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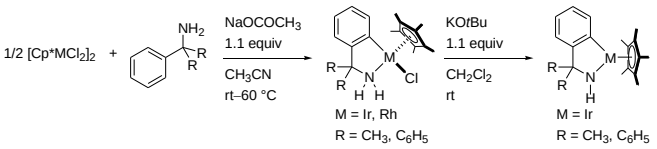
Comparative Study of Bifunctional Mononuclear and Dinuclear Amidoiridium Complexes with Chiral C–N Chelating Ligands for the Asymmetric Transfer Hydrogenation of Ketones

Yasuhiro Sato, Yoshihito Kayaki* and Takao Ikariya*[a]

Abstract: A series of new bifunctional C–N chelating Ir complexes possessing a metal/NH group was synthesized by cyclometalation of optically active primary benzylic amines such as *O*-silylated (*S*)-2-amino-2-phenylethanols (**1a** and **1a'**), (*R*)-5-amino-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**1b**), and (*R*)-1-phenyl-2,2-dimethylpropylamine (**1c**). Although treatment of KO^{t}Bu with the amine complexes originating from **1a** and **1a'** afforded amido-bridged dinuclear complexes (**3a** and **3a'**), more sterically hindered complexes were solely transformed into the coordinatively unsaturated mononuclear amido complexes (**3b** and **3c**), which can serve as real catalyst species in asymmetric transfer hydrogenation. The structural difference in the C–N chelate framework markedly affected the catalytic performance. Among them, the amido complex **3c** showed a pronounced ability to catalyze the transfer hydrogenation of acetophenone in 2-propanol, even at a low temperature of –30 °C. A hydridoiridium complex (**4c**) was also identified in the reaction of **3c** in 2-propanol, which provides mechanistic insights into the enantio-discriminating step in the hydrogen transfer to prochiral ketones.

Introduction

Group 8 and 9 metal complexes with multidentate protic amine ligands have been utilized as efficient catalysts for hydrogen transfer from alcohols and to carbonyl compounds.[1] Since the discovery of well-defined Ru catalysts bearing *N*-sulfonyldiamines (N–N chelates) two decades ago,[2] the metal/NH bifunctionality that allows the interconversion between 16e-amido and 18e-hydrido(amine) complexes has been widely credited as a powerful and versatile concept to facilitate H^+/H^- delivery.[2,3] The related C–N chelating Ir, Rh, and Ru complexes derived from benzylic amines have also been successfully synthesized (Scheme 1), and their marked catalytic abilities have been recognized.[4-9] We reported that the C–N chelating complexes could offer a beneficial enhancement in the transfer hydrogenation of ketones using 2-propanol[4] and in the aerobic oxidation of alcohols[5], compared to the original N–N chelating Ir and Rh complexes.[3] The rapid hydrogen transfer from alcohols to mononuclear amidoiridium and from hydrido(amine)iridium to ketones is induced by the high basicity of the amido complexes[4,6a] as well as by the enhanced nucleophilicity of the hydrido ligand,[6b] that arises from the strong σ-donor nature of the chelating carbon atom. Notably, these outstanding features accommodate the dynamic kinetic resolution of racemic secondary alcohols by combination with enzymatic transesterification.[8]



Scheme 1. Synthesis of C–N chelating complexes from achiral benzylic amines.

Azametalacycles with a NH group are applicable to the asymmetric transfer hydrogenation by introducing appropriate chirality into the C–N chelate frameworks.[4,5a,9] Pfeffer and coworkers developed the related cationic C–N chelating Ru complex that acted as a precatalyst for the asymmetric transfer hydrogenation of ketones and imines.[9a,f] In a mechanistic study of the Ru system, [Ru{(*R*)-κ^2(*N*,*C*)-1-(1-naphthyl)ethylamine}(η^6-benzene)(NCCH$_3$)](PF$_6$), treatment of the catalyst precursor with KO^{t}Bu in 2-propanol afforded a diastereomeric mixture of hydrido(amine) complexes with different configurations at the ruthenium center.[9d] The hydridoruthenium species presented similar catalytic behavior to that of the precatalyst and generated the corresponding mononuclear amidoruthenium species accompanied with 1-phenylethanol in a stoichiometric reaction with acetophenone. Although the coordinatively unsaturated amido complex was observed in solution by ^{1}H NMR spectroscopy, an attempt to isolate it from the reaction mixture of the precatalyst and KO^{t}Bu in CD_2Cl_2 resulted in crystallization of an amido-bridged dimer. For the relative chiral Rh and Ir systems, the concomitant formation of catalytically less active imine complexes via the dehydrogenation of benzylic amines during cyclometalation was reported.[9e] Among these derivatives, the 16e mononuclear chiral amido complexes have not been synthesized; therefore, the catalytic asymmetric hydrogen transfer requires a base additive such as KO^{t}Bu to generate active mononuclear intermediates of the hydrido(amine) and amido complexes from the precatalysts.

In this paper, we disclose the synthesis and characterization of new azairidacycles from optically active benzylamine derivatives possessing a chiral center at a position on the NH

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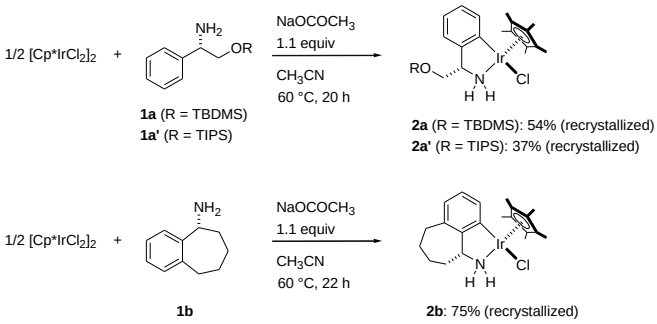
moiety and their deprotonation to isolate the amido complexes. Based on the relative reactivity and stereoselectivity of the isolated amido complexes in the hydrogen transfer from 2-propanol, we also address the mechanistic aspects of the asymmetric transfer hydrogenation of acetophenone to understand how the chiral azairidacycles lead to asymmetric induction.

Results and Discussion

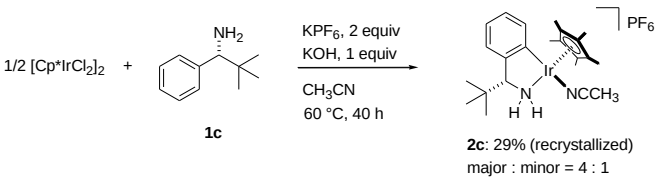
Cyclometalation of Optically Active Benzylic Amines

The C–N chelating framework was prepared by selective *ortho* C–H activation of benzylamines.[10] Analogous to our previous report on the synthesis of an azairidacycle (**2a**) from TBDMS-protected (*S*)-2-amino-2-phenylethanol (**1a**),[4] we newly performed the cyclometalation of TIPS-protected (*S*)-2-amino-2-phenylethanol (**1a'**) and (*R*)-5-amino-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**1b**)[11] using a stoichiometric amount of $[Cp^*IrCl_2]_2$ (ligand:Ir = 1:1) with a slight excess of sodium acetate in CH_3CN at 60 °C. After recrystallization, the corresponding C–N chelating chlorido complexes (**2a'**, and **2b**) were obtained as yellow crystals in 37% and 75% yields, respectively (Scheme 2). The ^{1}H NMR spectra of **2a**, **2a'**, and **2b** in $CDCl_3$ display that the signals due to the amine protons are shifted downfield compared with those of the respective parent amines **1a**, **1a'**, and **1b**. A set of nonequivalent NH_2 signals also indicates the chelating structure of the amine ligand. Coordination of the chiral C–N chelates led to the formation of diastereomers due to a central chirality at the iridium center. The diastereomeric ratios were determined to be 13:1 for **2a** and 10:1 for **2a'** by ^{1}H NMR analysis at room temperature. Less than 4% of the minor diastereomer was observed for **2b**.[12]



Scheme 2. Synthesis of the azairidacycles **2a**, **2a'**, and **2b** by cyclometalation of **1a**, **1a'**, and **1b**.

