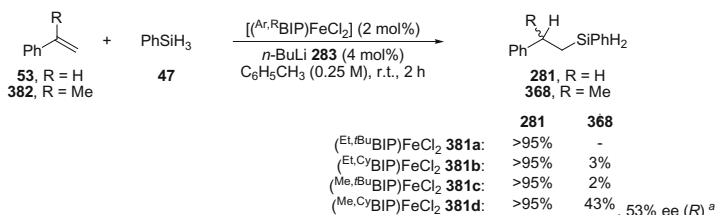
The enantiopure bis(imino)pyridine iron(II) chloride complexes were initially tested for base reactivity in the hydrosilylation of styrene **53** using phenylsilane **47** (Scheme 2.20). In each case quantitative conversion to the alkyl silane was obtained, and so the hydrosilylation of prochiral 1,1-disubstituted alkenes was investigated.



Scheme 2.18 Cobalt-catalysed enantioselective hydrogenation of prochiral 1,1-disubstituted aryl alkenes using an enantiopure cobalt(I) bis(imino)pyridine complex **376**



Scheme 2.19 Synthesis of enantiopure bis(imino)pyridine iron(II) chloride complexes **381a-d**. **a** Synthesis of enantiopure bis(imino)pyridine ligands **380a-d**. **b** Complexation with iron(II) chloride



^a Determined by chiral HPLC following conversion to 2-phenylpropanol **383**

Scheme 2.20 Hydrosilylation of styrene **53** and α -methylstyrene **382** using enantiopure bis(imino)pyridine iron(II) pre-catalysts **381a-d**

The complex bearing the most sterically-hindered enantiopure bis(imino)pyridine ligand, (Et,^tBuBIP)FeCl₂ **381a**, was inactive for the hydrosilylation of α -methylstyrene **382**. Reduction in the size of the enantiopure amine group to the cyclohexane derivative, (Et,CyBIP)FeCl₂ **381b**, gave an iron catalyst with minimal activity, with the alkyl silane **368** obtained in 3 % yield. Reduction in the size of the *N*-aryl substituents was then investigated. The iron(II) complex (Me,^tBuBIP)FeCl₂ **381c** also displayed minimal activity for hydrosilylation, however further reduction in the steric bulk of the ligand to (Me,CyBIP)FeCl₂ **381d** produced a moderately active catalyst. The hydrosilylation product **368** was obtained in 43 % yield, and 53 % enantiomeric excess. The absolute stereochemistry of the product was determined to

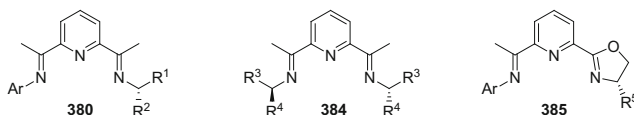


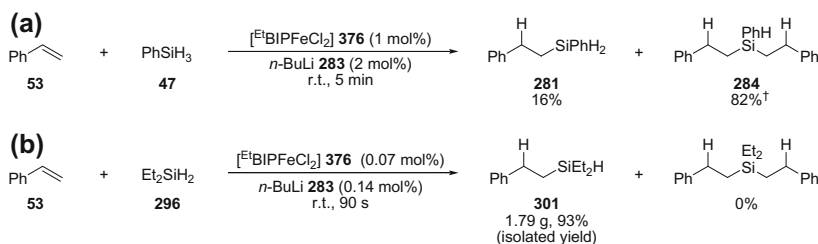
Fig. 2.1 Enantiopure C_1 - and C_2 -symmetric iminopyridine-based ligand structures which may be investigated for the development of asymmetric iron-catalysed hydrosilylation

be (*R*)-based upon chiral HPLC and optical rotation. The hydrosilylation of (*R*)-limonene was also tested with each of the enantiopure bis(imino)pyridine iron(II) pre-catalysts **368a-d**, however no hydrosilylation activity was observed.

It is apparent from this work that the more sterically-bulky bis(imino)pyridine ligands do not form a catalyst capable of the hydrosilylation of (prochiral) 1,1-disubstituted alkenes. Reducing the steric-hindrane of the ligand further may improve hydrosilylation activity, however enantioselectivity might be compromised if less sterically-hindered analogues also result in a wider binding cavity and lower facial selectivity. There is however good scope for further exploration of this class of C_1 -symmetric enantiopure ligand **380** due to the wide variety of aniline derivatives and enantiopure amines that are commercially-available (Fig. 2.1). It would also be worthwhile investigating the use of *N*-alkyl substituted C_2 -symmetric enantiopure ligands **384** for enantioselective hydrosilylation. Chirik has reported that *N*-alkyl substituted bis(imino)pyridine iron(0) bis(dinitrogen) complexes cannot be synthesised by sodium amalgam or sodium naphthalenide reduction [11, 25, 26], however the in situ reduction technique developed in this methodology may allow access to previously inaccessible catalyst structures. This work might also be extended by investigating the use of enantiopure iminopyridine oxazoline ligands **385**, following recent reports of their application in the enantioselective cobalt- [37] and iron-catalysed [38] hydroboration of 1,1-disubstituted alkenes.

Gram-Scale Hydrosilylation

The hydrosilylation reactions aimed at investigating chemo-, regioselectivity had been performed on a small scale (<1 mmol), and therefore the potential to perform the reaction on a preparative scale (10 mmol) was investigated. Performing the reaction on a larger scale also provided the opportunity to use the methodology developed for the hydrosilylation of 1,1 and 1,2-disubstituted alkenes, and conduct the reaction under ‘solvent-free’ conditions. From preliminary experiments, it was found that the hydrosilylation of styrene **53** using phenylsilane **47** was unselective towards multiple hydrosilylations, with a mixture of the mono-silylation product **281** and bis-silylation product **284** obtained (Scheme 2.21a). This indicated that the rate of hydrosilylation of styrene **53** by the secondary silane product **281** was competitive with the rate of hydrosilylation of styrene **53** by phenylsilane **47**. The hydrosilylation of styrene **53** was therefore investigated using diethylsilane **296**. Using just 0.07 mol% iron pre-catalyst $^{\text{Et}}\text{BIPFeCl}_2$ **367**, the hydrosilylation of



[†] Yield based on phenylsilane 47

Scheme 2.21 Gram-scale hydrosilylation of styrene **53** under ‘solvent-free’ conditions

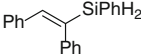
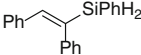
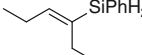
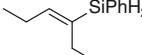
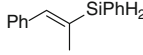
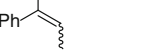
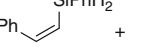
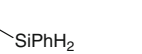
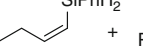
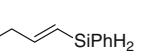
styrene **53** with diethylsilane **296** was complete within 90 s, giving the mono-silylation product **301** in quantitative conversion, and 93 % isolated yield (Scheme 2.21b). Under the ‘solvent-free’ reaction conditions it was apparent that the hydrosilylation reaction was highly exothermic, with the reaction temperature increasing almost instantaneously upon addition of the silane. The reaction was quenched when the reaction temperature ceased to increase, however the hydrosilylation reaction may have been complete much sooner. Under these unoptimised conditions, the catalyst turn-over-frequency was calculated as approximately 60,000 mol h⁻¹. Chirik has reported catalyst turn-over-frequencies of up to 100,000 mol h⁻¹ using isolated bis(imino)pyridine iron bis(dinitrogen) complexes [12a]. This demonstrates that the developed methodology provides access to iron catalysts with a similarly high activity for hydrosilylation, without the need to prepare and isolate highly air- and moisture sensitive iron complexes.

2.2.6 Hydrosilylation of Alkynes

The developed methodology was applied to the hydrosilylation of alkynes using phenylsilane (Table 2.7). Internal alkynes underwent diastereoselective hydrosilylation to give (*E*)-vinylsilane products (*syn*-addition of Si–H), whilst terminal alkynes gave a mixture of diastereoisomers, with the major (*Z*)-vinylsilane product arising from the formal *anti*-addition of the silicon–hydrogen bond.

Diaryl- and dialkyl alkynes gave (*E*)-vinylsilanes **386** and **387** in excellent yield, and with complete diastereochemical control. The stereochemistry of the vinylsilane products was confirmed by comparison with literature data, and by stereoretentive protodesilylation using tetrabutylammonium fluoride [39]. The unsymmetrically-substituted internal alkyne, 1-phenylpropyne, also underwent hydrosilylation to give a 9:1 mixture of regioisomers **β-388** and **α-388**. Both regioisomers were obtained as a single diastereoisomer, with the major regioisomer confirmed as the (*E*)-vinylsilane **β-388** by 1D nOe NMR spectroscopy. The hydrosilylation of terminal alkynes was regioselective for the addition of the silicon group to the terminal position,

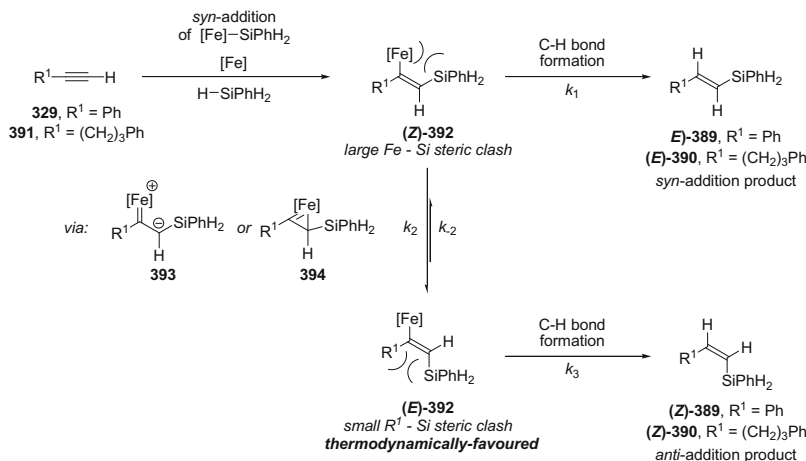
Table 2.7 Hydrosilylation of internal and terminal alkynes^a

