Iridium(I)-Catalysed Tandem Hydrosilylation-Protodesilylation of Imines

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In the presence of alkylsilanes, the cationic Ir^I complex [{Ir[bis(pyrazol-1-yl)methane](CO)$_2$}BPh$_4$] (**1**) catalyses the reduction of a range of imines, including *N*-alkyl and *N*-aryl imines, and both aldimines and ketimines. Excellent conversions directly to the product amines are achieved rapidly at room temperature in methanol solution.

Introduction

The catalysed reduction of imines is a useful method for the synthesis of primary and secondary amines. The amine products of the reductions are often useful building blocks for biologically and synthetically important compounds.[1] Hydrosilylation of imines, in which the Si–H bond is added across the C=N bond, is an attractive alternative approach to the hydrogenation of imines as it is experimentally simple, does not require high pressure or temperature, and makes use of readily available silanes. Most of the effective catalysts for imine hydrosilylation are transition metal complexes, using metals including Rh,[2–4] Ru,[5,6] Ti,[7,8] Cu,[9] and Ni[10] however a recent report, using high throughput screening methods, also identified a number of new Sn and Zn catalysts.[11] There have been only limited reports of imine hydrosilylation employing complexes of Ir,[12] although Ir complexes are known to promote the hydrogenation of imines.[13–22] The development of catalysts which are efficient for both *N*-aryl and *N*-alkyl imine substrates, as well as aldimines and ketimines, remains an important goal for hydrosilylation research.

Recently we reported the efficient hydrosilylation of a cyclic imine, 2-methyl-1-pyrroline, catalysed by the cationic Ir^I dicarbonyl complex [{Ir(bpm)(CO)$_2$}BPh$_4$] [**1**; bpm = bis-(pyrazol-1-yl)methane], as well as the use of this catalyst for a tandem hydroamination/hydrosilylation procedure, which indicated its potential as an imine hydrosilylation catalyst.[23] We report the catalytic activity of this Ir^I complex in the hydrosilylation of imines, including acyclic and cyclic imines (Figure 1).

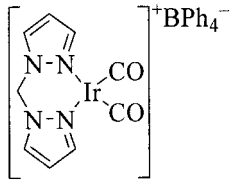

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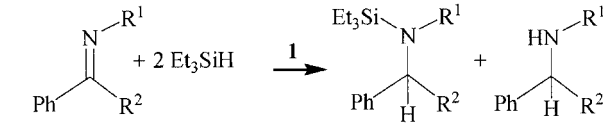
Figure 1. [{Ir(bpm)(CO)$_2$}BPh$_4$] [**1**; bpm = bis(pyrazol-1-yl)methane]

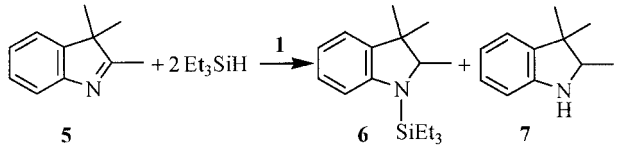
Results and Discussion

The hydrosilylation of the acyclic aldimine *N*-(benzylidene)aniline (**2a**) was explored using [{Ir(bpm)(CO)$_2$}-BPh$_4$] (**1**) as catalyst and the tertiary silane triethylsilane (Et_3SiH) as reducing agent in both [D_8]THF and CD_3OD solvents (Scheme 1). In [D_8]THF, a moderate conversion was achieved (52% after 24 h at 60 °C), giving a 1:1 mixture of the *N*-silylamine **3a** and the desilylated amine **4a**. On addition of water to this product mixture, in the presence of catalyst, almost quantitative conversion to the desilylated product was obtained in 2 h.



2a: R^1 = Ph, R^2 = H
2b: R^1 = Ph, R^2 = Me
2c: R^1 = *n*Bu, R^2 = H

3a–c **4a–c**



5 **6** **7**

Scheme 1.

