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PII: S1381-1169(16)30191-1
DOI: http://dx.doi.org/doi:10.1016/j.molcata.2016.05.020
Reference: MOLCAA 9895

To appear in: *Journal of Molecular Catalysis A: Chemical*

Received date: 4-3-2016
Revised date: 12-5-2016
Accepted date: 18-5-2016

Please cite this article as: Yoshiki Manabe, Kanako Shinohara, Hanako Nakamura, Hiro Teramoto, Satoshi Sakaguchi, Chiral N-heterocyclic carbene iridium catalyst for the enantioselective hydrosilane reduction of ketones, Journal of Molecular Catalysis A: Chemical http://dx.doi.org/10.1016/j.molcata.2016.05.020

Chiral N-heterocyclic carbene iridium catalyst for the enantioselective hydrosilane reduction of ketones

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Keywords:

Asymmetric catalysis

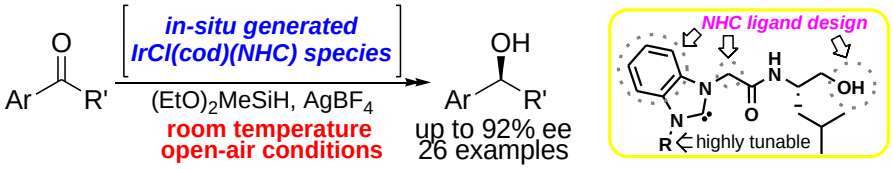
Hydrosilylation

N-Heterocyclic carbene

Ligand design

Iridium

Graphical abstract



Highlights

- Enantioselective hydrosilylation of ketones catalyzed by an Ir complex is developed.
- The *in-situ* generated *N*-heterocyclic carbene (NHC) Ir catalyst can be used .
- The attachment of hydroxyamide side arm is critical for the NHC ligand design.

Abstract

Enantioselective reduction of ketones with $(EtO)_2MeSiH$ catalyzed by an *in-situ* generated *N*-heterocyclic carbene (NHC) Ir complex at room temperature has been developed. A series of benzimidazolium salts were synthesized and screened in the asymmetric hydrosilylation reaction. As a result, propiophenone was efficiently reduced by the combined catalytic system of $[IrCl(cod)]_2$ and NHC–Ag complex derived from *N*-(1-naphthalenylmethyl)-substituted benzimidazolium salt **L12**, affording the corresponding alcohol in 92% yield and with 92% ee. Moreover, the evaluation of an Ir catalyst precursor showed that cationic $[Ir(cod)_2]BF_4$ complex could be used. Furthermore, the introduction of a chiral hydroxyamide side arm into the benzimidazolium salt was critical for the successful design of the NHC ligand.

1. Introduction

An important goal in homogeneous metal-mediated catalysis is the development of inexpensive and easy-to-use chiral ligands [1]. The progress in *N*-heterocyclic carbene (NHC) ligands is one of the most important advances in catalytic asymmetric reactions in the past decade [2,3]. The stereoselective hydrosilylation of ketones catalyzed by transition-metal complexes is an important method for the synthesis of optically active alcohols [4]. Since Hermann reported the first catalytic asymmetric hydrosilylation reaction in which the chiral induction was achieved using a chiral NHC [5], the enantioselective hydrosilylation of ketones with different types of chiral NHCs has been widely investigated [6]. Among the increasing number of the NHC–metal complexes, several NHC-containing well-defined Rh

complexes have been found to be efficient asymmetric catalysts for this transformation [7-10].

The *in-situ* generated chiral metal complexes offer several distinct advantages over the use of well-defined, preformed metal complexes as reported by Veige et al. [11]: (i) facilitation of benchtop chemistry, (ii) rapid screening of diverse chiral NHC precursors, (iii) avoiding additional catalyst synthetic steps. Despite the enormous progress of the catalytic reaction using the well-defined metal complexes [7-10], the asymmetric hydrosilylation with *in-situ* generated NHC–metal complexes has been rarely reported.

Previously, we developed a hydroxyamide-functionalized benzimidazolium salt as a chiral NHC ligand precursor [12,13]. Fortunately, the well-defined, monodentate IrCl(cod)(NHC) (cod = 1,5-cyclooctadiene) complex catalyzed the asymmetric hydrosilylation of ketones efficiently under mild conditions [10]. An attractive feature of this functionalized chiral NHC ligand is that an easy tuning of the *N*-functional groups of the NHC ring helped to develop diverse NHC ligands. Indeed, the azolium ligand precursors can be synthesized in two steps from enantiopure β-amino alcohols (*vide infra*). Based on these advantages, we now investigated the catalytic asymmetric hydrosilylation of ketones using *in-situ* generated NHC–Ir species from readily available functionalized benzimidazolium salts. This could be performed under operationally simple conditions because the independent preparation and purification of the IrCl(cod)(NHC) complex were not needed.

2. Experimental

2.1. General procedures

All of the reagents were purchased from Aldrich, Tokyo Chemical Industry Co., Ltd. (TCI), Wako Pure Chemical Industries, Ltd. and were used as received. All non-commercially available compounds were prepared and characterized as described in Section 2.2. Column chromatographies were performed with silica gel 60 (63-210 μm) purchased from Kanto Chemical Co., Inc. NMR spectra were recorded on JEOL ECA400 (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) spectrometer. Chemical shifts were reported downfield from TMS (δ= 0 ppm) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent used as an internal reference. Elemental analyses were performed at Osaka University.

*2.2. Procedure for Synthesis of Azolium Salt **L12***

The reaction mixture of 1-(1-naphthalenyl)-1H-benzimidazole (373 mg, 1.44 mmol) and α-chloroacetamide (279 mg, 1.44 mmol), derived from chloroacetyl chloride and L-luecinol, in 1,4-dioxane (4 mL) was heated to 110 °C and stirred for 24 h. After the reaction, the solvent was removed under reduced pressure. The azolium salt **L12** was purified by reprecipitation using CH_3OH and $CH_3CO_2C_2H_5$ affording white solid (yield: 472 mg, 72%). Other azolium salts could be prepared by the similar reaction procedure. Compounds **L1** [12c], **L6** [12c], **L16** [13b], **L17** [13b], **L18** [12c], **L19** [12a] and **L20** [12a] were reported in our previous publications (see also Appendix A. Supplementary data).

*2.2.1. Compound **L12***

^{1}H-NMR ($CDCl_3$): δ 10.52 (s, 1H), 9.05 (d, *J* = 8.2 Hz, 1H), 8.00-7.76 (m, 4H), 7.59-7.47 (m, 3H), 7.38-7.22 (m, 4H), 6.24 (d, *J* = 16.0 Hz, 1H), 6.06 (d, *J* = 16.4 Hz, 1H), 5.81 (d, *J* = 16.0 Hz, 1H), 5.62 (d, *J* = 16.4 Hz, 1H), 4.86 (br, 1H), 3.96-3.88 (m, 1H), 3.61-3.42 (m, 2H), 1.55-1.42 (m, 2H), 1.21-1.17 (m, 1H), 0.78 (d, *J* = 6.4 Hz, 3H), 0.72 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR: δ 164.7, 144.1, 133.6, 132.1, 130.9, 130.3, 129.7, 129.0, 127.9, 127.5, 127.1, 126.8, 126.5, 126.1, 125.3, 122.2, 114.2, 113.1, 64.3, 51.0, 49.8, 49.0, 39.7, 24.7, 22.7, 22.2. Anal. Calc. for $C_{26}H_{30}ClN_3O_2$•0.2H_2O: C, 68.54; H, 6.73; N, 9.22. Found: C, 68.37; H, 6.72; N, 9.21%. M.p. 181.3-183.1 °C.