$\text{R}^1\text{—}\text{C}\equiv\text{C—R}^2 + \text{H—SiPhH}_2 \xrightarrow[\text{EtMgBr } \mathbf{280} \text{ (2 mol\%), THF (0.25 M), r.t., 1 h}]{\text{FeCl}_2 \mathbf{279} \text{ (1 mol\%), } ^{\text{Et}}\text{BIP } \mathbf{273b} \text{ (1 mol\%)}}$		$\text{R}^1\text{—CH=CH—SiPhH}_2$	
(110 mol%)		Yield ^b (isolated yield)	
			
386		386	
>95% (90%)		>95% (90%)	
			
387 [#]		387 [#]	
>95% (95%)		>95% (95%)	
			
β-388		α-388	
>95% (87%)		9:1	
			
(Z)-389		(E)-389	
72–86% (74%)		4:1 → 8:1	
			
(Z)-390		(E)-390	
68–76% (66%)		6:1 → >100:1	

^aConditions: alkyne (0.7 mmol), FeCl₂ **279** (1 mol%), ^{Et}BIP **273b** (1 mol%), PhSiH₃ **47** (0.77 mmol), EtMgBr **280** (2 mol%), tetrahydrofuran (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; # = Result obtained by Dominik Frank

however, in contrast to internal alkynes, a mixture of diastereoisomers was obtained (Table 2.7). Phenylacetylene gave vinylsilane products (**Z**)-**389** and (**E**)-**389** in good to excellent yield, with the major product (**Z**)-**389** arising from the formal *anti*-addition of the silicon–hydrogen bond. (**Z**)-Vinylsilane (**Z**)-**389** could be reproducibly obtained in 4:1 to 8:1 diastereoselectivity. The hydrosilylation of the terminal alkyl-substituted alkyne, 5-phenylpentyn, also gave a mixture of diastereoisomers, however in this case a wider range of diastereoselectivities were observed. Under the optimised conditions, diastereoselectivities ranging from 6:1 to greater than 100:1 were obtained in favour of the (**Z**)-vinylsilane (**Z**)-**390** (formal *anti*-addition of the silicon–hydrogen bond).

The formation of the thermodynamically unfavoured (**Z**)-vinylsilane products (**Z**)-**389** and (**Z**)-**390** may be explained using the mechanisms proposed by Crabtree [4b, c] and Ojima [3c] for iridium- and rhodium-catalysed hydrosilylation (Scheme 2.22). *syn*-Silylmethallation of the terminal alkyne **329** or **391** would give the (**Z**)-metallavinylsilane intermediate (**Z**)-**392** regio- and diastereoselectively. This can undergo π -bond isomerisation via either the zwitterionic carbenoid **393** or metallocyclopropene **394** intermediate to give the (**E**)-metallavinylsilane (**E**)-**392**. If the rate of metallavinylsilane π -bond isomerisation (k_2) is significantly faster than the rate of carbon–hydrogen bond formation (k_1), then the ratio of hydrosilylation products will reflect the difference in thermodynamic stability between the (**Z**)- and (**E**)-metallavinylsilane intermediates (**Z**)-**392** and (**E**)-**392**. Assuming the iron catalyst has more steric bulk than the organic R¹ group, the (**E**)-metallavinylsilane



Scheme 2.22 Proposed mechanism for the hydrosilylation of terminal alkynes to explain diastereoselectivity for the formation of (Z)-vinylsilanes (Z)-389 and (Z)-390

intermediate (E)-392, where iron is *trans*- to the silicon group, and *cis*- to the hydrogen, should be the thermodynamically-favoured metallavinylsilane intermediate. An alternative explanation could be proposed where metallavinylsilane π -bond isomerisation is fast and reversible, but the rate of carbon–hydrogen bond formation from (E)-392 to give (Z)-389/390 (k_3), is significantly faster than the rate of carbon–hydrogen bond formation from (Z)-392 to give (E)-389/390 (k_1). This may be more significant if carbon–hydrogen bond formation occurs by an intermolecular process, and the rate of this process (k_1) is retarded by the greater steric congestion around iron in (Z)-metallavinylsilane intermediate (Z)-392 (Scheme 2.22). These justifications based upon differences in thermodynamic and kinetic parameters do not need to be mutually exclusive however, and it is likely that a combination of factors will influence the level of diastereoselectivity obtained in these reactions.

The (Z)-vinylsilane (Z)-390, obtained from the hydrosilylation of 5-phenylpentyne 391, was obtained in higher diastereoselectivity than the (Z)-vinylsilane (Z)-389 obtained from the hydrosilylation of phenylacetylene 329. This might be explained by considering the difference in thermodynamic stability of the respective (E)-metallavinylsilane intermediates (E)-392 (where $\text{R}^1 = \text{phenyl}$ or an alkyl chain). When the R^1 group is phenyl (following silylmethallation of phenylacetylene 329), there would be a larger steric clash with the silicon group in (E)-metallavinylsilane (E)-392 than that when the R^1 group is an alkyl chain (following silylmethallation of 5-phenylpentyne 391). This would result in a smaller difference in thermodynamic stability between the (E)- and (Z)-metallavinylsilane intermediates (E)- and (Z)-392 when the R^1 group is phenyl. A lower preference for (E)-metallavinylsilane (E)-392 would therefore lead to lower diastereoselectivity for (Z)-vinylsilane (Z)-389.

To investigate the inconsistent diastereoselectivities obtained for the hydrosilylation of 5-phenylpentyne, a range of variables were systematically altered,

Table 2.8 Effect of Grignard reagent loading on the diastereoselectivity of the hydrosilylation of 5-phenylpentyne^a

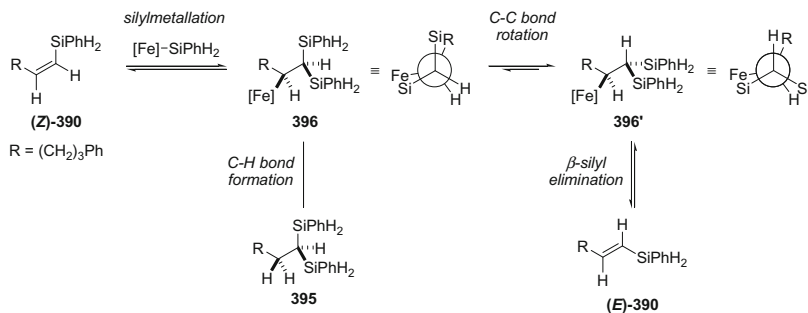
Entry	EtMgBr/mol %	Yield (%) ^{b,c}			Z: E diastereomeric ratio	Total yield of hydrosilylation products (%) ^{b,d}
		(Z)-390	(E)-390	395		
1	2	68	0.5	0	136:1	69
2	3	67	6.6	13	10:1	100
3	4	39	16	27	5:2	109

^aConditions: 5-phenylpentyne **391** (0.7 mmol), FeCl₂ **279** (1 mol%), ^{Et}BIP **273b** (1 mol%), PhSiH₃ **47** (0.77 mmol), EtMgBr **280** (2–4 mol%), tetrahydrofuran (0.25 M), r.t., 1 h; ^bYield determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard; ^cYield based on 5-phenylpentyne **391** (max yield = 100 %); ^dYield based on phenylsilane (max yield = 110 %)

including reaction concentration, equivalents of silane and amount of Grignard reagent. The only variable which resulted in a clear trend was the alteration of the amount of Grignard reagent used to activate the pre-catalyst (Table 2.8).

The standard reaction conditions gave the (*Z*)- and (*E*)-vinylsilanes (**Z**)-**390** and (**E**)-**390** in good yield and excellent diastereoselectivity for the (*Z*)-vinylsilane (**Z**)-**390** (Table 2.8, entry 1, Z:E = ~130:1). Increasing the quantity of Grignard reagent still gave the (*Z*)- and (*E*)-vinylsilanes (**Z**)-**390** and (**E**)-**390** in good yield, however the Z:E diastereoselectivity was reduced to just 10:1 (Table 2.8, entry 2). Increasing the quantity of Grignard reagent further resulted in even lower diastereoselectivity, with a preference of just 5:2 for the (*Z*)-vinylsilane (**Z**)-**390** obtained (Table 2.8, entry 3). In addition, a third product **395**, arising from the formal bis-hydrosilylation of the alkyne was obtained when increased amounts of Grignard reagent were used.