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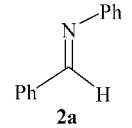
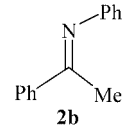
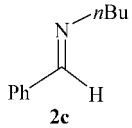
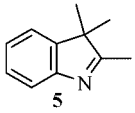
When the solvent was changed to methanol, a marked rate enhancement was observed, with quantitative conversion to the desilylated amine **4a** achieved in less than 10 min at room temperature (in air).

The efficiency of the hydrosilylation in methanol solvent for a representative set of imine substrates **2a**–**c** and **5** is given in Table 1 with 2 equivalents triethylsilane in the presence of 1 mol-% complex **1** in CD_3OD at room temperature (in air). The efficiency of conversion of the *N*-phenyl imines was higher than for the other imines studied.

Table 1. Efficiency of imine hydrosilylation using Et_3SiH, catalysed by $[Ir(bpm)(CO)_2][BPh_4]$ (**1**), in methanol solvent.

Imine	% Conversion to desilylated amines (**4**, **7**) after 12 min	Time to >98% conversion
 **2a**	quant.[a]	≤ 10 min[b]
 **2b**	quant.[a]	≤ 10 min[b]
 **2c**	66	27 min
 **5**	76	89 min

[a] Quantitative conversion. This is defined as >99% conversion. This is the time where no remaining substrate peaks are evident in the 300 MHz ^1H NMR spectrum of the reaction mixture. [b] The first NMR spectrum was recorded at 10 min, at which point these reactions had gone to completion. Therefore the actual time to completion may be significantly less than 10 min.

The reduction reaction is efficient and clean with >98% conversion to the desilylated amine product in less than 0.5 hour for all of the acyclic imine substrates examined, and only 1.5 hours for the cyclic indolenine. The silylated amine intermediates **3** were not observed in any of the reactions conducted in alcohol solution. In the absence of a metal catalyst there is only very minor conversion (<10%) of imine to amine after 30 min under identical reaction conditions.

By reducing the catalyst loading to 0.5 mol-% and recording the first NMR spectrum at 2 min a turnover frequency can be estimated for the hydrosilylation of ketimine **2b**. After 2 min the reaction had proceeded to 83% conversion, giving an initial turnover frequency of approximately 5000 h^{-1}. The results in Table 1 clearly indicate that in methanol solvent, the complex **1** is an efficient catalyst for the reduction of aldimines and ketimines, as well as *N*-aryl and *N*-alkyl imines.

Mechanistically, since only the desilylated amine is observed in methanol solvent, the reaction could proceed in a tandem fashion by hydrosilylation of the imine to give an intermediate *N*-silylamine, followed by a rapid methanolysis of the nitrogen–silicon bond. Nitrogen–silicon bonds are generally labile and silyl-protected amines are frequently deprotected with methanol or water or dilute acid. This reasoning is consistent with the fact that the *N*-silylamines are observed as the predominant reaction products when the reaction is carried out in the absence of a protic solvent. The reaction could also proceed by direct hydrogenation of the imine by hydrogen gas, produced in situ from the reaction between the silane and methanol since complex **1**, and related complexes, are known to catalyse the very rapid silanolysis of hydroxy groups in alcohols with the formation of H_2 and silyl ethers.[24] The iridium complex **1** does act as a catalyst for the direct hydrogenation of imines.[25] However, when the hydrosilylation reaction is conducted in CD_3OD as a solvent, there is no incorporation of deuterium at the imine carbon (by, ^2H NMR) and this indicates that the products are not formed by reduction of the imine with HD which would be formed in the reaction between CD_3OD and Et_3SiH. A third viable alternative is that methanol reacts directly with a metal-bound species in the cata-

