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Enantioselective catalytic hydrosilylation of propiophenone with a simple combination of a cationic iridium complex and a chiral azolium salt

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ABSTRACT

This study aims to propose a simple procedure for the development of enantioselective hydrosilylation of a ketone using catalytic amounts of $[Ir(cod)_2]BF_4$ and chiral azolium salt. Previously, catalytic asymmetric hydrosilylation reactions have used *well-defined* metal-N-heterocyclic carbene (NHC) complexes. The proposed method offers an important advantage of avoiding preparation of NHC-metal species. Several reaction parameters including the amount of reductant, solvent, catalyst loading and ligand structure were evaluated. In addition, the investigation of the reaction progress as a function of time revealed that an iridium species, which was generated after 5 h of reaction time, catalyzed the stereoselective reduction with almost perfect facial selection of the ketone. An attempt to obtain a catalytic active species from the reaction of $[Ir(cod)_2]BF_4$ and chiral azolium salt has been made. The newly obtained iridium species promoted the hydrosilylation of a ketone with high yield and enantioselectivity.

1. Introduction

Controlling the stereoselectivity of asymmetric metal-mediated catalytic processes depends on the design of a versatile ligand that strongly coordinates to a metal center. In recent years, chiral N-heterocyclic carbene ligands (NHCs) have attracted considerable attention owing to their strong σ-donating capability to metals and the ability to vary the substituents on the nitrogen atom [1]. In 1996, Hermann reported the asymmetric hydrosilylation reaction of acetophenone with diphenylsilane, which was the first catalytic process where chiral induction was achieved using a chiral NHC [2]. The use of a *well-defined* metal complex seems to be ideal for the strict stereocontrol in asymmetric catalysis. In 2003, Shi achieved a breakthrough in asymmetric catalysis (98% ee) by developing a bidentate axially chiral bis(NHC)-Rh(III) complex with a 1,1′-binaphthalenyl backbone [1j, 3]. Gade and co-workers introduced a bidentate oxazoline/NHC-Rh(I) complex that was obtained through the direct linkage of heterocycles [1l, 1r, 1v, 4]. In addition to these two important works, many investigators have developed different classes of *well-defined* metal-NHC over the past two decades [5]. On the contrary, to the best of our knowledge, there is only one report on the successful enantioselective hydrosilylation using an *in-situ generated* chiral metal-NHC complex. Andrus demonstrated asymmetric hydrosilylation catalyzed by $RuCl_2(PPh_3)_2$ combined with a monodentate chiral NHC ligand that contained planar [2.2] paracyclophane in the presence of AgOTf [6].

Previously, we reported the synthesis of hydroxyamide-functionalized azolium salt **1**, a precursor of an NHC, from commercially available (*S*)-leucine (Scheme 1) [7]. From **1**, the synthesis of the *well-defined* monodentate IrCl(NHC)(cod) complex **3** was successfully achieved. This *well-defined* iridium complex catalyzed the asymmetric hydrosilylation of ketones in the presence of $AgBF_4$ to afford the corresponding optically active alcohols with high enantioselectivities (Scheme 1).

In-situ generated chiral metal complexes offer several distinct advantages over *well-defined* metal complexes [8]. Because of a quick and easy synthesis of the hydroxyamide-functionalized azolium salt, a large library of compounds can be easily obtained by varying the substituents at the NHC ligand precursor. Therefore, *in-situ generated* catalysts would allow for rapid screening and tuning of diverse chiral NHC precursors. From this viewpoint, we have investigated catalytic asymmetric hydrosilylation using an *in-situ generated* IrCl(NHC)(cod) species **3′**, and an efficient procedure for this process has also been successfully developed (Scheme 2, method A) [9]. A typical procedure includes the treatment of the