Increasing the amount of Grignard reagent used to activate the pre-catalyst resulted in an increase in the total amount of silylated products, and therefore it is possible that more active catalyst (or a more active catalyst) was formed under the reaction conditions. The higher proportion of (*E*)-vinylsilane (**E**)-**390** produced may be explained by the formation of a catalytic species with different diastereoselectivity, or through isomerisation of the (*Z*)-vinylsilane product (**Z**)-**390** to the thermodynamically-favoured (*E*)-vinylsilane (**E**)-**390** under the reaction conditions. The disilylated product **395** was presumably formed following the hydrosilylation of a vinylsilane product ((**Z**)-**390** or (**E**)-**390**). The formation of this product may also provide an indication to the source of the variable Z:E diastereoselectivities observed (Scheme 2.23). *syn*-Silylmetallation of the (*Z*)-vinylsilane product (**Z**)-**390** would give the iron alkyl intermediate **396**, which following C–H bond

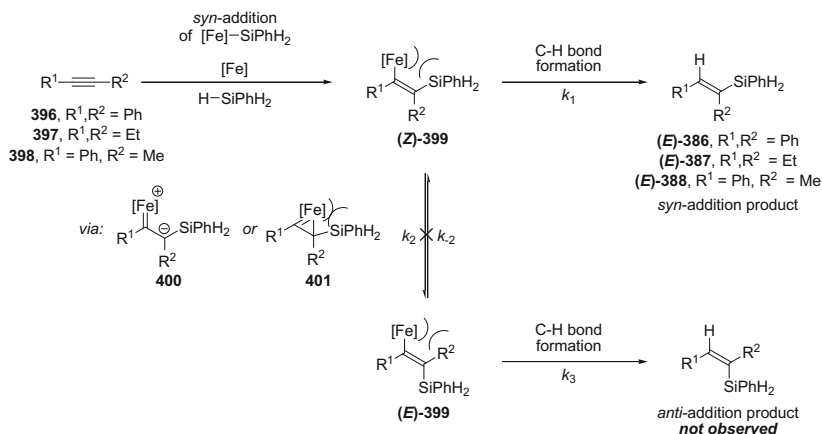


Scheme 2.23 Proposed mechanism for the isomerisation of (*Z*)-vinylsilane (**Z**)-**390** to give (*E*)-vinylsilane (**E**)-**390** via a disilylated intermediate **396**

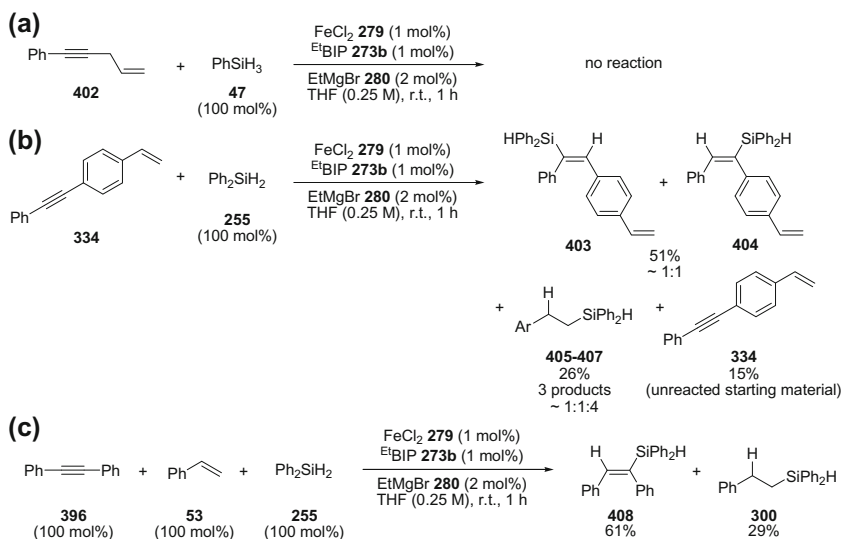
formation would give the disilylated product **395** (Scheme 2.23). Iron alkyl intermediate **396** suffers from significant steric clashes by the eclipsed arrangement of the silicon group and alkyl chain, however this steric clash can be decreased by C–C bond rotation to give iron alkyl intermediate **396'**. β-Silyl elimination from iron alkyl intermediate **396'** would then give the (*E*)-vinylsilane product (**E**)-**390**. Further evidence would be required to support this proposition. Kinetic data would allow quantification of product formation and interconversion, and application of (*Z*)-vinylsilane (**Z**)-**390** as a substrate would support of refute the proposal that isomerisation occurs under the reaction conditions.

In contrast to the hydrosilylation of terminal alkynes, the hydrosilylation of internal alkynes gave only a single diastereoisomer arising from the *syn*-addition of the silicon–hydrogen bond (Table 2.7). It is conceivable that terminal and internal alkynes may undergo hydrosilylation by different mechanisms, however the difference in diastereoselectivity can be rationalised using the same metallavinylsilane mechanism, if when using internal alkynes the rate of metallavinylsilane π-bond isomerisation (*k*₂) is significantly slower than the rate of carbon–hydrogen bond formation (*k*₁) (Scheme 2.24). This can be justified as the presence of a second organic group at the R² position will increase the steric congestion in the proposed zwitterionic carbenoid **400** or metallocyclopropene **401** intermediates, and make metallavinylsilane π-bond isomerisation less favourable. An increase in steric congestion might be expected to have a greater negative effect on the stability of the more sterically hindered metallocyclopropene **401** intermediate. These results therefore indicate that metallavinylsilane π-bond isomerisation may occur via a metallocyclopropene **401** intermediate, as originally proposed by Crabtree for rhodium-catalysed hydrosilylation [4b, c].

Having established reactivity for both the hydrosilylation of alkenes and alkynes, substrates were chosen which contained both functionalities in order to investigate the chemoselectivity between these groups (Scheme 2.25). The addition of 1-phenyl-4-pent-1-yne **402** to the iron pre-catalyst in tetrahydrofuran resulted in an immediate colour change from blue to yellow. This indicated decomplexation of the bis(imino)pyridine ligand from iron, and accordingly the subsequent



Scheme 2.24 Proposed mechanism for the hydrosilylation of internal alkynes to explain diastereoselectivity for the formation of (*E*)-vinylsilanes **(E)-386-388**



Scheme 2.25 Investigation of chemoselectivity of hydrosilylation between alkyne and alkene functionalities

hydrosilylation reaction failed (Scheme 2.25a). Ligand decomplexation was presumably caused by preferential binding between iron(II) with the excess 1-phenyl-4-pent-1-yne **402** substrate, potentially acting as a bidentate ligand.

This issue was circumvented by using 4-(phenylethynyl)styrene **334**, in which the alkene and alkyne functionalities were further apart. Initial hydrosilylation reactions using phenylsilane **47** resulted in a complex mixture of products, in which no remaining alkene functionalities were present. This complex mixture was attributed to

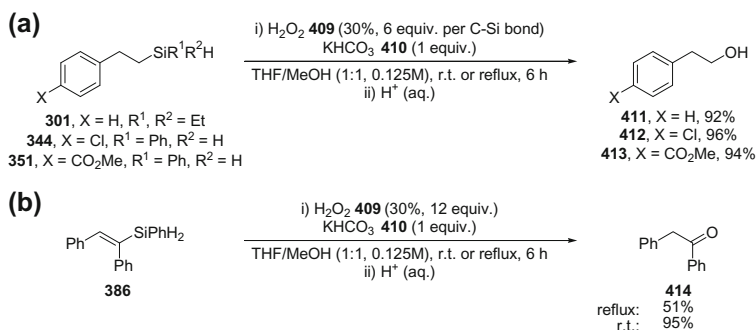
subsequent hydrosilylation reactions between the olefin and silane functionalities present in the secondary silane products and was therefore not informative about reaction chemoselectivity. This problem was partially solved by using a secondary silane, which would give a significantly less reactive tertiary silane product, however hydrosilylation using diphenylsilane **255** still gave a complex mixture of products (Scheme 2.25b). From ^1H NMR spectroscopy it was determined that three styrene derivatives were present in a 2:7:7 ratio, along with three distinguishable linear alkyl silane products in a 1:1:4 ratio. One of the styrene derivatives was identified as starting material **334**, whilst the other two products (51 % yield, approximately 1:1 ratio) were assigned as the two vinylsilane regioisomers **403** and **404**. The three alkyl silanes **405-407** could not be definitively assigned, however the major product was tentatively assigned as the product with alkyne functionality intact, with the other two, present in an approximately 1:1 ratio, assigned as being those where the alkyne had also undergone hydrosilylation. Overall this experiment indicated that alkyne hydrosilylation had occurred in 60 % of the material, whilst alkene hydrosilylation had occurred in 26 % of the material. This suggests a chemoselectivity in favour of alkyne hydrosilylation of approximately 2:1. As this product mixture had proved challenging to separate and definitively assign, diphenylacetylene and styrene were reacted with diphenylsilane in a simple competition experiment (Scheme 2.25c). Once again, chemoselectivity for alkyne hydrosilylation was observed, with vinylsilane **408** and alkylsilane **300** obtained in a ratio of approximately 2:1.

The level of chemoselectivity observed for the hydrosilylation of alkynes over alkenes could indicate that alkynes undergo hydrosilylation at a faster rate than alkenes using this catalyst. However, chemoselectivity could also arise due to a higher binding affinity between the low oxidation-state iron catalyst and the alkyne, thus preventing alkene coordination and inhibiting the rate of alkene hydrosilylation [40]. In order to delineate these possibilities, kinetic profiles for the hydrosilylation of styrene **53** and diphenylacetylene **396**, in combination and in isolation, would need to be obtained.