Orthometalation of (*R*)-1-phenyl-2,2-dimethylpropylamine (**1c**) possessing a sterically demanding *tert*-butyl group did not proceed with sodium acetate. Alternatively, Pfeffer's method[9a-c] proved to be feasible for the less reactive amine. Treatment of **1c** with a suspension of $[Cp^*IrCl_2]_2$, KOH, and excess KPF_6 in CH_3CN afforded the desired cationic azairidacycle (**2c**) which was isolated as yellow crystals in 29% yield after recrystallization from dichloromethane/diethyl ether (Scheme 3).



Scheme 3. Synthesis of the cationic azairidacycle **2c** by cyclometalation of **1c**.

In contrast to the C–N chelating chloridoiridium complexes **2a**, **2a'**, and **2b**, the ^{1}H NMR spectrum of the cationic complex **2c** displayed broad signals at room temperature, as shown in Figure 1. Lowering the temperature to –20 °C resulted in a peak separation with a ratio of approximately 4:1. The dynamic behavior is possibly due to the rapid stereochemical inversion at the Ir center, as depicted in Scheme 4. The labile acetonitrile group in the cationic complex **2c** readily dissociates in solution,[7] allowing the interconversion between the diastereomers.

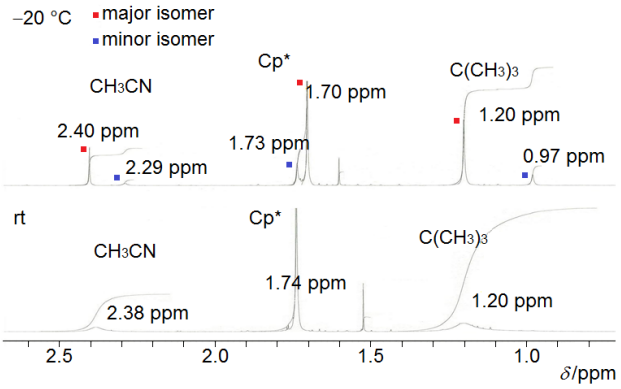
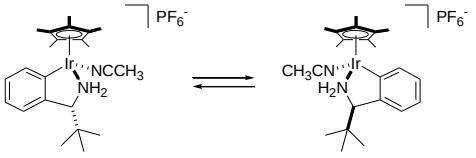


Figure 1. ^{1}H NMR spectra of **2c** at –20 °C and room temperature.

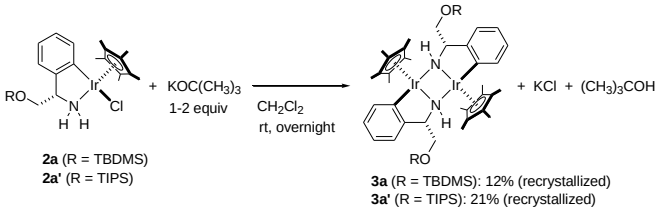


Scheme 4. Dynamic behavior of the cationic C–N chelating complex **2c**.

Synthesis of Amidoiridium Complexes via Deprotonation of Amine Ligands

Deprotonation of the precursor amine complexes was examined for conversion into optically active amidoiridium complexes, according to the reported method.[4] As shown in Scheme 5, addition of KO^{t}Bu to the C–N chelating chlorido complex **2a** or

2a' in dichloromethane turned the solution color from orange to red at room temperature. The resulting amido complexes (**3a** and **3a'**) were isolated as orange crystals in 12% and 21% yield, respectively, after purification by recrystallization from diethyl ether at –20 °C.



Scheme 5. Synthesis of the dinuclear C–N chelating amido complexes **3a** and **3a'**.

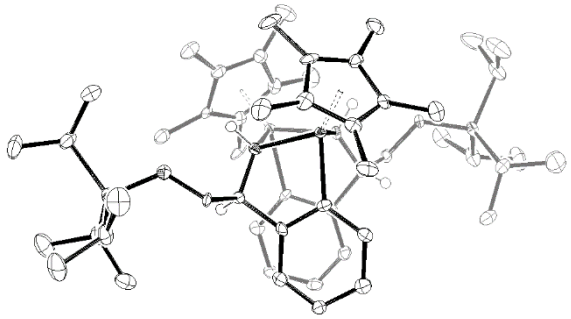
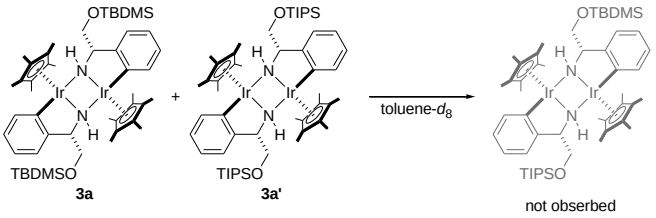


Figure 2. Molecular structure of [Cp*Ir{κ^2(*N,C*)-(*S*)-(NHCH(CH_2OTIPS)-2-C_6H_4)}]$_2$ (**3a'**) with 50% probability ellipsoids. All hydrogens except those attached to the chiral carbon and amine protons are omitted for clarity.

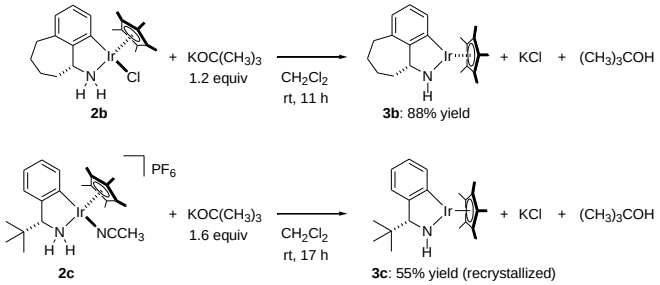
The ^{1}H NMR spectra of the amido complexes **3a** and **3a'** in CD_2Cl_2 exhibit a broad signal ascribed to the amido proton at 2.89 and 2.77 ppm, respectively. These chemical shifts are distinct from those of the mononuclear amidoiridium complexes, Cp*Ir[κ^2(*N,C*)-(N*H*C(C_6H_5)$_2$-2-C_6H_4)] and Cp*Ir[κ^2(*N,C*)-(N*H*C(CH_3)$_2$-2-C_6H_4)] (8.00 and 8.47 ppm),[4] possibly because the amido nitrogens in **3a** and **3a'** are sp^3 hybridized unlike the mononuclear amido complexes. Single-crystal X-ray diffraction of **3a'** possessing TIPS groups revealed that the amido ligand bridges to dimerize, as shown in Figure 2. The Ir_2N_2 core adopts a slightly distorted geometry, which is corroborated by a small dihedral angle of 24.936° between the triangle of Ir1-Ir2-N1 and the triangle of Ir1-Ir2-N2. The Cp* ligands arrange in a mutually *cis* orientation, and a pseudo C2 symmetric axis lies perpendicular to the Ir_2N_2 core. The absence of metal-metal bonding interactions is confirmed by a Ir–Ir distance of 3.3079(5) Å, which is longer than those of the reported amido-bridged Ir(I) complexes, for example, 2.8146(3) Å and 2.9577(4) Å in [Ir(μ_2-NH_2)L_2]$_2$ (L_2 = cod and $(CO)_2$);[13] 2.837 Å (mean value) in an amido/imido-bridged Ir(III) complex,[14] [Cp*Ir(μ_2-NHTs)(μ_2-NTs)IrCp*][OTf] (Tf = SO_2CF_3); and 2.584(1) Å in a bis(amido)-bridged Ir(II) complex,[15] [Cp*Ir{(μ_2-NH)$_2$$C_{10}H_6$-1,8}IrCp*]. The Ir–N bond lengths (2.127 Å, mean value) of **3a'** are distinct from that of the reported monomeric amidoiridium complex, Cp*Ir[κ^2(*N,C*)-(N*H*C(C_6H_5)$_2$-2-C_6H_4)] (1.903(2) Å),[4] and are closer to the Ir-sulfonylamido bonds in [Cp*Ir(μ_2-NHTs)(μ_2-NTs)IrCp*][OTf] (Tf = SO_2CF_3) (2.114(6) and 2.131(6) Å) or to the Ir-arylamido bonds in [Cp*Ir{(μ_2-NH)$_2$$C_{10}H_6$-1,8}IrCp*] (2.02-2.11 Å).[15]

To verify whether the dimeric amido complexes are accessible to the mononuclear amido species in solution, we performed crossover experiments using the isolated homodimers. ^{1}H NMR monitoring of a 1:1 mixture of the amido complexes **3a** and **3a'** in toluene-d_8 revealed that no scrambling process took place, even when increasing the temperature up to 100 °C (Scheme 6). It was also confirmed that the amido-bridging structure was maintained in other polar solvents including 2-propanol.