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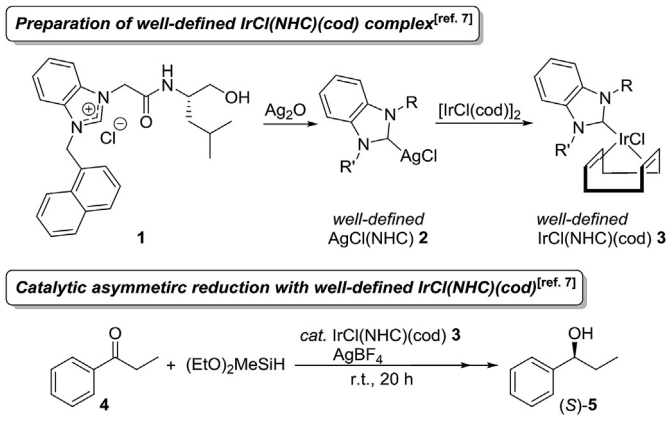
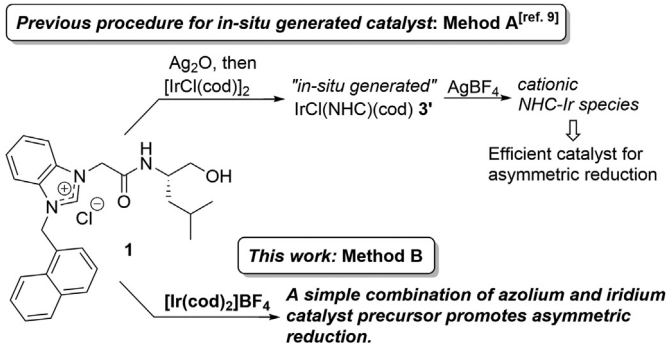


Scheme 1. Development of *well-defined* NHC-Ir complex for enantioselective hydrosilylation (Previous work).



Scheme 2. Development of *in-situ generated* catalyst under operationally simple conditions.

azolium salt **1** with Ag_2O to produce the corresponding NHC-Ag complex **2** through deprotonation of C-H bond at the C_2 position of **1**. Subsequently, the resulting NHC-Ag complex **2** was allowed to react with $[IrCl(cod)]_2$ to afford the IrCl(NHC)(cod) complex **3'**. Next, propiophenone (**4**) was combined with $(EtO)_2MeSiH$ in the presence of unpurified complex **3'** and $AgBF_4$ to yield (*S*)-1-phenyl-1-propanol ((*S*)-**5**) in 92% yield with 92% ee.

The previous procedure employed stepwise addition of Ag_2O, $[IrCl(cod)]_2$ and $AgBF_4$ to a THF solution of azolium salt **1** to generate IrCl(NHC)(cod) **3'** (Scheme 2, method A) [9]. We assumed that these components could be added simultaneously to the reaction vessel. During the course of these studies, we discovered that a simple combination of $[Ir(cod)_2]BF_4$ and the chiral azolium salt **1** promoted the catalytic asymmetric hydrosilylation (Scheme 2, method B). So far, it has been considered that Ag_2O was needed to deprotonate the C-H bond at the C_2 position of the azolium salt to afford a carbene species. Indeed, in some previous studies, the *well-defined* NHC-M (M = Rh or Ru) complexes for catalytic asymmetric hydrosilylation have been synthesized through the pretreatment of a chiral azolium salt with a base such as Ag_2O and ^{t}BuOK [3–5,7]. As such, we were surprised that pretreatment of the azolium salt with Ag_2O to form the corresponding NHC species was not needed for hydrosilylation with the $[Ir(cod)_2]BF_4$/azolium salt catalytic system (Scheme 2, method B). The proposed method offers the additional important advantage of avoiding advance preparation of NHC-metal species. In this study, we report an asymmetric reduction of a ketone with the $[Ir(cod)_2]BF_4$/azolium salt catalytic system.