*2.2.2. Compound **L2***

^{1}H-NMR ($CDCl_3$): δ 10.25 (s, 1H), 8.84 (d, *J* = 9.0 Hz, 1H), 7.95-7.92 (m, 1H), 7.67-7.64 (m, 1H), 7.58-7.53 (m, 2H), 5.71 (d, *J* = 16.2 Hz, 1H), 5.58 (d, *J* = 16.2 Hz, 1H), 4.57 (q, *J* = 7.3 Hz, 2H), 4.00-3.96 (m, 1H), 3.63-3.61 (m, 1H), 3.54-3.50 (m, 1H), 3.96-3.50 (br, 1H), 1.66 (t, *J* = 7.3 Hz, 3H), 1.62-1.53 (m, 1H), 1.50-1.45 (m, 1H), 1.28-1.22 (m, 1H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR: δ 164.9, 142.8, 132.1, 130.7, 127.0, 126.7, 114.1, 112.4, 64.2, 50.9, 49.5, 42.9, 39.7, 24.8, 22.8, 22.2, 14.4. Anal. Calc. for $C_{17}H_{26}ClN_3O_2$•2H_2O: C, 54.32; H, 8.04; N, 11.18. Found: C, 54.35; H, 7.69; N, 11.28%. M.p. 136.2-136.6 °C.

*2.2.3. Compound **L3***

^{1}H-NMR (DMSO): δ 10.00 (s, 1H), 8.78 (d, *J* = 8.7 Hz, 1H), 8.13-8.09 (m, 1H), 7.99-7.95 (m, 1H), 7.69-7.64 (m, 2H), 5.40 (d, *J* = 16.0 Hz, 1H), 5.34 (d, *J* = 16.0 Hz, 1H), 4.89 (t, *J* =

6.0 Hz, 1H), 4.56 (t, *J* = 7.1 Hz, 2H), 3.81-3.75 (m, 1H), 3.35-3.33 (m, 2H), 1.91-1.83 (m, 2H), 1.63-1.56 (m, 1H), 1.39-1.26 (m, 4H), 0.90 (t, *J* = 7.3 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR: δ 164.1, 143.3, 131.5, 130.7, 126.6, 126.5, 113.7, 113.6, 63.4, 49.7, 48.6, 46.4, 39.7, 30.5, 24.2, 23.2, 21.8, 19.0, 13.3. Anal. Calc. for $C_{19}H_{30}ClN_3O_2 \bullet H_2O$: C, 59.13; H, 8.36; N, 10.89. Found: C, 59.16; H, 8.35; N, 10.99%. M.p. 161.8-162.4 °C.

2.2.4. Compound ***L4***

^{1}H-NMR ($CDCl_3$): δ 10.34 (s, 1H), 8.95 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.66-7.55 (m, 3H), 5.77 (d, *J* = 16.2 Hz, 1H), 5.65 (d, *J* = 16.2 Hz, 1H), 4.35 (d, *J* = 7.6 Hz, 2H), 4.00 (br, 2H), 3.67-3.64 (m, 1H), 3.55-3.51 (m, 1H), 2.39-2.29 (m, 1H), 1.67-1.55 (m, 1H), 1.53-1.48 (m, 1H), 1.30-1.23 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR: δ 164.7, 143.5, 132.0, 131.1, 127.2, 126.8, 114.3, 112.5, 64.3, 55.4, 51.0, 49.6, 39.7, 28.8, 24.8, 22.9, 22.3, 19.8, 19.8. Anal. Calc. for $C_{19}H_{30}ClN_3O_2 \bullet 1.2H_2O$: C, 58.58; H, 8.38; N, 10.79. Found: C, 58.55; H, 8.35; N, 10.83%. M.p. 76.8-77.6 °C.

2.2.5. Compound ***L5***

^{1}H-NMR (DMSO): δ 9.94 (s, 1H), 8.76 (d, *J* = 8.7 Hz, 1H), 8.02-7.96 (m, 2H), 7.69-7.65 (m, 2H), 6.15-6.07 (m, 1H), 5.44-5.25 (m, 6H), 4.88 (t, *J* = 6.0 Hz, 1H), 3.81-3.75 (m, 1H), 3.37-3.32 (m, 2H), 1.62-1.57 (m, 1H), 1.38-1.30 (m, 2H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR: δ 164.0, 143.4, 131.6, 131.1, 131.0, 130.6, 126.7, 120.3, 113.8,

113.6, 63.4, 49.7, 48.7, 48.6, 39.7, 24.2, 23.2, 21.8. Anal. Calc. for $C_{18}H_{26}ClN_3O_2$•$0.7H_2O$: C, 59.32; H, 7.58; N, 11.53. Found: C, 58.98; H, 7.34; N, 11.46%. M.p. 159.5-160.0 °C.

*2.2.6. Compound **L7***

^{1}H-NMR ($CDCl_3$): δ 10.39 (s, 1H), 9.02 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.60-7.12 (m, 7H), 5.81 (d, *J* = 16.2 Hz, 1H), 5.74 (s, 2H), 5.57 (d, *J* = 16.2 Hz, 1H), 3.96 (br, 1H), 3.66-3.50 (m, 2H), 2.37 (s, 3H), 2.37 (br, 1H), 1.63-1.46 (m, 2H), 1.29-1.22 (m, 1H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR: δ 164.6, 143.7, 136.5, 132.3, 131.3, 130.9, 130.1, 129.4, 128.4, 127.4, 127.0, 126.9, 114.3, 113.1, 64.3, 51.1, 49.9, 39.7, 24.8, 22.8, 22.4, 19.4. Anal. Calc. for $C_{23}H_{30}ClN_3O_2$•$0.5H_2O$: C, 65.00; H, 7.35; N, 9.89. Found: C, 64.66; H, 7.29; N, 9.95%. M.p. 172.0-172.6 °C.

*2.2.7. Compound **L8***

^{1}H-NMR (DMSO): δ 10.10 (s, 1H), 8.87 (d, *J* = 8.5 Hz, 1H), 7.99-7.96 (m, 2H), 7.67-7.61 (m, 2H), 7.34-7.16 (m, 4H), 5.81 (s, 2H), 5.43 (d, *J* = 16.2 Hz, 1H), 5.37 (d, *J* = 16.2 Hz, 1H), 4.88 (t, *J* = 5.8 Hz, 1H), 3.83-3.75 (m, 1H), 3.35-3.34 (m, 2H), 2.27 (s, 3H), 1.65-1.55 (m, 1H), 1.40-1.27 (m, 2H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR: δ 164.1, 143.6, 138.3, 133.9, 131.7, 130.5, 129.4, 128.9, 128.8, 126.7, 126.7, 125.3, 113.9, 113.7, 63.5, 49.8, 49.7, 48.8, 39.7, 24.2, 23.2, 21.9, 20.9. Anal. Calc. for $C_{23}H_{30}ClN_3O_2$: C, 66.41; H, 7.27; N, 10.10. Found: C, 66.07; H, 7.30; N, 10.10%. M.p. 219.8-220.9 °C.