Scheme 6. A crossover experiment using the amidoiridium dimers **3a** and **3a'**.

In contrast, treatment of the C–N chelating (*R*)-amine complexes **2b** and **2c** with a stoichiometric amount of KO^{t}Bu in dichloromethane caused an immediate color change from yellow to purple, which implies formation of the corresponding mononuclear amido complexes (**3b** and **3c**) with a similar structure as the previously reported achiral complexes (Scheme 7).[4] In the ^{1}H NMR spectra of **3b** and **3c** in CD_2Cl_2, the amido NH signals appeared in lower fields at 8.21 and 8.36 ppm, respectively, compared to the NH_2 signals of the parent complexes (3.46 and 4.99 ppm for **2b**; 3.90 and 4.36 ppm for **2c**). This downfield shift is characteristic of the protons attached to nitrogen atoms with sp^2 hybridization in coordinatively unsaturated amido complexes. As illustrated in Figure 3, X-ray crystallographic analysis indicates that the amido complex possesses a monomeric structure with a planar geometry around the metal center. The amido complex **3c** has a relatively short Ir–N bond (1.902(4) Å) compared with that of a general C–N chelating chloroiridium complex (2.119 and 2.137 Å).[4] The substituents vicinal to the coordinating nitrogen are crucial for the structure of the amido complex. The monomeric (*R*)-amido complexes **3b** and **3c** possess a sterically constrained framework that hampers dimerization, as observed for the reported complexes derived from achiral tritylamine and cumylamine.[4]



Scheme 7. Synthesis of the mononuclear amido complexes **3b** and **3c**.

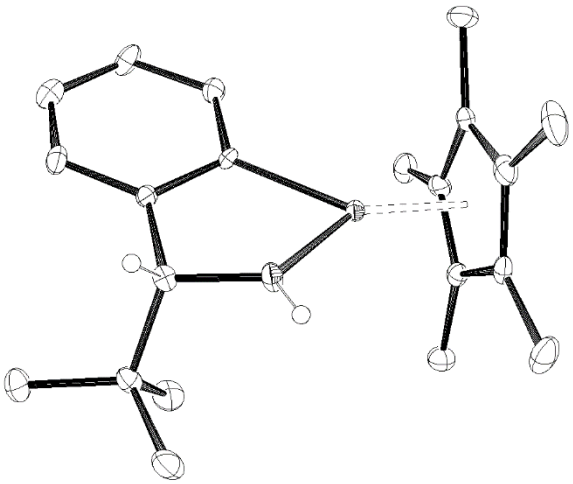


Figure 3. Molecular structure of Cp*Ir[κ^2(*N*,*C*)-(*R*)-{NHCH(C(CH$_3$)$_3$)-2-C$_6$H$_4$}] (**3c**) with 50% probability ellipsoids. All hydrogens except those attached to the chiral carbon and amine are omitted for clarity.

Catalytic Behavior of Amidoiridium Complexes

In order to compare the catalytic behavior of the isolated chiral amidoiridium complexes, asymmetric transfer hydrogenation of acetophenone (0.1 M) was carried out in 2-propanol using **3a**, **3b**, and **3c** with a substrate/catalyst (S/C) ratio of 200 at 30 °C. In all cases, (*S*)-1-phenylethanol was selectively formed, even in the absence of additional base; however, the catalytic activity of the dinuclear complex **3a** was remarkably lower than that of the mononuclear complexes **3b** and **3c**, as shown in Figure 4. The mononuclear amido complexes **3b** and **3c** exhibited outstanding performance, reaching almost complete conversion within 30 min, whereas the enantiomeric excess (ee) of the product decreased with time (Figure 5). Following the trend that the catalytic ability in the hydrogen transfer between ketones and alcohols is inherently associated with the ease of product racemization,[8d] **3c** exhibits superior activity over **3b** for the reduction.

When the transfer hydrogenation was conducted at a reduced catalyst concentration and the the S/C was increased from 200 to 1,000, the striking activity of the monomeric amido complexes **3b** and **3c** was maintained with an increase in the enantioselectivity. As summarized in Table 1, **3a**, **3b**, and **3c** provided the (*S*)-product in good ee of 61–69% (entries 1-3). Gratifyingly, **3c** effectively catalyzed the asymmetric transfer hydrogenation, even at –30 °C, and (*S*)-1-phenylethanol was smoothly produced within 4 h with an improved ee of 81% (entry 4).

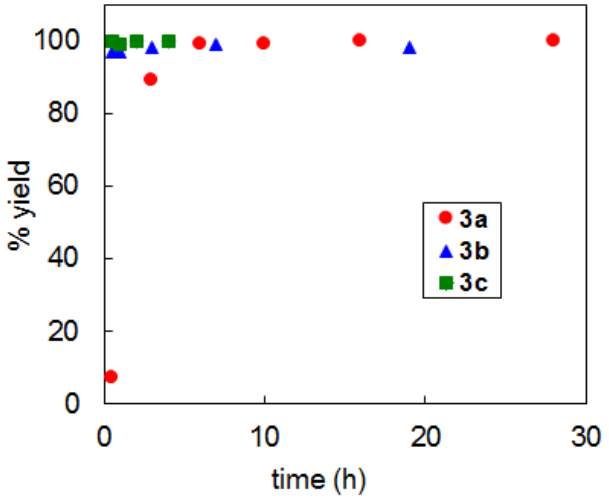


Figure 4. Time course of the yield of (*S*)-1-phenylethanol in the transfer hydrogenation of acetophenone catalyzed by **3a**, **3b**, and **3c** with a substrate/catalyst (S/C) ratio of 200.

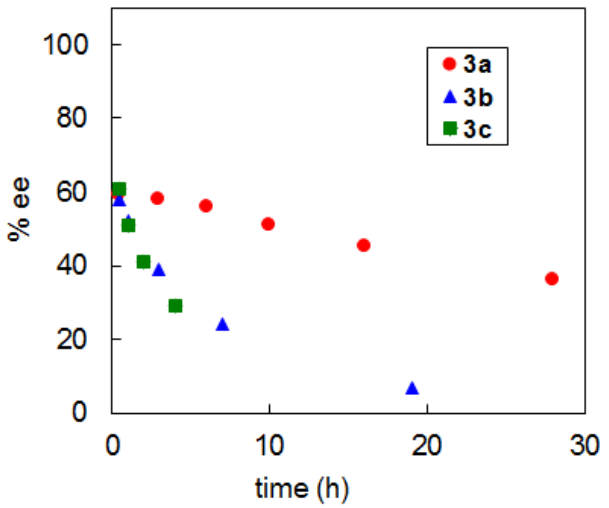


Figure 5. Time course of the optical purity of (*S*)-1-phenylethanol in the transfer hydrogenation of acetophenone catalyzed by **3a**, **3b**, and **3c** with a substrate/catalyst (S/C) ratio of 200.