2.2.7 Derivatisation of Hydrosilylation Products

The majority of the alkyl and vinyl silanes produced using this methodology were secondary and tertiary silanes, and could therefore be conveniently oxidised to the corresponding alcohols or ketones, as originally described by Tamao [41]. Using hydrogen peroxide **409** and potassium bicarbonate **410** in a mixed solvent system of tetrahydrofuran and methanol, alkyl silanes **301**, **344** and **351** were oxidised to give linear alcohols **411-413** in excellent yield (Scheme 2.26a).

The original procedure recommended heating the reactions at reflux, however it was found that the alcohol products were obtained in equal yield at room temperature. The oxidation of vinyl silane **386** gave a mixture of oxidised products when the reaction was heated at reflux. These were attributed to silicon-carbon bond oxidation to give the expected ketone product **414**, followed by

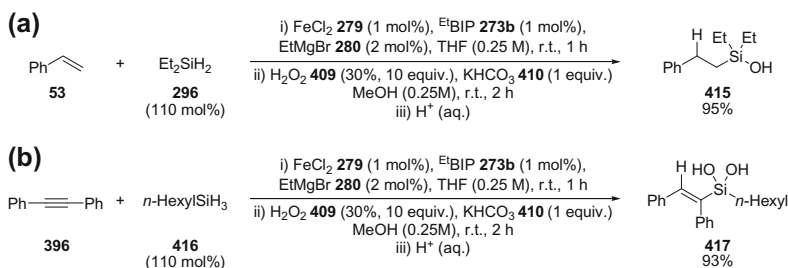


Scheme 2.26 Tamao oxidation of alkyl- and vinylsilanes **301**, **344**, **351** and **386** to give alcohol and ketone products **411–414**

Baeyer-Villiger rearrangement. The ketone product **414** could be obtained selectively by conducting the oxidation at room temperature (Scheme 2.26b).

The iron-catalysed hydrosilylation reaction was commonly conducted in tetrahydrofuran, and therefore the one-pot hydrosilylation-oxidation of alkenes was attempted by the simple addition of hydrogen peroxide **409**, potassium bicarbonate **410** and methanol following the hydrosilylation reaction. This would provide products from the formal anti-Markovnikov hydration of alkenes. Unexpectedly, the one-pot hydrosilylation-oxidation of styrene **53** did not give the linear alcohol **411**, but instead resulted in quantitative conversion to the silanol product **415** (Scheme 2.27a). This one-pot hydrosilylation-oxidation procedure was also applied to the hydrosilylation-oxidation of an alkyne, to give vinyl silanediol **417**, again in excellent yield (Scheme 2.27b). This synthetic sequence is potentially useful as alkylsilanols have numerous applications in materials chemistry [42], whilst vinylsilanols can be used as substrates in cross-coupling [43], Mizoroki–Heck [44], and carbonyl addition reactions [45].

The selectivity for silicon–hydrogen bond oxidation over silicon–carbon bond oxidation in this reaction is intriguing considering that the only difference between the isolated oxidation procedure and one-pot procedure is the presence of iron. This



Scheme 2.27 One-pot iron-catalysed hydrosilylation-oxidation of styrene **53** and diphenylacetylene **396** to give alkyl silanol **415** and vinyl silanol **417**, respectively

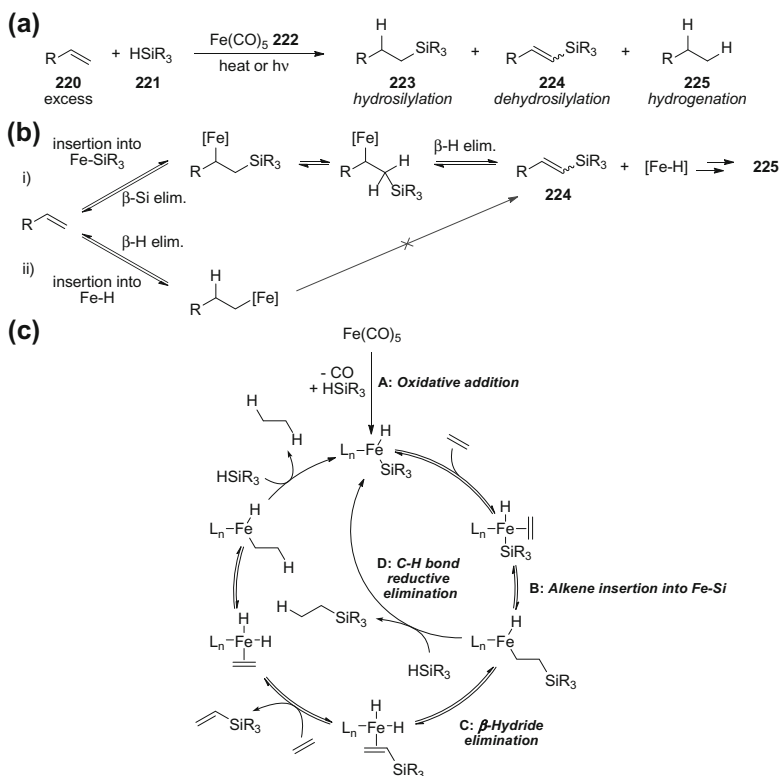
difference in reactivity may be explained by iron-catalysed decomposition of hydrogen peroxide [46], if the rate of decomposition is faster than the rate of silicon–carbon bond oxidation. Silicon–hydrogen bond oxidation may therefore occur through reaction with hydrogen peroxide at a faster rate than the rate of hydrogen peroxide decomposition, or through reaction with the hydroxyl radicals or iron-peroxide intermediates proposed during the iron-catalysed decomposition of hydrogen peroxide.

2.2.8 Preliminary Mechanistic Work

The mechanism of iron-catalysed hydrosilylation was originally studied by Wrighton, focussing on hydrosilylation reactions which used iron carbonyl pre-catalysts (Scheme 2.28a) [1b, c]. The concurrent formation of dehydrosilylation **224** and hydrogenation **225** products led Wrighton to propose that iron-catalysed hydrosilylation proceeded by alkene insertion into an iron–silicon bond (Scheme 2.28b, i), rather than insertion into an iron–hydrogen bond (Scheme 2.28b, ii). Following alkene insertion into the iron–silicon bond, β -hydride elimination would give the dehydrosilylation product **224** and produce an iron(di)hydride, which could react with a further equivalent of alkene **220** to produce the hydrogenation product **225**. The same products would not be obtained by alkene insertion into the iron–hydrogen bond, as β -hydride elimination would simply reform an alkene (Scheme 2.28b, ii).

To provide support for the proposed mechanism (Scheme 2.28c), Wrighton investigated the stoichiometric reactions of pentamethylcyclopentadienyl iron carbonyl complexes to assess the feasibility of the key steps of: **A** oxidative addition; **B** alkene insertion; **C** β -hydride elimination and **D** carbon–hydrogen bond reductive elimination (Scheme 2.29) [1c]. Near-UV irradiation of the iron(silyl)dicarbonyl complex **418** in the presence of trimethylsilane gave the iron(disilyl)hydride complex **419** (Scheme 2.29a). The formation of iron(disilyl)hydride complex **419** was proposed to occur following carbon monoxide dissociation from iron(silyl)dicarbonyl complex **418** and subsequent oxidative addition into the silicon–hydrogen bond of trimethylsilane. The formation of this complex provides evidence for the oxidative addition of coordinatively-unsaturated iron carbonyl complexes into a silicon–hydrogen bond.

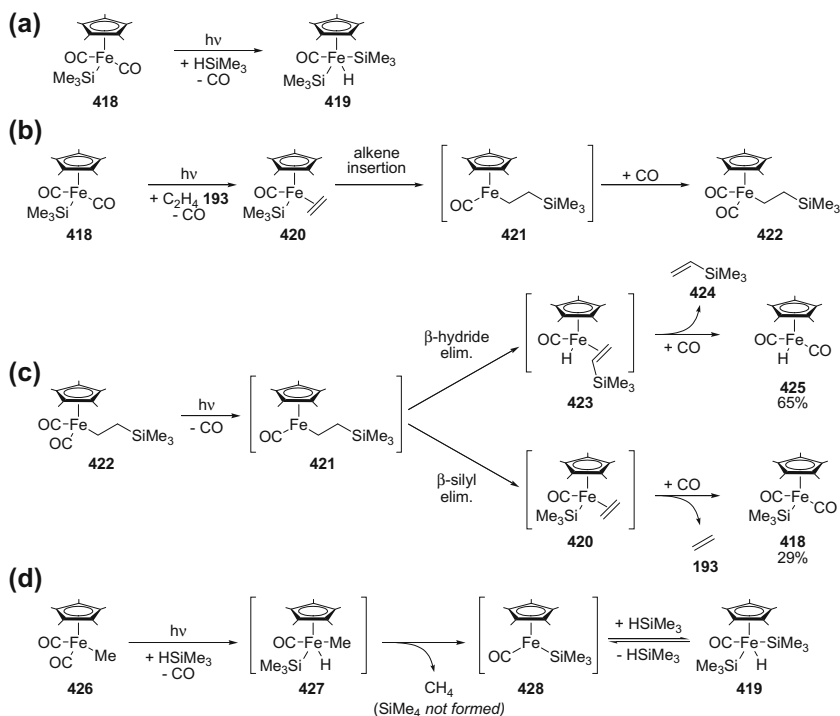
Near-UV irradiation of the iron(silyl)dicarbonyl complex **418** in the presence of ethylene **193** gave iron-alkyl complex **422**, which indicated the insertion of ethylene **193** into the iron–silicon bond (Scheme 2.29b). Near-UV irradiation of the isolated iron-alkyl complex **422** resulted in decomposition through β -hydride- and β -silyl elimination pathways to give iron(hydride)dicarbonyl **425** and iron(silyl)dicarbonyl **418** in 65 and 29 % yield, respectively (Scheme 2.29c). Vinylsilane **424** and ethylene **193** were released as by-products of these reactions. This experiment supported the proposed mechanism for the formation of dehydrosilylation products in iron-catalysed hydrosilylation, and also demonstrated that alkene insertion into