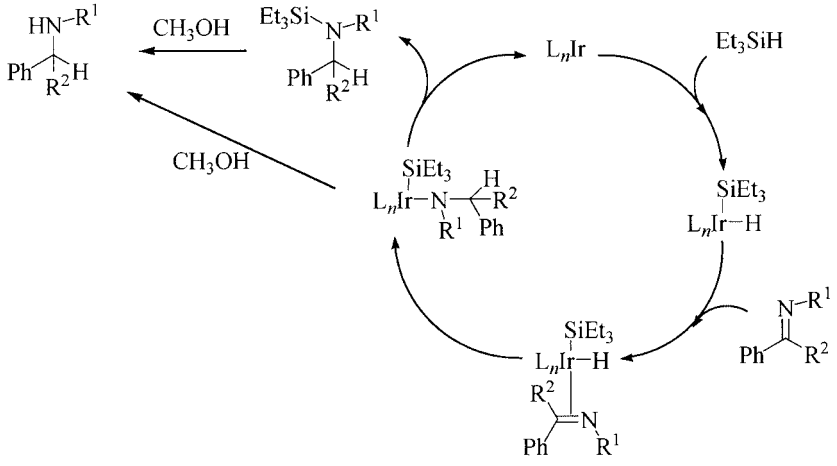


Figure 2. Proposed mechanism for hydrosilylation of an imine in methanol.

lytic cycle to give the free amine and a methoxysilane. This pathway would rationalise the marked rate enhancement which is observed in methanol if the release of product is the slow step in the reaction Scheme. A possible mechanistic Scheme is shown in Figure 2.

Experiments are underway to more clearly define the mechanism of the reaction and to determine the scope of metal complexes and silanes which are effective in the catalytic reduction of imines. The catalysed hydrogenation of imines is effective using this catalyst, giving quantitative yields, and is also being explored as an alternative means of reduction.[25]

Conclusions

In conclusion, an efficient process for the synthesis of amines using [{Ir(bpm)(CO)$_2$}BPh$_4$] (**1**) as an effective catalyst for the reduction of imines has been demonstrated. The hydrosilylation–protodesilylation of a range of imines afforded excellent conversions to the amines in short time periods on reaction in methanol. The synthesis of enantiomerically pure amines is also an important goal and studies of the enantioselective reduction of imines using related metal complexes incorporating chiral N-donor ligands are currently underway.

Experimental Section

Typical Experimental Procedure for Hydrosilylation in THF: The Ir complex **1** (3.7 mg, 5.2 μmol) and the imine **3a** (47.3 mg, 0.26 mmol) were weighed into a NMR tube fitted with a concentric Teflon valve. The tube was then evacuated and [D$_8$]THF (0.6 mL) was vacuum-transferred into the tube. Et$_3$SiH (84 mg, 0.72 mmol) was injected and the tube was frozen in liquid nitrogen before being taken to the NMR machine. After rapid thawing, the tube was inserted into the NMR probe heated to 60 °C and the reaction progress was monitored by ^{1}H NMR spectroscopy. Yields given are determined directly from the ^{1}H NMR spectra.

Typical Experimental Procedure for Hydrosilylation in MeOH: The Ir complex **1** (2.2 mg, 3.1 μmol) and the imine **3a** (56 mg, 0.31 mmol) were weighed into a 10-mL round-bottomed flask, which was then fitted with a rubber septum. CD$_3$OD (0.2 mL) was added to give a yellow suspension. A silane solution, Et$_3$SiH (74 mg, 0.64 mmol) in CD$_3$OD (0.8 mL), was injected into the flask containing the catalyst and imine. All of the solid dissolved and bubbles of gas were observed. After stirring for 5 minutes, the pressure was released through a needle, the yellow solution was transferred to the NMR tube and the progress of the reaction was monitored by ^{1}H NMR spectroscopy. The first spectrum was taken at 10 minutes after the start of the reaction, so that for the reactions in which quantitative conversion is quoted, reactions may have been complete before this time. All reactions were done at room temperature. Yields given are determined directly from the ^{1}H NMR spectra.

Acknowledgments

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[25] The Ir complex **1** (5.6 mg, 7.8 μmol) and the imine **3a** (71 mg, 0.39 mmol) were dissolved in THF (2 mL) and stirred at 60 °C in a stainless steel bomb under a hydrogen pressure of 120 psi for 20 min. The amine **4a** was formed in quantitative yield (by NMR spectroscopy).

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