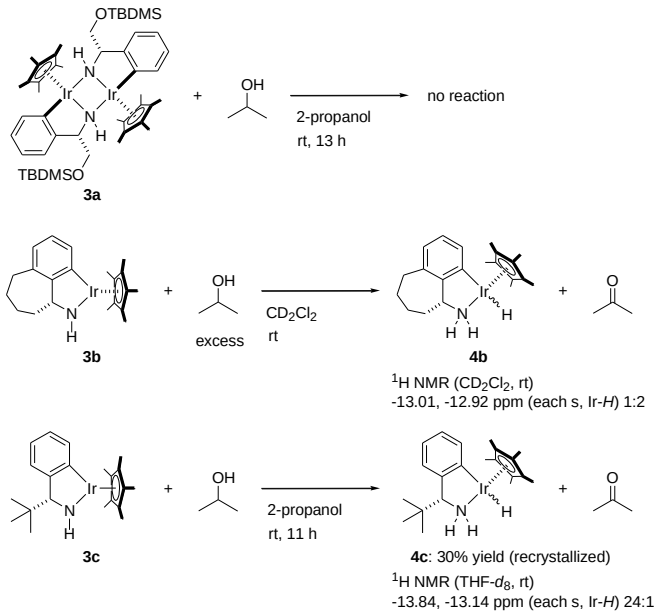
Table 1. Asymmetric transfer hydrogenation of acetophenone in 2-propanol catalyzed by **3a**, **3b**, and **3c** with a substrate/catalyst (S/C) ratio of 1000.

Entry	Catalyst	*t* [h]	Yield [%]	Ee [%]
1	**3a**	27.5	79	61
2	**3b**	1	88	63
3	**3c**	1	83	69
4[a]	**3c**	4	78	81

[a] This reaction was performed at –30 °C.

Dehydrogenation of 2-Propanol by Amidoiridium Complexes

The excellent hydrogen transfer ability of the mononuclear amidoiridium complexes **3b** and **3c** was also confirmed by the dehydrogenation of 2-propanol to furnish the corresponding hydrido(amine) complexes (**4b** and **4c**). In sharp contrast to the bridging amido complex **3a** being inert in 2-propanol at room temperature, the amido complex **3b**, formed *in-situ* from **2b** and KO^{t}Bu in CD_2Cl_2, was completely converted into **4b** by the addition of excess of 2-propanol. Two sets of signals corresponding to the diastereomers of **4b** were confirmed by the ^{1}H NMR spectrum, in which the Ir–H resonances appeared at –13.03 and –12.96 ppm with an integral ratio of 1:2.



Scheme 8. Attempts at the synthesis of the C–N chelating hydrido(amine) complexes **4** from the C–N chelating amido complexes **3a**, **3b**, and **3c**.

Although attempts to isolate **4b** were unsuccessful due to its instability, the structurally well-defined (*R*)-amido complex **3c** could smoothly react in 2-propanol to yield the corresponding hydrido complex (**4c**), which can be stored under an argon atmosphere at –20 °C for several months. Pale yellow crystals of **4c** were successfully obtained in 30% yield after crystallization from diethyl ether at –20 °C. In the ^{1}H NMR spectrum of **4c** in THF-d_8 at room temperature, a mixture of two diastereomers was observed at a ratio of 24:1. Preliminary X-ray crystallographic analysis of **4c** revealed a three-legged piano-stool structure of a single diastereomer possessing an *S* configuration at the iridium center, as shown in Figure S2, but further structural refinement was not possible due to the poor crystal quality. The chiral metal center is slightly fluxional in solution, as evident from the fact that the obtained crystals epimerized to the diastereomeric mixture upon dissolution in THF-d_8.

The crystallographic structure of the amido and hydrido complexes, **3c** and **4c**, could be rationalized with the enantiomeric outcome of the hydrogen transfer process. The S_{Ir}-isomer of **4c** was favorably generated because 2-propanol approached to the amido complex **3c** away from the spatially congested *tert*-butyl group as depicted in Figure 6a. The H^+/H^- transfer from **4c** to the *Re* face of acetophenone resulted in the formation of (*S*)-1-phenylethanol. From the extensive theoretical studies on the bifunctional Ru(η^6-arene) catalysts bearing aminoalcohol and *N*-sulfonyldiamine ligands, a C-H/π attraction between the η^6-arene ligand and the phenyl ring of acetophenone in a six-membered pericyclic transition structure was realized as the main origin of the enantioselectivity.[16] The enantioselection by **4c** is also likely governed by a congeneric C-H/π interaction involving the η^5-C_5Me_5 ligand,[17] as shown in Figure 6b. The model can explain the preferential formation of (*S*)-alcohol via the unique *Re* face selection derived from the C-H/π interaction, permitting a rather crowded transition state.

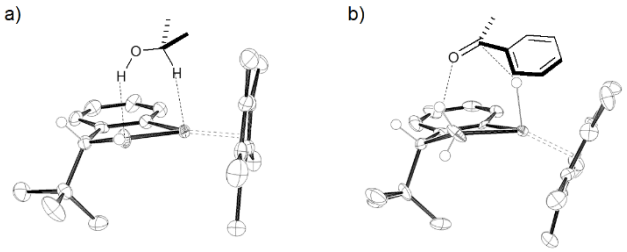


Figure 6. Conceptual drawings based on the ORTEP structures of **3c** and **4c**: a) H^+/H^- delivery from 2-propanol to the amido complex **3c** and b) subsequent transfer from the hydrido complex (S_{Ir})-**4c** to acetophenone to produce (*S*)-1-phenylethanol.

Conclusions

By changing the C–N chelating framework, mono- and dinuclear amidoiridium complexes were specifically synthesized via deprotonation of primary amine-Ir complexes derived from optically active benzylamines possessing a chiral center at the benzyl position. The coordinatively unsaturated amidoiridium complexes **3b** and **3c** exhibited outstanding catalytic

performance in the asymmetric transfer hydrogenation of acetophenone in 2-propanol to yield (*S*)-1-phenylethanol in good enantioselectivities up to 81% ee, whereas the bis(amido)-bridged diiridium complex **3a** exhibited lower hydrogen transfer ability. The catalytic utility of the mononuclear amido complex was in accord with the facile and highly selective formation of the hydrido complex (R_C, S_{Ir})-**4c** from **3c** in 2-propanol. The enhanced enantioselectivity observed for **3c** is attributable to the effective collision between the *tert*-butyl group and the hydrogen donor, 2-propanol, giving rise to highly diastereoselective formation of hydridoiridium species, which should be strongly contributed to the precise discrimination of the prochiral face of the ketone substrate. Further studies on the intimate stereochemical mechanism of this transfer hydrogenation are in progress to develop a new series of chiral C–N chelating ligands.

Experimental Section

General: All experiments were conducted under an argon atmosphere using Schlenk techniques. All deuterated NMR solvents were dried and degassed by appropriate methods. Solvents were purchased from Kanto Chemical and Nacalai Tesque, and dried by refluxing over sodium benzophenone ketyl (THF, toluene, diethyl ether), P_2O_5 (dichloromethane, acetonitrile), or CaH_2 (hexane, pentane) and distilled under argon. $[Cp^*IrCl_2]_2$,[18] (*R*)-5-amino-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (**1b**),[11] and Cp*IrCl[κ^2(*N,C*)-(*S*)-($NH_2CHCH_2OSi(CH_3)_2(C(CH_3)_3$-2-$C_6H_4$)] (**2a**)[4] were prepared according to the literature methods. ^{1}H, ^{19}F, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded on JEOL JNM-LA300 and JNM-ECX400 spectrometers and referenced to tetramethylsilane via the solvent resonance. Elemental analyses were carried out using a PE2400 Series II CHNS/O Analyzer (PerkinElmer). Analytical gas chromatography was performed with a Shimadzu GC-17A gas chromatograph equipped with an INNOWAX capillary column (30 m × 0.25 mm i.d.) purchased from Agilent Technologies. Mass spectra (MS) were obtained with a JEOL JMS-SX102A instrument. High performance liquid chromatography (HPLC) analysis was performed using a system comprised of a JASCO column oven: CO-1565, a low-pressure gradient unit: LG-1580-02, a pump: PU-1580, a degasser: DG 1580-53, a UV/VIS detector: UV-1570, and a CD detector: CD-2095. Analytical chiral HPLC was performed on a Chiralcel OD column (4.6 mm × 25 cm) purchased from Daicel Chemical Industries, Ltd. with hexane/2-propanol as the eluent where baseline separation was obtained.