2. Results and discussion

Representative results for the reaction of propiophenone (**4**) with $(EtO)_2MeSiH$ in the presence of catalytic amounts of $[Ir(cod)_2]BF_4$ and chiral ligand precursor **1** are summarized in Table 1. When **4** was allowed to react with 2 eq. of $(EtO)_2MeSiH$ in the presence of 4 mol % of $[Ir(cod)_2]BF_4$ and **1** in cyclopentyl methyl ether (CPME) at room temperature for 20 h, (*S*)-1-phenyl-1-propanol ((*S*)-**5**) was obtained in 49% yield with 88% ee (entry 1).

Several reaction parameters including amount of the reductant, solvent and catalyst loading were evaluated (Table 1). Although the use of 2 eq. of reductant with respect to ketone **4** resulted in a moderate yield of (*S*)-**5** (entry 1), 4 eq. of $(EtO)_2MeSiH$ was enough to achieve optimum conversion (entries 2–5). Various solvents were explored and THF, 2-MeTHF and diethylene glycol dimethyl ether (diglyme) proved to be superior (entries 6, 7 and 10). In contrast, the catalytic reaction in Et_2O, CH_2Cl_2 and DMSO resulted in lower yield of the reduced product (entries 9–13).

Increasing the amount of the azolium salt **1** (2 eq. with respect to $[Ir(cod)_2]BF_4$) resulted in a slightly lower yield of the desired product (*S*)-**5** with 90% ee (entry 14). Using half the amount of **1** with respect to the iridium catalyst precursor led to a poor yield and enantioselectivity of reduced product (entry 15). Moreover, a decrease in the catalyst loading (Ir/**1** = 2/2 mol%) did not result in a significant decrease in the product yield or ee (entry 6 vs. entry 16). It is noteworthy that almost no reaction occurred in absence of the azolium salt **1** (entry 18). This strong ligand-accelerated catalysis (LAC) facilitated by the NHC ligand will be discussed later.

The higher performance of the combined catalytic system of an Ir catalyst precursor and **1** motivated us to study catalysis using the chiral NHC ligand with the opposite configuration. As expected, when **4** was allowed to react with $(EtO)_2MeSiH$ in the presence of catalytic amounts of $[Ir(cod)_2]BF_4$ and *ent*-**1**, the corresponding alcohol such as (*R*)-**5** was preferentially obtained in 92% yield and 90% ee (entry 19).

Table 1
Evaluation of several reaction parameters.[a]

Entry	Silane [eq.]	Ir-cat./1 [mol %]	Solvent	Yield [%][b]	*ee* [%][c]
1	2	4/4	CPME	49	88
2	3	4/4	CPME	83	88
3	3.5	4/4	CPME	93	91
4	4	4/4	CPME	98	93
5	4.5	4/4	CPME	97	90
6	4.5	4/4	THF	97	93
7	4.5	4/4	2-MeTHF	98	93
8	4.5	4/4	1,4-dioxane	34	81
9	4.5	4/4	Et_2O	9	12
10	4.5	4/4	diglyme	87	92
11	4.5	4/4	toluene	57	79
12	4.5	4/4	CH_2Cl_2	16	59
13	4.5	4/4	DMSO	<1	
14	4.5	4/8	THF	80	90
15	4.5	4/2	THF	12	25
16	4.5	2/2	THF	90	91
17	4.5	1/1	THF	31	39
18	4.5	4/0	THF	<1	
19[d]	4.5	4/4	THF	92	90

[a] **4** (0.5 mmol), $(EtO)_2MeSiH$, $[Ir(cod)_2]BF_4$, **1**, solvent (2 mL) at room temperature for 20 h under Ar. After the reaction, K_2CO_3 (2 mg) and MeOH (2 mL) were added, and then the reaction mixture was stirred at room temperature for 2 h, affording (*S*)-**5**.
[b] Determined by GC using the internal standard method.
[c] Determined by GC on a chiral stationary phase.
[d] *Ent*-**1** in place of **1** was used, affording (*R*)-**5**.