*2.2.8. Compound **L9***

^{1}H-NMR ($CDCl_3$): δ 10.53 (s, 1H), 9.06 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.51-7.41 (m, 3H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 5.83-5.64 (m, 4H), 4.80 (br, 1H), 3.98-3.95 (m, 1H), 3.66-3.62 (m, 1H), 3.55-3.50 (m, 1H), 2.26 (s, 3H), 1.62-1.46 (m, 2H), 1.27-1.20 (m, 1H), 0.82 (d, *J* = 6.3 Hz, 3H), 0.76 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR: δ 164.8, 143.5, 139.0, 132.2, 130.6, 129.9, 129.5, 128.0, 127.0, 126.7, 114.1, 113.2, 64.3, 51.3, 51.0, 49.7, 39.7, 24.8, 22.7, 22.2, 21.0. Anal. Calc. for $C_{23}H_{30}ClN_3O_2$•0.1H_2O: C, 66.13; H, 7.29; N, 10.06. Found: C, 66.07; H, 7.19; N, 10.20%. M.p. 225.5-226.7 °C.

*2.2.9. Compound **L10***

^{1}H-NMR (DMSO): δ 10.15 (s, 1H), 8.79 (d, *J* = 8.7 Hz, 1H), 8.04-7.98 (m, 3H), 7.81 (d, *J* = 7.3 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.68-7.62 (m, 3H), 6.00 (s, 2H), 5.44 (d, *J* = 16.5 Hz, 1H), 5.37 (d, *J* = 16.5 Hz, 1H), 4.90 (br, 1H), 3.82-3.77 (m, 1H), 3.38-3.35 (m, 2H), 1.63-1.55 (m, 1H), 1.39-1.26 (m, 2H), 0.85 (d, *J* = 6.4 Hz, 3H), 0.78 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR: δ 164.0, 143.9, 135.4, 132.4, 131.7, 130.4, 130.1, 126.8, 126.7, 125.5, 125.2, 125.1, 122.6, 113.8, 63.4, 49.7, 49.0, 48.8, 39.8, 24.2, 23.2, 21.8. Anal. Calc. for $C_{23}H_{27}ClF_3N_3O_2$: C, 58.78; H, 5.79; N, 8.94. Found: C, 58.64; H, 5.74; N, 8.99%. M.p. 217.6-218.3 °C.

*2.2.10. Compound **L11***

^{1}H-NMR (DMSO): δ 10.15 (s, 1H), 8.76 (d, *J* = 8.7 Hz, 1H), 8.06-8.03 (m, 1H), 8.00-7.96 (m, 1H), 7.71-7.60 (m, 8H), 7.60-7.35 (m, 3H), 5.92 (s, 2H), 5.44 (d, *J* = 16.0 Hz, 1H), 5.38 (d, *J* = 16.0 Hz, 1H), 4.89 (t, *J* = 5.7 Hz, 1H), 3.83 (m, 1H), 3.37-3.30 (m, 2H), 1.65-1.58 (m, 1H), 1.39-1.29 (m, 2H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR: δ 164.0, 143.6, 140.5, 139.3, 133.1, 131.7, 130.5, 128.9, 128.9, 127.7, 127.2, 127.1, 126.7,

126.7, 113.9, 113.7, 63.5, 49.7, 49.4, 48.7, 39.8, 24.2, 23.2, 21.8. Anal. Calc. for $C_{28}H_{32}ClN_3O_2$•1.2H_2O: C, 67.31; H, 6.94; N, 8.41. Found: C, 67.16; H, 6.73; N, 8.53%. M.p. 167.8-168.6 °C.

*2.2.11. Compound ent-**L12***

^{1}H-NMR ($CDCl_3$): δ 10.57 (s, 1H), 9.16 (d, *J* = 7.3 Hz, 1H), 8.02-7.77 (m, 4H), 7.57-7.37 (m, 3H), 7.34-7.22 (m, 4H), 6.27 (d, *J* = 16.0 Hz, 1H), 6.08 (d, *J* = 16.4 Hz, 1H), 5.86 (d, *J* = 16.0 Hz, 1H), 5.66 (d, *J* = 16.4 Hz, 1H), 4.81 (br, 1H), 3.91 (br, 1H), 3.59-3.45 (m, 2H), 1.56-1.44 (m, 2H), 1.22-1.18 (m, 1H), 0.78 (d, *J* = 6.4 Hz, 3H), 0.71 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR: δ 164.8, 144.1, 133.7, 132.2, 131.0, 130.4, 129.8, 129.1, 127.8, 127.6, 127.2, 126.9, 126.5, 126.3, 125.4, 122.2, 114.3, 113.2, 64.4, 51.1, 49.9, 49.1, 39.7, 24.8, 22.8, 22.2. Anal. Calc. for $C_{26}H_{30}ClN_3O_2$: C, 69.09; H, 6.69; N, 9.30. Found: C, 68.61; H, 6.63; N, 9.25%. M.p. 181.3-182.9 ºC.

*2.2.12. Compound **L13***

^{1}H-NMR ($CDCl_3$): δ 10.49 (s, 1H), 9.02 (d, *J* = 8.5 Hz, 1H), 7.95 (t, *J* = 7.0 Hz, 2H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.55-7.43 (m, 3H), 7.34-7.28 (m, 2H), 7.26-7.18 (m, 2H), 6.25 (d, *J* = 16.2 Hz, 1H), 5.98 (d, *J* = 16.2 Hz, 1H), 5.81 (d, *J* = 16.2 Hz, 1H), 5.63 (d, *J* = 16.2 Hz, 1H), 4.10 (br, 1H), 3.90 (br, 1H), 3.59-3.45 (m, 2H), 1.54-1.40 (m, 2H), 1.19-1.12 (m, 1H), 0.76 (d, *J* = 6.3 Hz, 3H), 0.68 *J* = 6.3 Hz, 3H); ^{13}C-NMR: δ 164.7, 144.1, 133.6, 132.1, 130.9, 130.3, 129.6, 129.0, 128.0, 127.4, 127.1, 126.8, 126.4, 126.0, 125.2, 122.2, 114.2, 113.1, 64.3, 51.0, 49.8, 48.9, 39.7, 24.7, 22.7, 22.1. Anal. Calc.

for $C_{26}H_{30}ClN_3O_2$•0.1H_2O: C, 68.82; H, 6.71; N, 9.26. Found: C, 68.61; H, 6.64; N, 9.26%. M.p. 170.6-171.0 °C.