Synthesis of (*S*)-2-triisopropylsiloxy-1-phenylethylamine (1a'): To a solution of (*S*)-2-phenylglycinol (3.52 g, 25.7 mmol), triethylamine (3.12 g, 30.9 mmol), and 4-(dimethylamino)pyridine (0.323 g, 2.65 mmol) in CH_2Cl_2 (35 mL) was added triisopropylsilyl chloride (5.09 g, 26.4 mmol). After stirring for 3 days, the reaction mixture was diluted with water, and extracted with CH_2Cl_2. The combined organic layer was dried over sodium sulphate, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane/CH_2Cl_2), giving the amine **1a'** (0.456 g, 6% yield) as a colorless oil. $[\alpha]_D^{25}$ +170 (c 0.045, $CHCl_3$). ^{1}H NMR (399.8 MHz, $CDCl_3$, RT): δ 1.04-1.05 (m, 21H; OSi(C*H*(CH_3)$_2$)$_3$), 1.96 (br, 2H; N*H*$_2$), 3.61 (m, 1H; OC*H*$_2$CHNH$_2$), 3.81 (m, 1H; OC*H*$_2$CHNH$_2$), 4.10 (m, 1H; OCH$_2$C*H*NH$_2$), 7.23-7.39 (m, 4H; C_6H_5); ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, RT): δ 12.0 (OSi(*C*H(CH_3)$_2$)$_3$), 18.1 (OSi(CH(*C*H$_3$)$_2$)$_3$), 58.0 (OCH$_2$*C*HNH$_2$), 69.9 (OCH$_2$CHNH$_2$), 127.0, 127.4, 128.4, 142.5 (C_6H_5). HRMS (ESI+) calcd for $C_{17}H_{32}NOSi$ [M+H]+: 294.2253. Found: 294.2247.

Synthesis of (*R*)-1-phenyl-2,2-dimethylpropylamine (1c): A mixture of 2,2-dimethylpropiophenone (5.01 g, 30.9 mmol), (*S*)-1-phenylethylamine (7.51 g, 62.1 mmol), and trifluoroacetic acid (1.00×10^{-1} mL) was refluxed in toluene (30 mL) for 14 h with azeotropic removal of water using a Dean-Stark trap. The solvent and unreacted amine were removed under reduced pressure, and toluene (20 mL) was added to the residue. The resulting mixture was added dropwise to a solution of sodium borohydride (1.45 g, 38.4 mmol) in anhydrous ethanol (50 mL) at –20 °C. After stirring at room temperature for 45 h, water was added to the mixture and the solvents were evaporated to dryness. The residue was extracted with diethyl ether, dried over sodium sulphate, and concentrated under reduced pressure. The crude product was mixed with Pd/C (0.62 g), acetic acid (6 mL), water (6 mL), and methanol (45 mL) and was then shaken at room temperature for 38 h under atmospheric pressure of hydrogen. After filtration of the resulting mixture through a plug of Celite, the solvents were removed under reduced pressure, and the residue dissolved in chloroform. The organic phase was washed with an aqueous solution of NH_3 and dried over sodium sulphate. After evaporation of the filtrate to dryness, the desired (*R*)-amine **1c** (3.76 g, 75% yield) was obtained as a pale yellow oil. The spectral data were in accord with those reported for the racemic **1c**.[19] $[\alpha]_D^{25}$ +48 (c 0.066, $CHCl_3$), 96% ee (Chiralcel OD-H, 2-propanol/hexane = 5/95; 30 ºC, 1 mL/min, detection at 254 nm; t_R 5.1 min (*R* form) and 8.6 min (*S* form)). ^{1}H NMR (399.8 MHz, $CDCl_3$, RT): δ 0.90 (s, 9H; C(CH_3)$_3$), 1.50 (br, 2H; NH_2), 3.70 (s, 1H; C*H*NH$_2$), 7.25-7.29 (m, 4H; C_6H_5); ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, RT): δ 26.6 (C(*C*H$_3$)$_3$), 35.1 (*C*(CH$_3$)$_3$), 65.4 (*C*HNH$_2$), 126.8, 127.6, 128.3, 143.9 (C_6H_5).

Synthesis of Cp*IrCl[κ^2(*N,C*)-(*S*)-($NH_2CHCH_2OSi(CH(CH_3)_2)_3$-2-$C_6H_4$)] (2a'): A mixture of $[Cp^*IrCl_2]_2$ (0.39 g, 0.49 mmol), (*S*)-2-triisopropylsiloxy-1-phenylethylamine (**1a'**) (0.28 g, 0.96 mmol), and NaOAc (85 mg, 1.0 mmol) in CH_3CN (20 mL) was stirred at 60 °C for 20 h. The solvent was removed under reduced pressure. After the residue diluted with CH_2Cl_2, the resulting mixture was filtered through a Celite pad. Evaporation of the filtrate to dryness gave the iridacycle product **2a'**. Orange crystals were obtained by slow diffusion of hexane into the solution in toluene. Yield: 37% (0.23 g, 0.36 mmol) as a 10:1 mixture of diastereomers. ^{1}H NMR (399.8 MHz, $CDCl_3$, RT, major diastereomer): δ 1.07-1.20 (m, 21H; OSi(C*H*(CH_3)$_2$)$_3$), 1.74 (s, 15H; $C_5(CH_3)_5$), 3.12-3.17 (dd, 1H; NH_2CHCH_2OSi), 3.73-3.76 (m, 1H; NH_2CHCH_2OSi), 4.16-4.20 (m, 1H; NH_2CHCH_2OSi), 4.46, 4.75 (each br, 1H; N*H*$_2$CHCH$_2$OSi), 6.79-7.50 (m, 4H; C_6H_4); ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, RT, major diastereomer): δ 9.4 ($C_5(CH_3)_5$), 12.0 (OSi(*C*H(CH_3)$_2$)$_3$), 17.8, 18.1 (OSi(CH(*C*H$_3$)$_2$)$_3$), 66.0 (NH_2CHCH_2OSi), 67.6 (NH_2CHCH_2O), 86.8 ($C_5(CH_3)_5$), 120.6, 122.3, 127.7, 136.7, 147.4, 155.8 (C_6H_4). Anal. Calcd for $C_{27}H_{45}ClIrNOSi$: C, 49.48; H, 6.92; N, 2.14. Found: C, 49.66; H, 6.92; N, 2.31.

Synthesis of Cp*IrCl[κ^2(*N,C*)-(*R*)-{$NH_2CH(CH_2)_4$-2-C_6H_3}] (2b): A mixture of $[Cp^*IrCl_2]_2$ (0.81 g, 1.0 mmol), (*R*)-5-amino-6,7,8,9-tetrahydro-

5*H*-benzocycloheptene (**1b**) (0.33 g, 2.0 mmol), and NaOAc (0.17 g, 2.1 mmol) in CH_3CN (20 mL) was stirred at 60 °C for 22 h. The solvent was removed under reduced pressure. After the residue diluted with CH_2Cl_2, the resulting mixture was filtered through a Celite pad. Evaporation of the filtrate to dryness gave the iridacycle product **2b**. Orange crystals were obtained by slow diffusion of hexane into the solution in CH_2Cl_2. Yield: 75% (0.79 g, 1.5 mmol) as a >25:1 mixture of diastereomers. ^{1}H NMR (399.8 MHz, $CDCl_3$, RT, major diastereomer): δ 1.19-1.29 (m, 1H; $NH_2CH(CH_2)_4C_6H_3$), 1.49-2.03 (m, 5H; $NH_2CH(CH_2)_4C_6H_3$), 1.70 (s, 15H; $C_5(CH_3)_5$), 2,61-2.76 (m, 2H; $NH_2CH(CH_2)_4C_6H_3$), 4.50 (m, 1H; $NH_2CH(CH_2)_4C_6H_3$), 3.46, 4.99 (each br, 1H; $NH_2CH(CH_2)_4C_6H_3$), 6.54-7.32 (m, 3H; $NH_2CH(CH_2)_4C_6H_3$); ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, RT): δ 9.4 ($C_5(CH_3)_5$), 27.6, 29.9, 36.5, 37.1 ($NH_2CH(CH_2)_4C_6H_3$), 65.8 ($NH_2CH(CH_2)_4C_6H_3$), 86.7 ($C_5(CH_3)_5$), 123.0, 127.1, 134.4, 135.6, 152.0, 153.3 (C_6H_3). Anal. Calcd for $C_{21}H_{29}ClIrN$: C, 48.21; H, 5.59; N, 2.68. Found: C, 48.28; H, 5.71; N, 2.71.