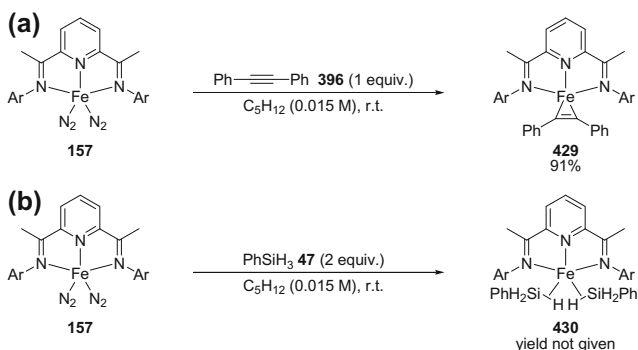
Scheme 2.28 Iron-catalysed hydrosilylation using iron pentacarbonyl as a pre-catalyst. **a** General reaction scheme. **b** Significance of alkene insertion into an iron-silicon bond for the formation of dehydrosilylation products. **c** Proposed hydrosilylation mechanism, with ‘key steps’ (**A–D**) highlighted

the iron–silicon bond was reversible. Finally, near-UV irradiation of iron(alkyl) dicarbonyl complex **426** in the presence of trimethylsilane resulted in the formation of methane and iron(disilyl)hydride complex **419** (Scheme 2.29d). The pentacoordinate iron(silyl)(hydride) intermediate **427** was proposed based upon UV-visible absorption spectroscopy. Significantly, tetramethylsilane (SiMe₄) was not observed, suggesting that carbon–hydrogen bond reductive elimination was kinetically favoured over carbon–silicon bond reductive elimination.

In-depth mechanistic studies have not been undertaken for bis(imino)pyridine iron-catalysed hydrosilylation reactions. Chirik has reported the stoichiometric reactions of bis(imino)pyridine iron bis(dinitrogen) complex **157** with diphenylacetylene **396** and phenylsilane **47** to give the isolatable acetylene- and bis(silane) complexes **429** and **430** (Scheme 2.30a, b) [8]. Both complexes were effective pre-catalysts for hydrosilylation, showing similar activity to bis(imino)pyridine iron bis(nitrogen) complexes. This demonstrates that both complexes are in equilibrium with catalytically-active species in solution, however in the absence of kinetic data further conclusions on the catalytic significance of these complexes is difficult.



Scheme 2.29 Stoichiometric reactions of pentamethylcyclopentadienyl iron carbonyl complexes to demonstrate each of the ‘key steps’ (A–D) highlighted in Scheme 2.28c. **a** Oxidative addition of HSiR_3 , **b** alkene insertion into Fe-SiR_3 , **c** β -hydride- and β -silyl elimination from iron alkyl, **d** reductive elimination of C–H bond



Scheme 2.30 Stoichiometric reactions of bis(imino)pyridine iron bis(dinitrogen) complex **157** with phenylacetylene **396** and phenylsilane **47** to give iron complexes **429** and **430**, respectively

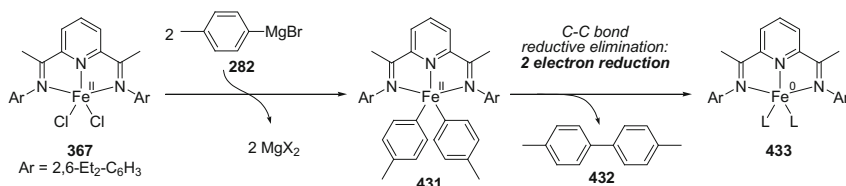
Analysis of the crystal structure of the diphenylacetylene complex **429** showed pyramidalisation of the acetylenic carbons and elongation of the carbon–carbon triple bond, consistent with considerable π -back bonding from the iron centre. The (bis)silane σ -complex **430** contained two phenylsilane molecules, each bound to iron through a silicon–hydrogen σ -bond. Single crystal X-ray analysis showed significant elongation of the coordinated silicon–hydrogen σ -bond. Although the reaction of the bis(imino)pyridine iron bis(dinitrogen) complex **157** with phenylsilane **47** had given a (bis)silane σ -complex **430**, Chirik suggested that iron-catalysed hydrosilylation may instead proceed by oxidative addition of the iron catalyst into the silicon–hydrogen bond to give an iron(silyl)(hydride) intermediate. The yield was not given for the synthesis of the (bis)silane σ -complex **430**, and so it is conceivable that an iron(silyl)(hydride) complex may have also been formed, but was not isolated.

We sought to investigate some mechanistic aspects of the developed methodology for iron-catalysed hydrosilylation. Rather than focussing on the stoichiometric reactions of isolated complexes, we chose to study catalytic reactions where analysis of the reaction products and by-products could be used to provide mechanistic insight.

2.2.8.1 Reduction of Iron(II) Pre-catalyst

Using the developed in situ pre-catalyst reduction technique, we were presented with an opportunity to calculate the average oxidation-state of the iron catalyst in the reaction by using *p*-tolylmagnesium bromide as the pre-catalyst reductant. Arylation of the iron(II) pre-catalyst $^{\text{Et}}\text{BIPFeCl}_2$ **367** by *p*-tolylmagnesium bromide **282** would give an iron(II)diaryl intermediate **431**, which following carbon–carbon bond reductive elimination would result in a two electron reduction of iron, and the formation of 4,4'-dimethylbiphenyl **432** as a by-product (Scheme 2.31) [47]. Quantification of the formation of 4,4'-dimethylbiphenyl **432** could then be used to calculate the average number of electrons that had been transferred to iron during pre-catalyst reduction (Eq. 2.1).

$$\text{Number of electrons transferred to iron} = \frac{\% \text{ Yield of } \mathbf{432} \times 2}{\text{mol\% of } ^{\text{Et}}\text{BIPFeCl}_2 \text{ } \mathbf{367} \text{ used}} \quad (2.1)$$



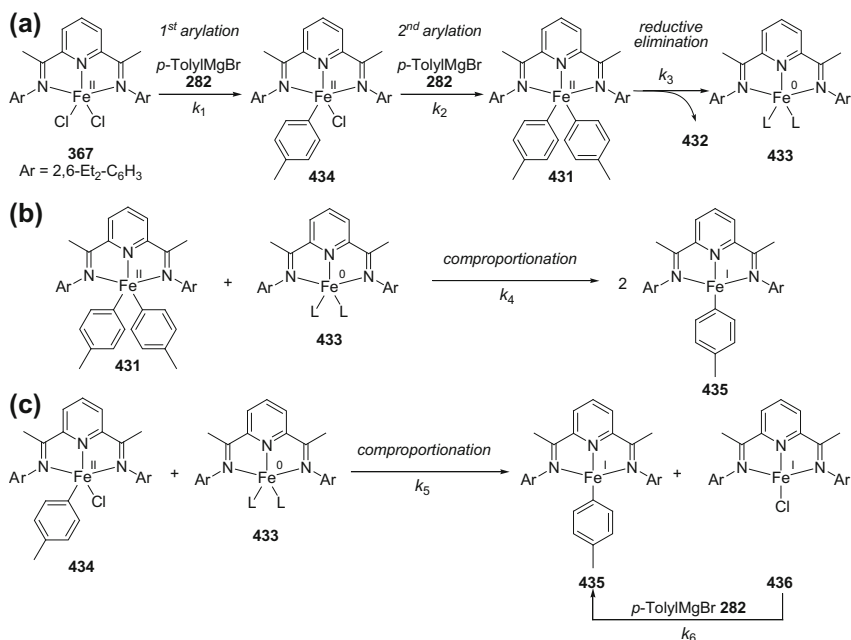
Scheme 2.31 Reduction of iron(II) pre-catalyst using *p*-tolylmagnesium bromide

In keeping with the initial reaction optimisation studies it was found that maximum catalytic activity was observed when two equivalents of *p*-tolylmagnesium bromide **282** were used (Table 2.9, entry 2). At this loading of Grignard reagent, 4,4'-dimethylbiphenyl **432** was obtained in a 2.25 % yield, corresponding to a 0.9 electron reduction of the iron(II) pre-catalyst to an average formal oxidation-state of 1.1. This was intriguing as the quantity of 4,4'-dimethylbiphenyl **432** obtained accounted for only half of the *p*-tolylmagnesium bromide that had been used. Use of 5 mol% *p*-tolylmagnesium bromide **282** (1 equivalent with respect to iron) did not give an active catalyst and resulted in the formation of only a trace amount of 4,4'-dimethylbiphenyl **432** (Table 2.9, entry 1). This indicates that more than one equivalent of *p*-tolylmagnesium bromide **282** is needed for the reductive elimination of 4,4'-dimethylbiphenyl **432** to take place, and is consistent with the proposed pre-catalyst reduction pathway (Scheme 2.31). The addition of more than two equivalents of *p*-tolylmagnesium bromide **282** with respect to iron resulted in

increasingly poor catalytic activity and the formation of more 4,4'-dimethylbiphenyl **432** (Table 2.9, entries 3–5). The lowest catalytic activity was observed using 25 mol% *p*-tolylmagnesium bromide **282** (5 equivalents with respect to iron). In this case, 4,4'-dimethylbiphenyl **432** was obtained in a 4.45 % yield, suggesting that reduction below iron(0) was unfavourable even in the presence of excess Grignard reagent (Table 2.9, entry 5).