*2.2.13. Compound **L14***

^{1}H-NMR (DMSO): δ 9.00 (s, 1H), 8.92 (s, 1H), 8.49 (d, *J*= 8.5 Hz, 1H), 8.40 (d, *J* = 8.1 Hz, 2H) 8.35 (d, *J* = 8.1 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.81-7.71 (m, 2H), 7.66-7.60 (m, 4H), 6.78 (s, 2H), 5.14 (d, *J* = 16.2 Hz, 1H), 5.07 (d, *J* = 16.2 Hz, 1H), 4.77 (t, *J* = 5.4 Hz, 1H), 3.72-3.64 (m, 1H), 3.25 (br, 2H), 1.55-1.45 (m, 1H), 1.26-1.22 (br, 2H), 0.80 (d, *J* = 6.3 Hz, 3H), 0.72 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR: δ 163.9, 142.2, 131.8, 131.4, 131.2, 131.0, 130.5, 129.5, 127.9, 127.0, 126.7, 125.7, 123.4, 121.9, 114.3, 113.7, 63.4, 49.5, 48.6, 43.5, 39.7, 24.2, 23.2, 21.8. Anal. Calc. for $C_{30}H_{32}ClN_3O_2$•2.6H_2O: C, 65.65; H, 6.83; N, 7.86. Found: C, 65.39; H, 6.49; N, 7.80%. M.p. 159.1-160.2 °C.

*2.2.14. Compound **L15***

^{1}H-NMR ($CDCl_3$): δ 10.49 (s, 1H), 9.07 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 6.7 Hz, 2H), 7.66-7.59 (m, 6H), 5.97 (d, *J* = 16.2 Hz, 1H), 5.79 (d, *J* = 16.2 Hz, 1H), 4.01-3.93 (m, 1H), 3.67-3.63 (m, 1H), 3.54-3.50 (m, 1H), 3.45 (br, 1H), 1.68-1.58 (m, 1H), 1.56-1.48 (m, 1H), 1.29-1.22 (m, 1H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR: δ 164.7, 142.8, 133.0, 132.1, 131.0, 130.7, 130.5, 127.6, 127.4, 125.0, 114.5, 112.9, 64.2, 51.2, 49.9, 39.7, 24.8, 22.8, 22.3. Anal. Calc. for $C_{21}H_{26}ClN_3O_2$•1.1H_2O: C, 61.86; H, 6.97; N, 10.31. Found: C, 61.47; H, 6.48; N, 10.34%. M.p. 177.3-177.5 °C.

2.3. Typical Procedure for Asymmetric Hydrosilane Reduction

2.3.1. Procedure Using [IrCl(cod)]$_2$ as an Ir Catalyst Precursor

A flask was charged with azolium salt **L12** (0.02 mmol, 9.1 mg), Ag_2O (0.01 mmol, 2.4 mg) and CH_2Cl_2 (1 mL). After stirring the resulting mixture at room temperature for 2 h in the dark, CH_2Cl_2 was removed in vacuo. Then, a THF (1 mL) solution of $[IrCl(cod)]_2$ (0.01 mmol, 6.9 mg) was added to the reaction vessel. The resulting mixture was stirred at room temperature for an additional 4 h in the dark, filtered through a membrane filter, and evaporated to dryness in vacuo. Subsequently, to the resulting flask containing yellow solid of the unpurified IrCl(cod)(NHC) complex, a solution of $AgBF_4$ (0.025 mmol, 4.9 mg) in CPME (2 mL) was added, and then stirred at room temperature for 1 h. Finally, propiophenone (0.5 mmol, 66 mg) and $(EtO)_2MeSiH$ (2.25 mmol, 294 mg) were added to the resulting CPME solution (see Appendix A. Supplementary data for details). After stirring at room temperature for 20 h under open-air conditions, K_2CO_3 (2 mg) and MeOH (2 mL) were added. Then, the resulting mixture was stirred at room temperature for 2 h. After evaporation of the solvents, the residue obtained was purified by column chromatography on silica gel (Et_2O/*n*-hexane = 3:7) to give (*S*)-1-phenyl-1-propanol (61 mg, 91% isolated yield). The ee was measured by chiral GLC.

2.3.2. Procedure Using [Ir(cod)$_2$]BF$_4$ as an Ir Catalyst Precursor

A flask was charged with azolium salt **L12** (0.02 mmol, 9.1 mg), Ag_2O (0.01 mmol, 2.4 mg) and CH_2Cl_2 (1 mL). After stirring the resulting mixture at room temperature for 2 h in the dark, CH_2Cl_2 was removed in vacuo. Then, a CPME (1 mL) solution of $[Ir(cod)_2]BF_4$ (0.02 mmol, 9.9 mg) was added to the reaction vessel. The resulting mixture was stirred at room temperature for an additional 4 h in the dark. Subsequently, propiophenone (0.49 mmol, 66

mg), $(EtO)_2MeSiH$ (2.19 mmol, 294 mg) and CPME (1 mL) were added to the reaction vessel. After stirring at room temperature for 20 h under open-air conditions, K_2CO_3 (2 mg) and MeOH (2 mL) were added. Then, the resulting mixture was stirred at room temperature for 2 h.

3. Results and discussion

3.1. Establishment of an experimental procedure for the hydrosilylation by the in-situ generated NHC–Ir catalyst

First, a series of azolium chlorides were synthesized from a commercially available β-amino alcohol (Scheme 1). The reaction of (*S*)-leucinol with chloroacetyl chloride afforded the corresponding α-chloroacetamide derivative **1** in an almost quantitative yield. Then, compound **1** was coupled to a substituted benzimidazole. Thus, a small library of the chiral NHC precursor **L1**–**L15** was easily obtained via this synthetic route. Notably, these newly synthesized azolium ligand precursors are completely air and moisture stable products; thus, they can be handled under air atmosphere and stored as solids without any special precaution.

(Scheme 1)

The aim of this study is the development of an asymmetric catalytic reaction using the NHC–Ir species generated *in situ*. After several trials, a highly tunable chiral NHC Ir

catalyst could be generated *in situ* for the enantioselective hydrosilane reduction of ketones (Scheme 2).

(Scheme 2)

A representative reaction was carried out according to the following procedure. The treatment of azolium chloride **L12** with Ag_2O in CH_2Cl_2 at room temperature afforded the corresponding NHC–Ag complex. After the removal of the solvent, a THF solution of $[IrCl(cod)]_2$ was added to the resulting Ag complex. The mixture was stirred at room temperature, filtered through a membrane filter to remove the AgCl formed, and evaporated to dryness under vacuum, affording the crude IrCl(cod)(NHC) complex. Next, the Ir complex was treated with $AgBF_4$ in cyclopentyl methyl ether (CPME) at room temperature for 1 h. Finally, the reaction of propiophenone (**2**) with 4.5 equiv of $(EtO)_2MeSiH$ was carried out at room temperature for 20 h in a CPME solution containing the Ir species thus obtained. Using this procedure, (*S*)-1-phenyl-1-propanol ((*S*)-**3**) was obtained in 92% yield and with 92% ee (standard reaction conditions, see Appendix A. Supplementary data for details).

The procedure has the advantage of operational simplicity, allowing easy ligand screening without the purification of the NHC–Ir complex (*vide infra*). In addition, one significant benefit of this procedure is that the isolation and spectroscopic characterization of a pure NHC–Ir complex are not needed.

3.2. Evaluation of NHC ligand

Based on the results of the reduction of **2** with $(EtO)_2MeSiH$ using the *in-situ* generated NHC–Ir catalyst, a series of benzimidazolium salts **L1**–**L15** were screened in the asymmetric hydrosilylation reaction (Table 1).