Synthesis of [Cp*Ir{κ^2(*N,C*)-(*R*)-($NH_2CHC(CH_3)_3$-2-C_6H_4)}(CH_3CN)]PF_6 (2c): Optically acitve (*R*)-amine **1c** (0.68 g, 4.18 mmol) was added to a suspension of $[Cp^*IrCl_2]_2$ (1.57 g, 1.97 mmol), KOH (0.23 g, 4.11 mmol), and KPF_6 (1.53 g, 8.29 mmol) in CH_3CN (20 mL), and the resulting mixture was stirred at 60 °C under Ar atmosphere for 95 h. The solvent was removed under reduced pressure. After the residue diluted with CH_2Cl_2, the resulting mixture was filtered through a Celite pad. The filtrate was evaporated under reduced pressure. The residue was washed with hexane and diethyl ether and dried under vacuum. Recrystallization from CH_2Cl_2 and diethyl ether afforded yellow crystals in 29% yield (0.77 g, 1.1 mmol) as a 4:1 mixture of diastereomers. ^{1}H NMR (399.8 MHz, $CDCl_3$, –20 °C, major diastereomer): δ 1.23 (s, 9H; $C(CH_3)_3$), 1.72 (s, 15H; $C_5(CH_3)_5$), 2.42 (s, 3H; CH_3CN), 3.41-3.44 (m, 1H; NH_2CH), 3.87-3.93, 4.34-4.36 (each br, 1H; NH_2), 6.99-7.48 (m, 4H; C_6H_4); ^{1}H NMR (399.8 MHz, $CDCl_3$, –20 °C, minor diastereomer): δ 1.00 (s, 9H; $C(CH_3)_3$), 1.76 (s, 15H; $C_5(CH_3)_5$), 2.30 (br, 3H; CH_3CN), 3.97-3.98 (m, 1H; NH_2CH), 3.79-3.82, 5.21-5.26 (each br, 1H; NH_2), 6.91-7.48 (m, 4H; C_6H_4); ^{13}C{^{1}H} NMR (399.8 MHz, $CDCl_3$, –20 °C, major diastereomer): δ 4.3 (CH_3CN), 9.2 ($C_5(CH_3)_5$), 27.1 ($C(CH_3)_3$), 35.2 ($C(CH_3)_3$), 76.4 ($CHNH_2$), 89.3 ($C_5(CH_3)_5$), 117.8 (CH_3CN), 123.3, 124.5, 127.5, 137.0, 146.6, 152.7 (C_6H_4). Anal. Calcd for $C_{23}H_{34}IrN_2PF_6$: C, 40.88; H, 5.07; N, 4.15. Found: C, 40.67; H, 5.06; N, 4.02.

Synthesis of [Cp*Ir{κ^2(*N,C*)-(*S*)-($NHCHCH_2OSi(CH_3)_2(C(CH_3)_3$-2-$C_6H_4$)}]$_2$ (3a): A mixture of Cp*IrCl[κ^2(*N,C*)-(*S*)-($NH_2CHCH_2OSi(CH_3)_2(C(CH_3)_3$-2-$C_6H_4$)] (**2a**) (0.34 g, 0.55 mmol) and $KOC(CH_3)_3$ (75 mg, 0.67 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 11 h. The solvent was removed under reduced pressure. After the residue was dissolved in diethyl ether, insoluble material was removed by filtration. Evaporation of the filtrate to dryness gave the product **3a**. Recrystallization from diethyl ether at –20 °C afforded orange crystals. Yield: 12% (37 mg, 32 μmol). ^{1}H NMR (399.8 MHz, CD_2Cl_2, RT): δ 0.03, 0.04 (each s, 6H; $OSi(CH_3)_2C(CH_3)_3$), 0.90 (s, 18H; $OSi(CH_3)_2C(CH_3)_3$), 1.63 (s, 30H; $C_5(CH_3)_5$), 2.44 (m, 2H; $NHCHCH_2$), 2.86 (br, 2H; $NHCHCH_2$), 2.89, 3.74 (each m, 2H; $NHCHCH_2$), 6.02-7.12 (m, 8H; C_6H_4); ^{13}C{^{1}H} NMR (100.5 MHz, CD_2Cl_2, RT): δ -5.4, -5.1 ($OSi(CH_3)_2C(CH_3)_3$), 9.4 ($C_5(CH_3)_5$), 18.6 ($OSi(CH_3)_2C(CH_3)_3$), 26.0 ($OSi(CH_3)_2C(CH_3)_3$), 68.9 (NH_2CHCH_2O), 76.4 (NH_2CHCH_2O), 85.3 ($C_5(CH_3)_5$), 119.4, 120.5, 124.3, 133.6, 155.7, 157.0 (C_6H_4). Anal. Calcd for $C_{48}H_{76}Ir_2N_2O_2Si_2$: C, 49.97; H, 6.64; N, 2.43. Found: C, 49.93; H, 7.10; N, 2.61.

Synthesis of [Cp*Ir{κ^2(*N,C*)-(*S*)-($NHCHCH_2OSi(CH(CH_3)_2)_3$-2-$C_6H_4$)}]$_2$ (3a'): A mixture of Cp*IrCl[κ^2(*N,C*)-(*S*)-($NH_2CHCH_2OSi(CH(CH_3)_2)_3$-2-$C_6H_4$)] (**2a'**) (0.21 g, 0.33 mmol) and $KOC(CH_3)_3$ (61 mg, 0.54 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 11 h. The solvent was removed under reduced pressure. After the residue was dissolved in diethyl ether, insoluble material was removed by filtration. Evaporation of the filtrate to dryness gave the product. Recrystallization from diethyl ether at –20 °C afforded orange crystals. Yield: 21% (43 mg, 35 μmol). ^{1}H NMR (399.8 MHz, CD_2Cl_2, RT): δ 1.04-1.08 (m, 42H; $OSi(CH(CH_3)_2)_3$), 1.64 (s, 30H; $C_5(CH_3)_5$), 2.55 (m, 2H; $NHCHCH_2$), 2.74 (br, 2H; $NHCHCH_2$), 2.97, 3.81 (each m, 2H; $NHCHCH_2$), 6.00-7.13 (m, 8H; C_6H_4); ^{13}C{^{1}H} NMR (100.5 MHz, CD_2Cl_2, RT): δ 9.44 ($C_5(CH_3)_5$), 12.3 ($OSi(CH(CH_3)_2)_3$), 18.0, 18.1 ($OSi(CH(CH_3)_2)_3$), 69.1 ($NHCHCH_2O$), 77.0 ($NHCHCH_2O$), 85.2 ($C_5(CH_3)_5$), 119.4, 120.6, 124.3, 133.3, 155.7, 156.9 (C_6H_4). Anal. Calcd for $C_{54}H_{88}Ir_2N_2O_2Si_2$: C 52.39, H 7.17, N 2.26. Found: C 52.75, H 7.17, N 2.26.