These results suggest that the iron(II) pre-catalyst **367** was reduced to an iron(I) species following reaction with two equivalents of *p*-tolylmagnesium bromide **282**. Only one equivalent of the *p*-tolylmagnesium bromide **282** could be accounted by the formation of 4,4'-dimethylbiphenyl **432**, however pre-catalyst reduction with just one equivalent of *p*-tolylmagnesium bromide **282** did not give an active catalyst. This could indicate the formation of an iron(I) aryl complex, where the first equivalent of *p*-tolylmagnesium bromide **282** is needed for the one electron reduction of the iron(II) pre-catalyst **367**, and the second equivalent remains bound to iron.

These results can be explained if the reaction of *p*-tolylmagnesium bromide **282** with the iron(II) dichloride pre-catalyst EtBIPFeCl_2 **367** gives an iron(II)(aryl) (chloride) intermediate **434** which is arylated at a slower rate than the iron(II) dichloride complex EtBIPFeCl_2 **367** (Scheme 2.32a, $k_1 > k_2$). Therefore the addition of just one equivalent of *p*-tolylmagnesium bromide **282** results in a catalytically inactive iron(II) species **434** and the formation of only small quantities of 4,4'-dimethylbiphenyl **432**. Upon addition of a second equivalent of *p*-tolylmagnesium

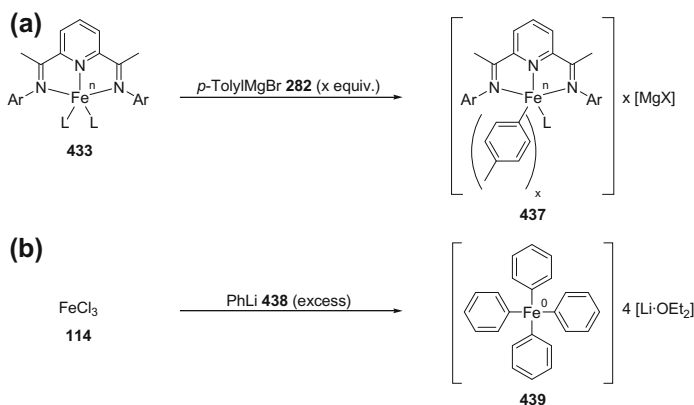


Scheme 2.32 Proposed formation of an iron(I) aryl complex **435** following the reduction of the iron(II) pre-catalyst **367** using *p*-tolylmagnesium bromide

bromide **282**, the diarylated iron(II) complex **431** is formed, which can undergo carbon–carbon bond reductive elimination to give 4,4'-dimethylbiphenyl **432** and a formally iron(0) complex **433**. Comproportionation between the formally iron(0) complex **433** and the diaryl iron(II) complex **431** would give two equivalents of the proposed iron(I) aryl complex **435** (Scheme 2.32b). The formation of an iron(I) aryl complex under the reaction conditions might suggest that the rate of comproportionation is comparable, or faster than, the rate of reductive elimination of 4,4'-dimethylbiphenyl **432** from the diaryl iron(II) complex **431** ($k_4 \geq k_3$). Alternatively, if the rate of the second arylation (k_2) is slower than all other processes, the concentration of the iron(II)(aryl)(chloride) intermediate **434** will be high. Comproportionation may therefore take place between iron(0) complex **433** and iron(II)(aryl)(chloride) intermediate **434** to give the iron(I) aryl complex **435** and the iron(I) chloride complex **436**. The iron(I) chloride complex **436** may then be converted to the iron(I) aryl complex **435** following reaction with another equivalent of *p*-tolylmagnesium bromide (Scheme 2.32c). According to either reduction pathway, two equivalents of *p*-tolylmagnesium bromide **282** would be required to give the iron(I) aryl complex **435**.

Chirik has shown that the analogous reaction of a bis(imino)pyridine iron(II) dibromide complex with two equivalents of phenyllithium also results in a one electron reduction to give a bis(imino)pyridine iron(I) phenyl complex, with concurrent formation of half an equivalent of biphenyl [49]. Chirik has also recently reported that bis(imino)pyridine iron(I) methyl complexes are suitable pre-catalysts for the hydrogenation of alkenes, without the need for any further reductant [50]. Although formally assigned as an iron(I) complex it is important to consider the redox-activity of the bis(imino)pyridine ligand. The reduction of the iron(II) pre-catalyst may in reality result in a one-electron reduction of the bis(imino)pyridine ligand to leave the iron centre in an oxidation-state of +2. Chirik has reported this effect with analogous bis(imino)pyridine iron (mono)alkyl complexes, where the electronic structures were determined to be high spin iron(II) centres coupled to bis(imino)pyridine radical anions [51].

The lower formal oxidation-states calculated when using excess *p*-tolylmagnesium bromide **282** (Table 2.9, entries 3–5) suggests that a larger quantity of the iron (0) complex **433** was formed. This could indicate that the rate of the second arylation (k_2) is the rate limiting process, and therefore an increase in the concentration of *p*-tolylmagnesium bromide **282** leads to an increase in the concentration of the diaryl iron(II) complex **431**. This would increase the rate of reductive elimination (k_3) to give iron(0) complex **433**. Based upon Chirik's work however it would be expected that an iron(0) complex, such as **433**, should also be an effective pre-catalyst for the hydrosilylation of alkenes. The reduction in catalytic activity observed upon the use of excess *p*-tolylmagnesium bromide **282** might therefore be attributed to further arylation of the iron(0) or iron(I) complexes formed to give catalytically inactive aryl-ferrate species **437** (Scheme 2.33a) [49]. Reductive elimination from iron(0) aryl complexes to give lower oxidation-state iron complexes has not been reported, and therefore coordinatively saturated aryl-ferrate species, such as **437**, may be the dominant species in solution in the presence of excess *p*-tolylmagnesium bromide



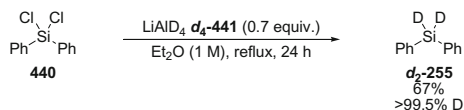
Scheme 2.33 Exhaustive arylation of iron species by aryl-metal reagents. **a** Proposed deactivation of iron (pre-)catalyst in the presence of excess *p*-tolylmagnesium bromide **282**. **b** Reported reaction of iron(III) chloride **114** with phenyllithium **438** to give iron(0) tetraphenylferrate **439** [52]

282. This is supported by the reaction of iron(III) chloride **114** with excess phenyllithium **438**, which leads to the formation of the highly arylated square-planar iron(0) tetraphenylferrate complex **439** (Scheme 2.33b) [52].

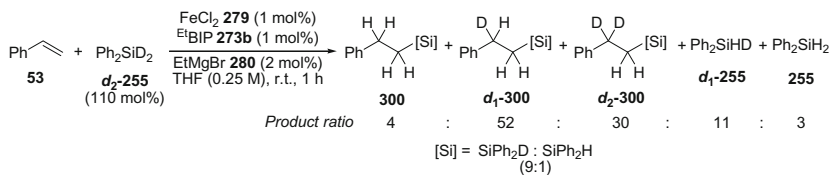
2.2.8.2 Hydrosilylation Using Deuterium-Labelled Silane

The deuterium-labelled silane, diphenyl(silane- d_2) ***d*₂-255**, was conveniently prepared by lithium aluminium deuteride ***d*₄-441** reduction of dichlorodiphenylsilane **440** (Scheme 2.34).

The hydrosilylation of styrene **53** using diphenyl(silane- d_2) ***d*₂-255** was investigated to ascertain if any useful mechanistic insight could be gained from this simple reaction (Scheme 2.35). The expected addition product ***d*₁-300** with a single deuterium incorporated at the benzylic position was obtained as the major product, however addition products with two deuteriums ***d*₂-300** and two hydrogens **300** in the benzylic position were also obtained. In addition, mono-deuterated diphenyl (silane- d_1) ***d*₁-255** and non-deuterated diphenylsilane **255** were also recovered, where deuterium–hydrogen exchange had occurred on silicon. The hydrosilylation products ***d*₀₋₂-300** were also obtained as a mixture, where the silyl group contained



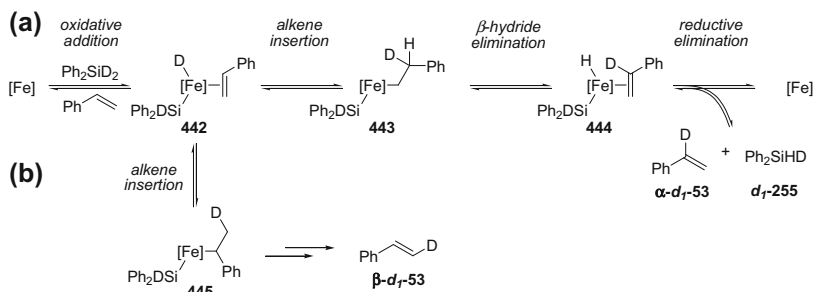
Scheme 2.34 Reduction of dichlorodiphenylsilane **440** with lithium aluminium deuteride ***d*₄-441** to give diphenyl(silane- d_2) ***d*₂-255**



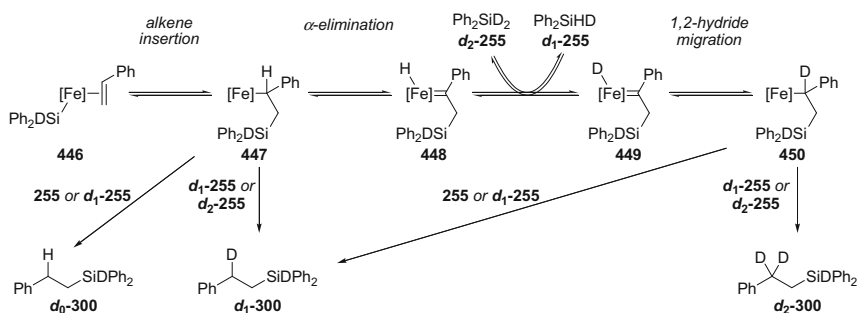
Scheme 2.35 Hydrosilylation of styrene **53** using diphenyl(silane- d_2) **d}_2\text{-255}**

either a silicon–deuterium or silicon–hydrogen bond. Significantly, ^2H NMR spectroscopy confirmed the presence of deuterium only on silicon and in the benzylic position, with no deuterium incorporation observed at the homobenzylic position (α - to the silyl group).