(Table 1)

The initial ligand screening showed that the introduction of a methyl substituent to the azolium ring, far from the stereogenic center of the chiral ligand, significantly decreased the catalytic activity of the Ir species. Thus, the Ir-catalyzed reaction of **2** with $(EtO)_2MeSiH$ under the influence of chiral NHC ligand derived from **L1** afforded (*S*)-**3** in a poor yield and enantioselectivity (entry 1). Similarly, the chiral ligand bearing an ethyl substituent (azolium **L2**) afforded a racemic mixture of the corresponding alcohol in 25% yield (entry 2). When the linear alkyl substituent (N-^{n}Bu, azolium **L3**) was replaced with a branched alkyl substituent (N-^{i}Bu, azolium **L4**) on the NHC ring, the catalytic activity of the Ir complex remained unchanged (entries 3 and 4). Allyl-substituted azolium salt **L5** was also synthesized and evaluated. However, the reduction with **L5** failed under the standard reaction conditions (entry 5).

A promising result was obtained when **L6** (R = benzyl) was used, affording (*S*)-**3** with an excellent enantioselectivity (94% ee) (entry 6). This result may suggest that π-π stacking between the benzylic moiety on the NHC ring and phenyl group of the substrate **2** is an important factor for the asymmetric hydrosilylation reaction. Another possibility is that the NHC-Ir complex having a hemilabile benzylic moiety generated a vacant site in the iridium coordination sphere during the reaction [14]. Therefore, the effect of a series of *N*-benzyl analogs of the NHC ligand on the catalytic activity was next investigated. The

corresponding *o*-, *m*-, and *p*-toluylmethyl-substituted NHC ligand precursors (azolium chlorides **L7**, **L8**, and **L9**) were synthesized. The reduction reaction using **L7** occurred in a similar manner as that using **L6** (entry 7). A highly enantioselective hydrosilylation reaction was also achieved when **L8** or **L9** was used (entries 8 and 9). The introduction of an electron-withdrawing group such as a CF_3 group at the *meta* position of the benzylic moiety (azolium **L10**) improved the yield and enantioselectivity of the catalytic reaction. Thus, **2** could be reduced efficiently by the *in-situ* generated Ir species from α,α,α-trifluoro-*m*-toluylmethyl-substituted azolium ligand precursor **L10**, affording (*S*)-**3** in 84% yield and with 92% ee (entry 10). An almost similar result was obtained when the reduction was carried out using an Ir complex derived from benzimidazolium salt **L11** bearing a 4-biphenylbenzyl group (entry 11).

A further ligand screening showed that the use of azolium chloride bearing an *N*-naphthalenylmethyl substituent increased the enantioselectivity of the hydrosilylation reaction. **2** was reduced efficiently with the combined catalytic system of $[IrCl(cod)]_2$ and NHC–Ag complex derived from *N*-(1-naphthalenylmethyl)-substituted benzimidazolium salt **L12**, affording (*S*)-**3** in 92% yield and with 92% ee (entry 12). Similarly, the enantioselective reaction using **L13** bearing a 2-naphthalenylmethyl group afforded (*S*)-**3** with 93% ee (entry 13). These results prompted us to prepare a ligand precursor bearing an *N*-anthracenylmethyl substituent such as **L14**. However, the reaction using **L14** afforded (*S*)-**3** in a moderate yield (53%) and with a low ee (16%), probably because of steric effect (entry 14).

Furthermore, the benzyl moiety on the NHC ring was replaced with a phenyl moiety. The synthesis of phenyl-substituted azolium chloride **L15** illustrates the ease of ligand

variation via the synthetic route shown in Scheme 1. The hydrosilylation of **2** with $(EtO)_2MeSiH$ was then carried out using the *in-situ* generated Ir-catalyst from **L15** under the standard reaction conditions. However, a poor catalytic activity was observed for the NHC–Ir complex containing an *N*-phenyl group at the NHC ring (entry 15).

Finally, based on the high performance of **L12**, the synthesis of (*R*)-**3** in the asymmetric catalytic hydrosilylation of **2** was investigated using the chiral ligand with the opposite configuration. (*R*)-Leucinol could be easily obtained from the commercial source, allowing an effortless preparation of the chiral ligand precursor, *ent*-**L12**. As expected, the reaction of **2** with $(EtO)_2MeSiH$ in the presence of a catalytic amount of NHC–Ir complex generated *in situ* from *ent*-**L12** under the standard reaction conditions afforded (*R*)-**3** in 95% yield and with 91% ee (entry 16). Thus, this method that utilizes inexpensive and readily available enantiomers of α-amino acids has potential benefits.

3.3. Evaluation of substrate

Scheme 3 summarizes the reactions of different substrates with the *in-situ* generated NHC–Ir species under the standard reaction conditions.

(Scheme 3)

The reduction of butyrophenone (**4**) smoothly afforded (*S*)-1-phenyl-1-butanol ((*S*)-**5**) in an excellent yield (97%). Similarly, butyl phenyl ketone (**6**) was converted into (*S*)-1-phenyl-1-pentanol ((*S*)-**7**) in a quantitative yield and with 90% ee. This *in-situ* generated catalytic system was also suitable for the asymmetric hydrosilane reduction of alkyl aryl

ketones bearing a branched alkyl group. The reduction of isopropyl phenyl ketone (**8**) and cyclohexyl phenyl ketone (**10**) yielded the corresponding optically active alcohols, (*S*)-**9** and (*S*)-**11**, with 92% ee and 93% ee, respectively. However, unfortunately, the reactions of 2,2-dimethylpropiophenone under the standard reaction conditions using **L6** and **L12**, respectively, did not occur at all, probably due to the steric effect. On the other hand, the reduction of aryl methyl ketones afforded the corresponding alcohols with slightly lower stereoselectivities. Acetophenone (**18**) was transformed into (*S*)-1-phenylethanol ((*S*)-**19**) in 92% yield and with 86% ee, whereas 89% ee was achieved in the reduction of *p*-butylphenyl methyl ketone (**20**).

The introduction of an electron-donating substituent such as methoxy group to acetophenone in the hydrosilylation afforded the corresponding reduced alcohols in higher yields. Thus, the reduction of *p*-methoxyacetophenone (**22**) and *m*-methoxyacetophenone (**24**) smoothly afforded (*S*)-**23** and (*S*)-**25** in excellent yields and with 86% ee and 84% ee, respectively. In contrast, the reduction of an aryl methyl ketone bearing an electron-withdrawing group such as *p*-chloroacetophenone (**26**) with $(EtO)_2MeSiH$ using this catalytic system afforded (*S*)-**27** in a slightly lower yield and enantioselectivity. Moreover, the reduction of *o*-chloroacetophenone (**28**) proceeded slowly, affording the corresponding alcohol in a moderate yield (63%) and stereoselectivity (47% ee), probably because of both electronic and steric effects.

We also investigated the reactivity of alkyl aryl ketone bearing different arene moieties using this catalytic system. Although the enantioselective reduction of 2-acetylnaphthalene (**32**) was successful, the reduction of 1-acetylnaphthalene (**34**) afforded the corresponding alcohol, (*S*)-**35**, in a moderate yield and enantioselectivity. The yields obtained in the reactions of **34** and **28** were comparable. These results probably indicate that

the reactivity of the NHC–Ir catalyst is affected by the steric factor of the arene moiety on the substance.