Synthesis of Cp*Ir[κ^2(*N,C*)-(*R*)-{$NHCH(CH_2)_4$-2-C_6H_3}] (3b): A mixture of Cp*IrCl[κ^2(*N,C*)-(*R*)-{$NH_2CH(CH_2)_4$-2-C_6H_3}] (**2b**) (0.45 g, 0.86 mmol) and $KOC(CH_3)_3$ (0.11 g, 1.0 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 11 h. The solvent was removed under reduced pressure. After the residue was dissolved in diethyl ether, insoluble material was removed by filtration. Evaporation of the filtrate to dryness gave the product **3b**. Recrystallization from diethyl ether at –20 °C afforded purple crystals in 88% yield (0.37 g, 0.76 mmol). ^{1}H NMR (399.8 MHz, CD_2Cl_2, RT): δ 1.93 (s, 15H; $C_5(CH_3)_5$), 0.81-2.76 (m, 9H; $NHCH(CH_2)_4C_6H_3$), 6.54-7.88 (m, 3H; $NHCH(CH_2)_4C_6H_3$), 8.19 (br, 1H; $NHCH(CH_2)_4C_6H_3$); ^{13}C{^{1}H} NMR (100.5 MHz, CD_2Cl_2, RT): δ 10.0 ($C_5(CH_3)_5$), 28.2, 31.2, 33.9, 37.6 ($NHCH(CH_2)_4C_6H_3$), 82.4 ($NHCH(CH_2)_4C_6H_3$), 87.0 ($C_5(CH_3)_5$), 123.2, 124.8, 134.5, 136.0, 159.0, 163.6 (C_6H_3). Anal. Calcd for $C_{21}H_{28}IrN$: C, 51.83, H 5.80, N 2.88. Found: C 51.43, H 5.96, N 2.87.

Synthesis of Cp*Ir[κ^2(*N,C*)-(*R*)-($NHCHC(CH_3)_3$-2-C_6H_4)] (3c): A mixture of [Cp*Ir{κ^2(*N,C*)-(*R*)-($NH_2CHC(CH_3)_3$-2-C_6H_4)}(CH_3CN)]PF_6 (**2c**) (0.21 g, 0.32 mmol) and $KOC(CH_3)_3$ (56 mg, 0.50 mmol) in CH_2Cl_2 (15 mL) was stirred at room temperature for overnight. The solvent was removed under reduced pressure. After the residue was dissolved in diethyl ether, insoluble material was removed by filtration. Evaporation of the filtrate to dryness gave the product. Dark red crystals suitable for X-ray crystallography were obtained by cooling the ethereal solution at –20 °C in 55% yield (85 mg, 0.17 mmol). ^{1}H NMR (399.8 MHz, CD_2Cl_2, RT): δ 0.80 (s, 9H; $C(CH_3)_3$), 1.93 (s, 15H; $C_5(CH_3)_5$), 2.36 (d, $^3J_{HH}$ = 3.1 Hz, 1H; $NHCH$) , 6.74-8.04 (m, 4H; C_6H_4), 8.36 (br, 1H; NH); ^{13}C{^{1}H} NMR (100.5 MHz, CD_2Cl_2, RT): δ 10.0 ($C_5(CH_3)_5$), 27.1 ($C(CH_3)_3$), 32.4 ($C(CH_3)_3$), 86.7 ($NHCH$), 88.6 ($C_5(CH_3)_5$), 121.2, 122.0, 124.4, 136.1, 157.1, 166.2 (C_6H_4). Anal. Calcd for $C_{21}H_{30}IrN$: C 51.61, H 6.19, N 2.87. Found: C 51.51, H 6.14, N 3.00.

Synthesis of Cp*IrH[κ^2(*N,C*)-(*R*)-($NH_2CHC(CH_3)_3$-2-C_6H_4)] (4c): Cp*Ir[κ^2(*N,C*)-(*R*)-($NHCHC(CH_3)_3$)] (**3c**) (56 mg, 0.12 mmol) dissolved in 2-propanol (3 mL) was stirred at room temperature for 12 h. The solvent was removed under reduced pressure. The residue was washed with pentane and dried under reduced pressure. Pale yellow crystals suitable

for X-ray crystallography were obtained by cooling the solution in diethyl ether at –20 °C. Yield 30% (17 mg, 35 μmol) as a 24:1 mixture of diastereomers. ^{1}H NMR (399.8 MHz, THF-d_8, RT, major diastereomer): δ –13.84 (s, 1H; Ir*H*), 0.92 (s, 9H; $NH_2CHC(CH_3)_3C_6H_4$), 1.85 (s, 15H; $C_5(CH_3)_5$), 3.35 (br, 2H; $NH_2CHC(CH_3)_3C_6H_4$), 5.68 (br, 1H; NH2C*H*C$(CH_3)_3C_6H_4$), 6.49-7.30 (m, 4H; $NH_2CHC(CH_3)_3C_6H_4$). Anal. Calcd for $C_{21}H_{32}$IrN: C 51.40, H 6.57, N 2.85. Found: C 51.52, H 6.48, N 2.96.

NMR Monitoring of a Mixture of 3a and 3a': An NMR tube equipped with a J-Young valve was charged with **3a** (4.3 mg, 3.7 μmol) and **3a'** (4.7 mg, 3.8 μmol) in 0.5 mL of toluene-d_8 at room temperature. The reaction mixture was analyzed by ^{1}H NMR spectra after heating at 60 and 100 °C.

General Procedure of Transfer Hydrogenation of Acetophenone in 2-Propanol Catalyzed by Amidoiridium Complexes: A 100-mL Schlenk flask was charged with an appropriate amount of the iridium catalyst (**3a**, **3b**, and **3c**), durene (0.11 g, 0.83 mmol; an internal standard) and 2-propanol (100 mL) under Ar atmosphere. After addition of acetophenone (1.2 g, 10 mmol), the reaction mixture was stirred at 30 °C for an appropriate period. The yield of (*S*)-1-phenylethanol was determined by GC analysis and the optical purity was determined by HPLC analysis (Chiralcel OD, 2-propanol/hexane = 5/95; 30 ºC, 0.5 mL/min, detection at 254 nm; t_R 8.0 min (*R* isomer) and 9.0 min (*S* isomer)).

X-ray Structure Determination of 3a', 3b, 3c, and 4c: X-ray diffraction studies were conducted using a Rigaku Saturn 70 CCD area detector equipped with graphite-monochromated Mo-$K\alpha$ radiation (λ = 0.71070 Å) under a nitrogen stream at 193 K. Indexing was performed from seven images. The crystal-to-detector distance was 45.05 mm. Data were collected to a maximum 2θ value of 55.0°. A total of 720 oscillation images were collected. A sweep of the data was carried out by using ω scans from –110.0 to 70.0° in 0.5° steps at χ = 45.0° and ϕ = 0.0°. A second sweep was performed by using ω scans from –110.0 to 70.0° in 0.5° steps at χ = 45.0° and ϕ = 90.0°. Intensity data were collected for the Lorentz-polarization effects as well as for the absorption. Structure solution and refinement were performed using the CrystalStructure program package. The heavy-atom positions were determined by a direct-program method (SIR2002), and the remaining non-hydrogen atoms were determined by the subsequent use of Fourier techniques (DIRDIF99). An empirical absorption correction based on equivalent reflections was applied to all data. All non-hydrogen atoms were refined anisotropically by full-matrix least-squared techniques based on F^2. The low-temperature data collection enabled a hydrogen attached to the iridium center in **4c** to be located from the Fourier difference map and refined isotropically. All other hydrogen atoms were constrained to be attached to their parent atom. The relevant crystallographic data are compiled in Table S1. CCDC 1487515 (**3a'**), CCDC 1487554 (**3b**), CCDC 1487552 (**3c**), and CCDC 1487553 (**4c**) contain the supplementary crystalographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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Keywords: asymmetric catalysis • cooperative effects • hydrogen transfer • iridium • ketones

[1] a) K. Muñiz, *Angew. Chem.* **2005**, *117*, 6780-6785; *Angew. Chem. Int. Ed.* **2005**, *44*, 6622-6627; b) T. Ikariya, A. J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300-1308; c) T. Ikariya, *Bull. Chem. Soc. Jpn.* **2011**, *84*, 1-16; d) B. Zhao, Z. Han, K. Ding, *Angew. Chem.* **2013**, *125*, 4844-4889; *Angew. Chem. Int. Ed.* **2013**, *52*, 4744-4788; e) A. Bartoszewicz, N. Ahlsten, B. Martín-Matute, *Chem. Eur. J.* **2013**, *19*, 7274-7302; f) D. Wang, D. Astruc, *Chem. Rev.* **2015**, *115*, 6621-6686; g) F. Foubelo, C. Nájera, M. Yus, *Tetrahedron: Asymmetry* **2015**, *26*, 769-790.