The observation of H–D transfer between the benzylic position of styrene and the silane can be most easily explained by reversible styrene insertion into an iron–hydride/deuteride bond and reversible oxidative addition/reductive elimination of the silane (Scheme 2.36a). Insertion of styrene into the iron–deuterium bond of iron complex **442** would give the iron–alkyl intermediate **443**, which contains both a hydrogen and deuterium atom β - to iron. β -Deuteride elimination would reform the original iron–deuteride complex **442**, however β -hydride elimination would give iron–hydride complex **444** and α -deuteriostyrene α -**d}_1\text{-53}**. Diphenyl(silane- d_1) **d}_1\text{-255}** could also be formed following silicon–hydrogen bond reductive elimination. The formation of these two products represents the formal hydrogen transfer from styrene to diphenylsilane, and deuterium transfer from diphenylsilane to styrene, and could therefore be used to account for the mixture of products obtained (Scheme 2.35). A possible weakness with this mechanism is that no deuterium incorporation was observed in the homobenzylic position of the hydrosilylation products **d}_{0,2}\text{-300}**. This would imply that alkene insertion into the iron–deuteride bond of iron complex **442** would need to be 100 % regioselective. If styrene insertion took place with the opposite regioselectivity, iron–benzyl intermediate **445** would be formed, which would lead to products with deuterium incorporation in the



Scheme 2.36 Reversible β -hydride elimination mechanism to explain hydrogen–deuterium exchange in the hydrosilylation of styrene using deuterium-labelled silane

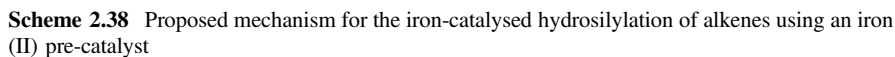


Scheme 2.37 Reversible α -elimination mechanism, via iron carbenoid intermediates **448** and **449**, to explain hydrogen–deuterium exchange in the hydrosilylation of styrene **53** using Ph_2SiD_2 d_2 -**255**

homobenzylic position (Scheme 2.36b). Iron-alkyl complexes have been shown to rearrange to the most thermodynamically-favoured species [53], and therefore it would be expected that formation of the iron-benzyl species **445**, and not iron-alkyl species **443**, would be more favourable.

An alternative proposal which involves the intermediacy of iron carbenoid species [54] could be used to account for the regioselectivity of deuterium incorporation in hydrosilylation products d_{0-2} -**300** (Scheme 2.37). Alkene insertion into the iron–silicon bond of iron–silyl complex **446** would give the iron–benzyl intermediate **447**. Carbon–hydrogen bond formation from this intermediate would give hydrosilylation product d_1 -**300**. If iron-benzyl intermediate **447** also had a deuteride ligand this product could be formed by reductive elimination, however in the absence of a deuteride ligand an intermolecular reaction with another equivalent of silane would be required to release the hydrosilylation product d_1 -**300**. Alternatively, iron-benzyl intermediate **447** may decompose by an α -elimination pathway to give the (hydrido)iron carbenoid intermediate **448**. Hydride–deuteride ligand exchange could take place by reaction with another equivalent of silane d_2 -**255**, through an oxidative addition–reductive elimination or σ -bond metathesis process. A 1,2-deuteride migration of iron carbenoid intermediate **449** would give the iron-benzyl intermediate **448** with deuterium incorporation in the benzylic position. Carbon–deuterium bond formation from this intermediate would give hydrosilylation product d_2 -**300** with two deuterium in the benzylic position. Although β -hydride elimination is probably the most commonly considered decomposition pathway for metal-alkyl species, α -elimination processes are also thermodynamically favourable through the conversion of a metal-alkyl into a relatively more stable metal carbenoid complex [55]. The proposed iron carbenoid intermediate **448** might be classified as a Fischer carbene, based upon the low oxidation-state of iron and strong π -accepting abilities of the bis(imino)pyridine ligand [56]. It would therefore be expected that the formation of the iron carbenoid complex **448** would be favoured by the stabilising effects of the adjacent aromatic ring and silane group [57].

During this work a number of observations were made that provide some mechanistic insight, and allow a possible mechanism to be proposed (Scheme 2.38). In the proposed mechanism the formal oxidation-state of iron has been given in each instance,



for iron complexes bearing a neutral bis(imino)pyridine ligand. It is important to appreciate that the bis(imino)pyridine ligand can also exist in reduced forms, meaning that the true oxidation-state of iron in these complexes could be higher.

The oxidation-state studies show that the iron(II) pre-catalyst EtBIPFeCl_2 **367** reacts with two equivalents of *p*-tolylmagnesium bromide **282** to give half an equivalent of 4,4'-dimethylbiphenyl **432**. This accounts for just half of the *p*-tolylmagnesium bromide **282** used, and indicates a one electron reduction of the pre-catalyst. These two observations together suggest the formation of the iron(I)-*p*-tolyl complex **435**. This species would still be only a pre-catalyst, and require conversion to an active catalyst. The diastereoselective hydrosilylation of terminal alkynes to give (*Z*)-vinylsilane products (Table 2.7), and the dehydrosilylation of 4-phenylbutene **361** using secondary silanes (Scheme 2.16), suggests that alkene/alkyne insertion into an iron–silicon bond takes place. It is therefore plausible that iron(I)-*p*-tolyl complex **435** is converted to an active iron(I) silyl complex **453** following reaction with an equivalent of silane. This may take place by an oxidative addition-reductive elimination pathway, via an iron(III) complex **451**, or by a σ -bond metathesis between the iron–aryl and silicon–hydrogen bonds **452**. In the latter process, the silane may first coordinate to iron to give a silane σ -bond complex, similar to those reported by Chirik [8].

As the hydrosilylation of terminal alkenes gave linear silane products exclusively using this methodology, alkene insertion into the iron–silicon bond must take place regioselectively to give the iron alkyl complex **456**. This regioselectivity could arise from a preference for alkene coordination with the large alkyl group orientated away from the large silyl group to reduce steric hindrance in iron complex **454**. Following formation of iron alkyl complex **456** a number of processes can take place. Reversible α -elimination would give the iron carbenoid complex **457**, proposed based upon the reactions using deuterium-labelled silane, whilst β -hydride elimination would give iron–hydride **458**. Alkene exchange would release the dehydrosilylation product **459** and give an iron–hydride alkene complex **460**, which could lead to the hydrogenation product **461**, following alkene insertion and reaction with a further equivalent of silane.

Iron alkyl complex **456** may alternatively react with a further equivalent of silane to give the hydrosilylation product **464**. This may take place by oxidative addition of iron into the silicon–hydrogen bond to give an iron(III) intermediate **463**. Regioselective oxidative addition of the silicon–hydrogen bond should give the iron complex with the silicon and alkyl groups *trans*- to one another in order to limit steric clashes. The resulting *cis*- relationship between the hydride and alkyl groups would be suitable for carbon–hydrogen bond reductive elimination. The strong *trans*- influence of the silicon group would be expected to weaken the iron–carbon bond and favour reductive elimination of the hydrosilylation product **464** [58]. Alternatively, carbon–hydrogen bond formation may take place by a σ -bond metathesis process [59]. Transition-metal-silane σ -complexes are well known [60], and the reaction of a bis(imino)pyridine iron bis(dinitrogen) complex has been shown to give a bis(silane) σ -complex [8], where the silicon–hydrogen bonds were significantly elongated. Silane σ -bond complexation to iron alkyl complex **456**