Enantiomerically pure secondary alcohols containing heteroaromatic substituents are often used in the synthesis of biologically active compounds [15]. This catalytic system was applied to the enantioselective reduction of 2-acetylthiophene (**36**) and 2-acetylfuran (**38**), affording the corresponding alcohols, (*S*)-**37** and (*S*)-**39**, with 86% ee and 80% ee, respectively.

Finally, to evaluate the substrate scope and limitations of this method, the asymmetric hydrosilylation of diverse ketones such as alkyl aryl ketones containing a heteroatom-substituted alkyl moiety, cyclic ketone, dialkyl ketone, and diary ketone was investigated. The reaction of ketones bearing chloro-substitutent afforded the corresponding products with moderate enantioselectivity. When phenacyl chloride (**40**) was reacted with $(EtO)_2MeSiH$ under the same reaction conditions, (*R*)-2-chloro-1-phenylethanol ((*R*)-**41**) was obtained in 67% yield and with 50% ee. Based on this result, the reduction of β-chloro-substituted ketone such as 3-chloropropiophenone (**42**) was investigated. This reaction afforded the corresponding optically active alcohol ((*S*)-**43**) in a slightly higher yield (82%) and stereoselectivity (66%). Optically active halo alcohols are especially significant structural elements for the formation of biologically active compounds, such as chiral epoxides, diols, and amino alcohols. Recently, Cu-catalyzed asymmetric hydrosilylation of α- or β-halo-substituted ketones was successfully achieved [16].

Moreover, the reduction of α-hydroxy ketones such as phenacyl alcohol (**44**) afforded phenylethylene glycol ((*R*)-**45**) in 59% yield and with 44% ee. The enantioselective reduction of cyclic ketones such as 4-chromanone (**46**) was difficult under the standard

reaction conditions. The hydrosilylation of α,β-unsaturated carbonyl compound such as chalcone resulted in a complex mixture of several unidentified products.

The NHC–Ir complex was not a suitable catalyst for the hydrosilylation of dialkyl ketones. For example, the reaction of 2-octanone (**48**) with $(EtO)_2MeSiH$ in the presence of a catalytic amount of chiral Ir complex at room temperature afforded a racemic mixture of 2-octanol (**49**) in 31% yield. The reduction of benzyl butyl ketone (**50**) afforded 1-phenyl-2-hexanol ((*R*)-**51**) in a poor yield. Again, it seems that π-π stacking between the benzylic moiety on the NHC ring and phenyl group of the substrate is a critical factor for the successful hydrosilylation reaction. In contrast, the present catalytic system facilitated the enantioselective hydrosilylation of diaryl ketone. The reduction of 2,4'-dichlorobenzophenone (**52**) afforded the corresponding diaryl methanol derivative, (*R*)-**53**, in a moderate yield (55%) and enantioselectivity (59% ee). In recent years, highly enantioselective Cu-catalyzed reduction of diaryl ketones with polymethylhydrosiloxane has been successfully achieved using a chiral phosphine ligand [17]. The reduction products such as optically active diarylmethanols have been used in the synthesis of many physiologically and biologically active compounds.

3.4. Performance of Ir catalyst precursor

Another advantage of the catalytic reaction using the *in-situ* generated catalyst is the ability to screen diverse metal-ion precursors rapidly. Therefore, several Ir precursors were evaluated in the asymmetric hydrosilylation of **2** with $(EtO)_2MeSiH$ under the standard reaction conditions (Table 2).

(Table 2)

The replacement of a neutral η^4-diene ligand such as 1,5-cyclooctadiene (cod) on the Ir center with an η^2-diene ligand significantly decreased the catalytic activity. When the reduction was carried out using an Ir catalyst precursor such as $(IrClL_2)_2$ (L = cyclooctene (coe) or ethene), the reduction product was formed in a lower yield (entries 2 and 3). The ee value of the product also slightly decreased. These results indicate that the bidentate η^4-cod ligand plays an important role in the highly enantioselective transformation. Moreover, this catalytic hydrosilylation reaction was carried out using a cationic Ir species, which was formed by treating a neutral IrCl(cod)(NHC) complex with $AgBF_4$ (entry 1). Therefore, the performance of commercially available bis(1,5-cyclooctadiene)iridium(I) tetrafluoroborate ($[Ir(cod)_2]BF_4$) was evaluated as the catalyst precursor. After the treatment of azolium salt **L12** with Ag_2O, cationic $[Ir(cod)_2]BF_4$ was added to the reaction vessel containing the resulting NHC–Ag species. Then, the reaction of **2** with $(EtO)_2MeSiH$ was carried out using the resulting NHC–Ir species (see Section 2.3.2). To our delight, this reaction afforded the desired (*S*)-**3** in an excellent yield and enantioselectivity (entry 4). This provides an alternative, simplified reaction procedure for the *in-situ* generation of cationic NHC–Ir species using $[Ir(cod)_2]BF_4$ as the Ir precatalyst.

3.5. Performance of NHC ligand precursor

The results of the screening of chiral ligand precursor indicate that the catalytic activity of the Ir species derived from *m*-toluylmethyl-substituted azolium precursor **L8** may be similar to that of the Ir species derived from azolium salt **L10** bearing an α,α,α-trifluoro-*m*-toluylmethyl substituent under the standard reaction conditions (Table 1, entry 8 vs. entry 10). It was assumed that through the choice of an appropriate ligand, a large range of electronic effects could be imparted to the metal center. Therefore, any difference in the activity of these catalyst systems in the initial stage of the asymmetric hydrosilylation would be observed. Indeed, the reduction of **2** with $(EtO)_2MeSiH$ using **L8-**based catalyst for 3 h afforded (*S*)-**3** in 19% yield, whereas the reaction catalyzed by the NHC–Ir species derived from **L10** bearing ad electron-withdrawing group such as a CF_3 substituent afforded (*S*)-**3** in 52% yield (Scheme 4). These results probably indicate that the catalytic activity of an Ir complex increased with an increase in the Lewis acidic sites.

(Scheme 4)

The reduction of *o*-chloroacetophenone (**28**) with $(EtO)_2MeSiH$ using the combined catalytic system of $[IrCl(cod)]_2$ and azolium salt **L12** bearing a *N*-1-naphthalenylmethyl substituent afforded (*S*)-**29** with moderate enantioselectivity (47% ee) (Scheme 3). As mentioned in the introduction, the development of an *in-situ* generated catalytic system helped in the rapid screening of diverse NHC ligand precursors. To improve the enantioselectivity of the reduction of **28**, three sets of chiral azolium ligand precursors were evaluated (Scheme 5). Fortunately, the reduction of **28** using the combined catalytic system of $[IrCl(cod)]_2$ and **L6** afforded (*S*)-**29** with a slightly increased stereoselectivity of 62% ee. The reduction of 4-chromanone (**46**) by the use of several azolium salts was also

investigated. However, unfortunately, **46** was difficult to be reduced with high stereoselectivity at this stage. Among the chiral ligands examined, azolium salt **L12** gave the corresponding optically active alcohol with 30% ee (Scheme 5).

(Scheme 5)

Adolfsson pointed out that high-throughput screening of the chiral ligand library is a convenient way to find the optimum catalyst for a certain substrate or transformation [18]. We believe that the hydroxy-amide functionalized NHC ligands are highly tunable, thus allowing the facile synthesis of ligand libraries and finding suitable catalysts for diverse substrates.