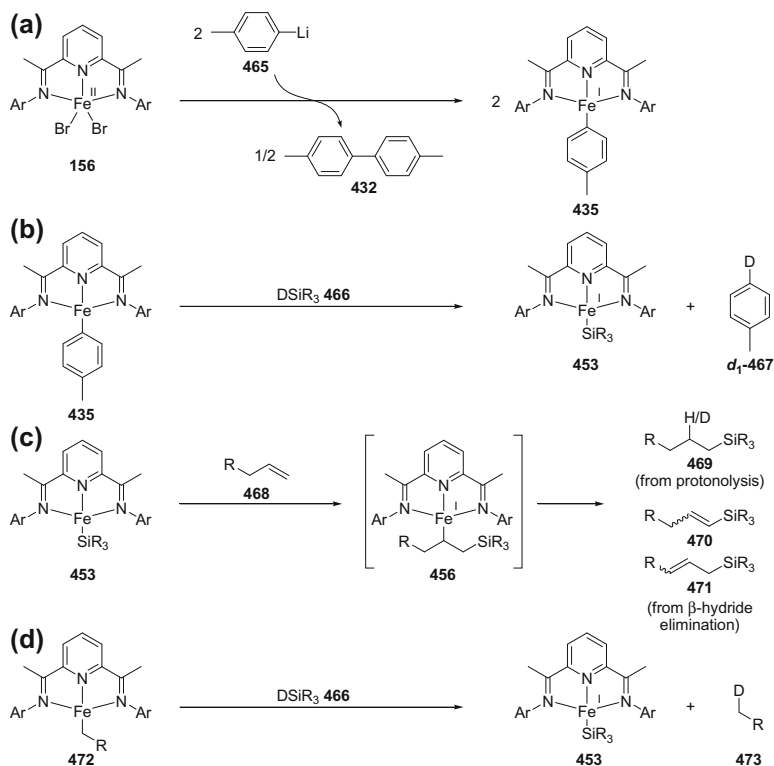
would give the iron(alkyl)(silane) complex **462**. Elongation and weakening of the coordinated silicon–hydrogen bond would activate it to σ -bond metathesis with the iron–alkyl bond to release the hydrosilylation product **464**. Although formally proposed as a redox-neutral process, it is possible that the transition-state structure of the σ -bond metathesis process may be asynchronous. This could result in a transition-state structure for σ -bond metathesis that may resemble the iron(III) intermediate **463**. The two mechanisms may therefore be distinguished by whether an iron(III) complex, such as **463**, is a reaction intermediate or a transition-state structure (local minima or saddle point on a potential energy surface).

2.2.8.4 Future Directions for Further Elucidation of the Hydrosilylation Mechanism

The mechanism of the developed methodology may be investigated further by a combination of studying the kinetic profile of catalytic reactions and by using the stoichiometric reactions of isolated iron complexes as evidence for the suggested primary steps of the catalytic cycle.

Following the kinetic profile of the hydrosilylation of alkenes will provide information about the rate of catalyst formation during pre-catalyst reduction and the rate of catalyst decomposition in the presence of different quantities of activating agents and functionalised substrates. A range of electronically-differentiated styrene derivatives were applicable in the reaction, providing an opportunity to assess the effect of these groups on the rate of reaction and perform a Hammett analysis. The hydrosilylation of electronically unsymmetrical diarylalkynes would also be interesting to assess not only the rate of reaction, but also the regio- and diastereoselectivity of the process. The source of diastereoselectivity in the hydrosilylation of terminal alkynes could also be investigated more thoroughly through a kinetic analysis approach. Significantly the diastereoselectivity of the reaction could be assessed at all points of the reaction, potentially providing evidence on whether the two diastereoisomers are formed concurrently and in a consistent ratio. It is possible that the formation of each diastereoisomer may give independent kinetic profiles, which could indicate isomerisation between the two diastereoisomers or the presence of multiple catalytically-active species in the reaction.

Key to the suggested catalytic cycle was the formation of an iron(I) aryl pre-catalyst **435**. This complex can be independently synthesised through the reaction of a bis(imino)pyridine iron(II) bromide complex **156** and *p*-tolyllithium **465** (Scheme 2.39a) [49]. The reaction of this complex with a silane could provide evidence to support or refute the suggested pre-catalyst conversion to an iron(I) silyl complex **453** (Scheme 2.39b). Using a deuterium-labelled silane may aid analysis of the reaction products and by-products. Applying both of these complexes as (pre-) catalysts in hydrosilylation reactions would provide data on the catalytic competence of the two complexes. Kinetic analysis would provide quantification of the relative induction periods. Isolation of an iron alkyl complex **456** following alkene insertion into an iron–silicon bond may be challenging due to the various decomposition

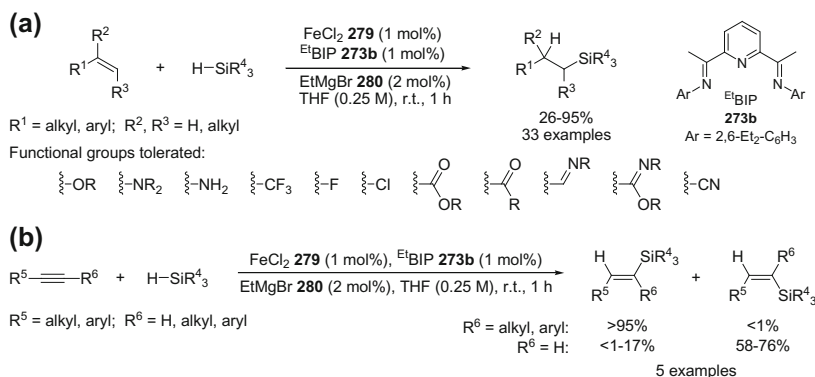


Scheme 2.39 Proposed stoichiometric reactions of isolated iron complexes to validate or disprove each step of the proposed catalytic cycle

pathways identified (Scheme 2.39c). If isolation of the iron alkyl intermediate **456** did prove overly-challenging then analysis of the decomposition products could still be sufficiently informative to provide mechanistic insight. The synthesis of iron alkyl complexes has been reported however [49], therefore if isolation of iron alkyl complex **456** was not possible, an independently synthesised iron alkyl complex **472** could be used as a model complex to validate the final step through reaction with another equivalent of deuterium-labelled silane (Scheme 2.39d).

2.3 Conclusions

A methodology for the iron-catalysed hydrosilylation of alkenes and alkynes using primary, secondary and tertiary silanes has been developed, using the in situ activation of a bench-stable bis(imino)pyridine iron(II) pre-catalyst with an organometallic reagent (Scheme 2.40). This provides a convenient approach to iron-catalysed hydrosilylation, without the need to synthesise and isolate air- and



Scheme 2.40 Iron-catalysed hydrosilylation of alkenes and alkynes using in situ reduction of an iron(II) pre-catalyst with ethylmagnesium bromide

moisture sensitive iron complexes. Oxidation of the alkyl- and vinyl silane products using hydrogen peroxide in the presence of the iron catalyst resulted in chemoselective silicon–hydrogen bond oxidation to give alkyl- and vinyl silan(edi)ol products. This serendipitously-discovered one-pot process provides simple access to these synthetically-useful products.

Terminal, 1,1- and 1,2-disubstituted alkenes underwent hydrosilylation to give linear silane products in good to excellent yield and with complete control of regioselectivity (Scheme 2.40a). A range of potentially reducible functional groups were tolerated, and catalyst turnover frequencies of up to 60,000 mol h^{−1} were recorded. The first example of enantioselective iron-catalysed hydrosilylation was obtained using an enantiopure C₁-symmetric bis(imino)pyridine iron(II) pre-catalyst. The hydrosilylation of α -methylstyrene gave the linear silane product in 43 % yield and 53 % ee. During this work, Huang reported an iron-catalysed hydrosilylation methodology displaying a similar range of functional group tolerance [16]. Higher levels of chemoselectivity for the hydrosilylation of alkenes in the presence of ketones were reported, however the methodology was only applicable to terminal alkenes, and the phosphinite-iminopyridine iron(II) pre-catalysts used were air-sensitive, and prepared by a 5-step synthesis.

The hydrosilylation of internal alkynes gave (*E*)-vinyl silanes with complete control of diastereoselectivity, whilst the hydrosilylation of terminal alkynes gave (*Z*)-vinyl silanes in a range of diastereoselectivities (*Z*:*E* = 4:1 → 100:1) (Scheme 2.40b). Further work could focus on the regio- and diastereoselectivity of the hydrosilylation of unsymmetrical di-substituted alkynes. This work would extend the synthetic utility of the process, and may provide further mechanistic insight. Previous iron-catalysed methodologies for the hydrosilylation of alkynes developed by either Enthaler [5] or Plietker [6], have only reported diastereoselectivities for the hydrosilylation of internal alkynes. These methodologies were applied to a much broader range of alkynes, however variable levels of diastereo- and regioselectivity were reported.

Preliminary mechanistic studies indicated that a one-electron reduction of the iron(II) pre-catalyst takes place to give an active catalyst in the formal oxidation-state of iron(I). The use of deuterium-labelled diphenylsilane, Ph_2SiD_2 , resulted in a mixture of deuterated- and non-deuterated hydrosilylation products, which may indicate the intermediacy of an iron-carbenoid species (on- or off-cycle). Further mechanistic studies could focus on stoichiometric reactions using isolated iron-complexes to provide support for, or refute, the proposed steps of the catalytic cycle. Kinetic analysis of the hydrosilylation reactions should be undertaken using a range of electronically-differentiated styrene- and diaryl alkyne derivatives. The hydrosilylation reaction profile using these substrates could be obtained in isolation (to provide absolute rates) and in competition experiments (to provide information about competitive binding and reaction inhibition).

Having developed a methodology in which a highly-active low oxidation-state iron catalyst was formed in situ, the potential to extend the process to other hydrofunctionalisation reactions was investigated.

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Alkynes

Greenhalgh, M.

2016, XVI, 306 p. 145 illus., 18 illus. in color., Hardcover

ISBN: 978-3-319-33662-6