In order to obtain further information, two functionalized azolium salts such as **L16** and **L17** were synthesized from commercially available L-alaninol and (*S*)-1-methoxy-2-propanamine, respectively. The hydrosilylation of **2** catalyzed by *in-situ* generated NHC–Ir catalyst derived from **L16** afforded (*S*)-**3** in 68% yield and with 88% ee. In contrast, when the OH group (azolium **L16**) was replaced with an OCH_3 group (azolium **L17**) in the chiral ligand, the enantioselectivity significantly decreased (Scheme 6). These results strongly indicate that the hydroxyl functionality on the NHC ligand induced a high stereoselectivity in the hydrosilylation reaction.

(Scheme 6)

Our strategy for the design of NHC ligands was based on the introduction of a chiral hydroxyamide side arm into the substituted *benzimidazole* derivative. In addition to these

ligand precursors, the corresponding *imidazolium* salt, **L18**, could be easily synthesized from 3-benzylimidazole using the synthetic route shown in Scheme 2. However, the asymmetric hydrosilane reduction of **2** using **L18**-based NHC–Ir catalyst afforded (*S*)-**3** in 36% yield and with 81% ee (Scheme 6). This is probably because the σ-donating ability of imidazol-2-ylidene NHC increased than that of benzimidazol-2-ylidene NHC [3k].

Moreover, for design of ligands, a methylene (CH_2) linker was used between the hydroxyamide group and NHC ring. To investigate the effect of different linkers of the chiral ligand on the catalytic activity, two hydroxyamide-functionalized azolium salts bearing a $(CH_2)_2$ linker (azolium **L19**) and $C(CH_3)_2$ linker (azolium **L20**) were synthesized and evaluated. In both the cases, the asymmetric hydrosilylation with the *in-situ* generated catalyst resulted in a poor yield and stereoselectivity (Scheme 6).

Wills et al. reported the enantioselective transfer hydrogenation of ketone catalyzed by a Ru(II) complex bearing polydentate ligand involving a hydroxyamide functionality [19]. They proposed that the hydroxyamide functionality is transformed into a cyclic form by intramolecular nucleophilic addition of hydroxy group to amide carbonyl moiety during the catalytic reaction. As shown in Scheme 6, the hydroxy moiety and the methylene linker of the chiral ligand system were critical in the present asymmetric hydrosilylation. Therefore, we speculated that a similar catalytic active species suggested by Wills is generated in the present asymmetric reduction catalyzed by NHC–Ir complex (Scheme 7). First, an iridium complex **B** involving a carbene and an amidato group might be generated from an cationic NHC–Ir catalyst precursor **A** [12d]. Because almost no reaction occurred under the influence of **L19** or **L20** (Scheme 6), the formation of the six-membered amidato iridium complex **B** might be important for successful catalytic reaction. Then, intramolecular nucleophilic addition of hydroxy group to amide carbonyl moiety might give

a cyclic form **C**, in which the stereodirecting group would be locked in a fixed conformation. The resulting **C** would act as an active catalyst of the asymmetric hydrosilylation.

(Scheme 7)

4. Conclusion

An enantioselective silane reduction of ketones catalyzed by an *in-situ* generated NHC–Ir complex under operationally simple conditions was investigated. A small library could be generated with ease via the modular synthesis of chiral NHC ligands by the use of easily available leucine. The attachment of the hydroxyamide side arm to the benzimidazolidene through a methylene (CH_2) linker was important for achieving a high enantioselectivity in the catalytic reaction. Further investigations on the asymmetric reduction of various carbonyl compounds, especially diaryl ketones, by using $[Ir(cod)_2]BF_4$ precatalyst are currently underway.

Acknowledgments

This work was financially supported by a Grant-in-Aid for Scientific Research (C) (26410254) from Japan Society for the Promotion of Science (JSPS).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi.

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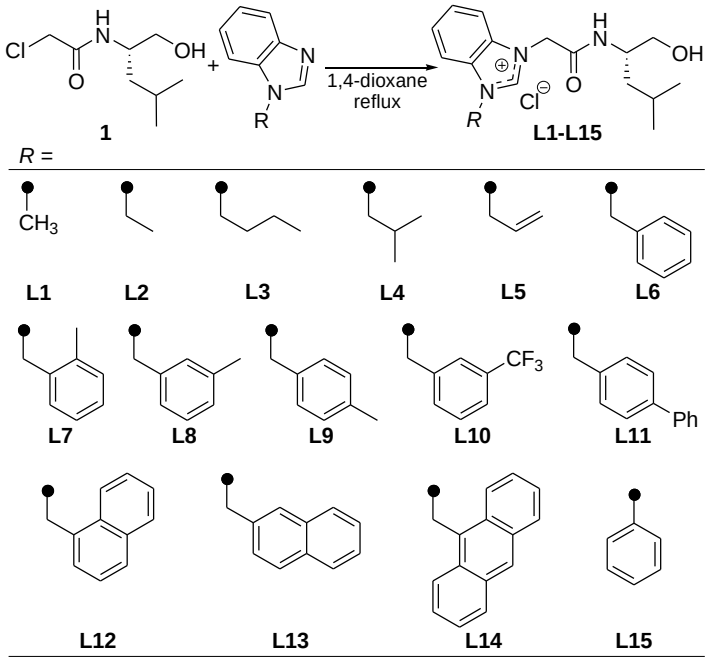
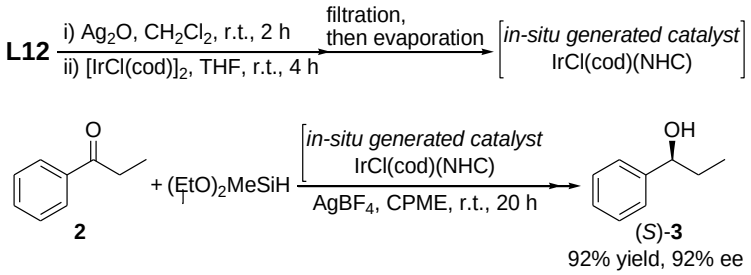


Scheme 1. A small library of the chiral NHC precursor.



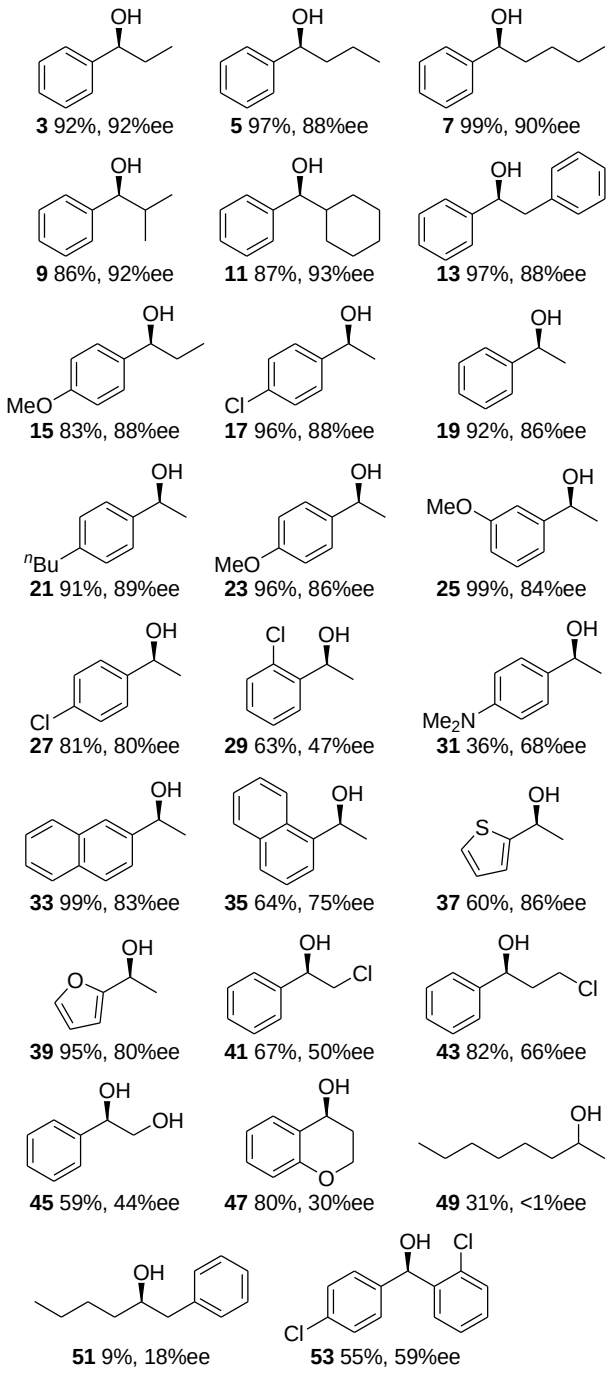
Scheme 2. Asymmetric hydrosilane reduction by *in-situ* generated IrCl(cod)(NHC) catalyst.

Table 1

Evaluation of NHC ligand precursor.[a]

Entry	Ligand Precursor	Yield [%][b]	Ee [%][c]	Config.[d]
1	**L1**	24	12	*S*
2	**L2**	25	<2	-
3	**L3**	13	14	*R*
4	**L4**	19	<2	-
5	**L5**	11	<2	-
6	**L6**	80	94	*S*
7	**L7**	83	90	*S*
8	**L8**	77	90	*S*
9	**L9**	77	89	*S*
10	**L10**	84	92	*S*
11	**L11**	82	90	*S*
12	**L12**	92	92	*S*
13	**L13**	90	93	*S*
14	**L14**	53	16	*S*
15	**L15**	27	27	*S*
16	*ent*-**L12**	95	91	*R*

[a] **2** (0.5 mmol), $(EtO)_2MeSiH$ (2.25 mmol), *in-situ* generated NHC–Ir precatalyst (4 mol %), $AgBF_4$ (4 mol %), CPME (2 mL), room temperature, 20 h. [b] Determined by GLC by the internal standard method. [c] Determined by chiral GLC (see Appendix A. Supplementary data. for details). [d] Absolute configuration.



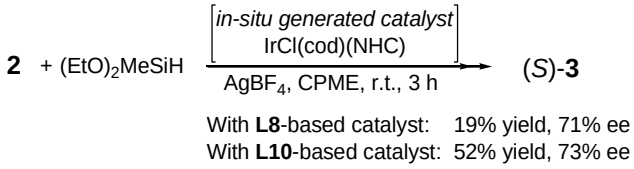
Scheme 3. Reduced product, isolated yield and enantiomeric excess from the asymmetric hydrosilylation reaction of ketone. Reaction conditions: ketone (0.5 mmol), $(EtO)_2MeSiH$ (2.25 mmol), *in-situ* generated NHC–Ir precatalyst (4 mol %) from **L12**, $AgBF_4$ (4 mol %), CPME (2 mL), room temperature, 20 h.

Table 2

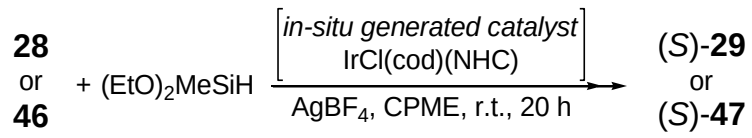
Evaluation of Ir catalyst precursor.[a]

Entry	Ir Catalyst Precursor	Yield [%]	Ee [%]
1[b]	$[IrCl(cod)]_2$	92	92
2	$[IrCl(coe)_2]_2$	66	83
3	$[IrCl(ethene)_2]_2$	77	85
4[c]	$[Ir(cod)_2]BF_4$	90	90

[a] **2** (0.5 mmol), $(EtO)_2MeSiH$ (2.25 mmol), *in-situ* generated NHC–Ir precatalyst (4 mol %) from **L12**, $AgBF_4$ (4 mol %), CPME (2 mL), room temperature, 20 h. [b] Data were shown in Table 1, entry 12. [c] Without $AgBF_4$.

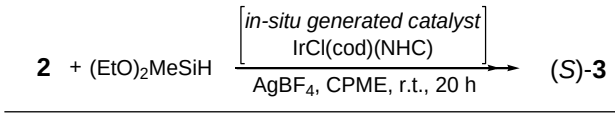


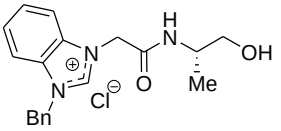
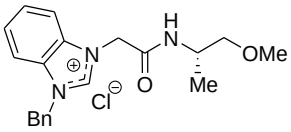
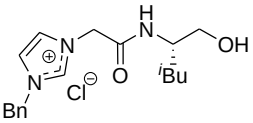
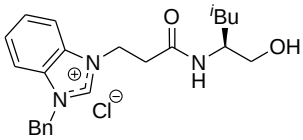
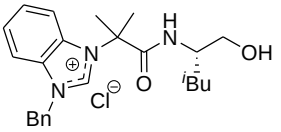
Scheme 4. Asymmetric hydrosilane reduction at the initial stage of the catalytic reaction.



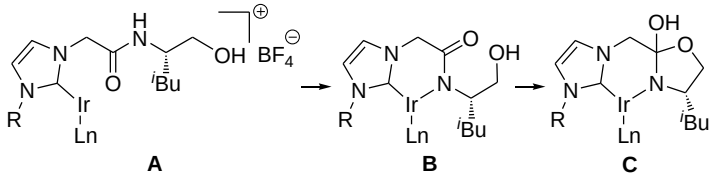
	28 → (*S*)-**29**	**46** → (*S*)-**47**
With **L12**-based catalyst:	63% yield, 47% ee	80% yield, 30% ee
With **L10**-based catalyst:	62% yield, 45% ee	
With **L13**-based catalyst:		<5% yield
With **L6**-based catalyst:	47% yield, 62% ee	58% yield, 6% ee

Scheme 5. Chiral ligand screening for the reduction of the selected ketones such as *o*-chloroacetophenone (**28**) and 4-chromanone (**46**)



Ligand Precursor		Product Yield [%]	Ee [%]
	**L16**	68% yield	88% ee
	**L17**	58% yield	*ent*-27% ee
	**L18**	36% yield	81% ee
	**L19**	<5% yield	
	**L20**	9% yield	*ent*-24% ee

Scheme 6. Evaluation of ligand precursors **L16–L20**.



Scheme 7. A plausible pathway.