[2] a) S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 7562-7563; b) A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1996**, *118*, 2521-2522; c) N. Uematsu, A. Fujii, S. Hashiguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1996**, *118*, 4916-4917; d) K.-J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya, R. Noyori, *Angew. Chem.* **1997**, *109*, 297-300; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 285-288; e) S. Hashiguchi, A. Fujii, K.-J. Haack, K. Matsumura, T. Ikariya, R. Noyori, *Angew. Chem.* **1997**, *109*, 300-303; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 288-290.

[3] a) K. Mashima, T. Abe, K. Tani, *Chem. Lett.* **1998**, *27*, 1119-1200; b) K. Mashima, T. Abe, K. Tani, *Chem. Lett.* **1998**, *27*, 1201-1202; c) K. Murata, T. Ikariya, *J. Org. Chem.* **1999**, *64*, 2186-2187.

[4] S. Arita, T. Koike, Y. Kayaki, T. Ikariya, *Organometallics* **2008**, *27*, 2795-2802.

[5] a) S. Arita, T. Koike, Y. Kayaki, T. Ikariya, *Angew. Chem.* **2008**, *120*, 2481-2483; *Angew. Chem. Int. Ed.* **2008**, *47*, 2447-2449; b) S. Arita, T. Koike, Y. Kayaki, T. Ikariya, *Chem. Asian J.* **2008**, *3*, 1479-1485.

[6] a) A. Ueno, Y. Kayaki, T. Ikariya, *Organometallics* **2014**, *33*, 4479-4485. b) A. Matsunami, S. Kuwata, Y. Kayaki, *ACS Catal.* **2016**, *6*, 5181-5185.

[7] Y. Sato, Y. Kayaki, T. Ikariya, *Organometallics* **2016**, *35*, 1257-1264.

[8] a) R. M. Haak, F. Berthiol, T. Jerphagnon, A. J. A. Gayet, C. Tarabiono, C. P. Postema, V. Ritleng, M. Pfeffer, D. B. Janssen, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *J. Am. Chem. Soc.* **2008**, *130*, 13508-13509; b) T. Jerphagnon, A. J. A. Gayet, F. Berthiol, V. Ritleng, N. Mršić, A. Meetsma, M. Pfeffer, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Chem. Eur. J.* **2009**, *15*, 12780-12790; c) T. Jerphagnon, R. Haak, F. Berthiol, A. J. A. Gayet, V. Ritleng, A. Holuigue, N. Pannetier, M. Pfeffer, A. Voelklin, L. Lefort, G. Verzijl, C. Tarabiono, D. B. Janssen, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Top. Catal.* **2010**, *53*, 1002-1008; d) Y. Sato, Y. Kayaki, T. Ikariya, *Chem. Commun.* **2012**, *48*, 3635-3637.

[9] a) J.-B. Sortais, V. Ritleng, A. Voelklin, A. Holuigue, H. Smail, L. Barloy, C. Sirlin, G. K. M. Verzijl, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, M. Pfeffer, *Org. Lett.* **2005**, *7*, 1247-1250; b) J.-B. Sortais, N. Pannetier, A. Holuigue, L. Barloy, C. Sirlin, M. Pfeffer, N. Kyritsakas, *Organometallics* **2007**, *26*, 1856-1868; c) J.-B. Sortais, N. Pannetier, N. Clément, L. Barloy, C. Sirlin, M. Pfeffer, N. Kyritsakas, *Organometallics* **2007**, *26*, 1868-1874; d) N. Pannetier, J.-B. Sortais, P. S. Dieng, L. Barloy, C. Sirlin, M. Pfeffer, *Organometallics* **2008**, *27*, 5852-5859; e) L. Barloy, J.-T. Issenhuth, M. G. Weaver, N. Pannetier, C. Sirlin, M. Pfeffer, *Organometallics* **2011**, *30*, 1168-1174; f) N. Pannetier, J.-B. Sortais, J.-T. Issenhuth, L. Barloy, C. Sirlin, A. Holiigue, L. Lefort, L. Panella, J. G. de Vries, M. Pfeffer, *Adv. Synth. Catal.* **2011**, *353*, 2844-2852; g) E. Féghali, L. Barloy, J.-T. Issenhuth, L. Karmazin-Brelot, C. Bailly, M.

Pfeffer, *Organometallics* **2013**, *32*, 6186-6194; h) S. Sabater, M. Baya, J. A. Mata, *Organometallics* **2014**, *33*, 6830-6839.

[10] Y.-F. Han, G.-X. Jin, *Chem. Soc. Rev.* **2014**, *43*, 2799-2823.

[11] A. L. Gutman, M. Etinger, G. Nisnevich, F. Polyak, *Tetrahedron: Asymmetry* **1998**, *9*, 4369-4379.

[12] The relative ratio could not be precisely determined for **2b** owing to overlapping NMR signals.

[13] I. Mena, E. A. Jaseer, M. A. Casado, P. García-Orduña, F. J. Lahoz, L. A. Oro, *Chem. Eur. J.* **2013**, *19*, 5665-5675.

[14] K. Ishiwata, S. Kuwata, T. Ikariya, *Organometallics* **2006**, *25*, 5847-5849.

[15] H. Matsuzaka, K. Ariga, H. Kase, T. Kamura, M. Kondo, S. Kitagawa, M. Yamazaki, *Organometallics* **1997**, *16*, 4514-4516.

[16] a) M. Yamakawa, I. Yamada, R. Noyori, *Angew. Chem.* **2001**, *113*, 2900-2903; *Angew. Chem. Int. Ed.* **2001**, *40*, 2818-2821; b) R. Noyori, M. Yamakawa, S. Hashiguchi, *J. Org. Chem.* **2001**, *66*, 7931-7944; c) C. A. Sandoval, T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, R. Noyori, *Chem. Asian. J.* **2006**, *1*, 102-110; d) J. Václavík, M. Kuzma, J. Přech, P. Kačer, *Organometallics* **2011**, *30*, 4822-4829; e) P. A. Dub, T. Ikariya, *J. Am. Chem. Soc.* **2013**, *135*, 2604-2619; f) A. Matsuoka, C. A. Sandoval, M. Uchiyama, R. Noyori, H. Naka, *Chem. Asian. J.* **2015**, *10*, 112-115; g) P. A. Dub, J. C. Gordon, *Dalton Trans.* **2016**, *45*, 6756-6781.

[17] a) M. Nordin, R.-Z. Liao, K. Ahlford, H. Adolfsson, F. Himo, *ChemCatChem* **2012**, *4*, 1095-1104; b) D. Madrigal, A. L. Cooksy, R. Somanathan, *Comput. Theor. Chem.* **2012**, *999*, 105-108.

[18] J. W. Kang, K. Moseley, P. M. Maitlis, *J. Am. Chem. Soc.* **1969**, *91*, 5970-5977.

[19] D. R. J. Hose, M. F. Mahon, K. C. Molloy, T. Raynham, M. Wills, *J. Chem. Soc., Perkin Trans. 1* **1996**, 691-703.

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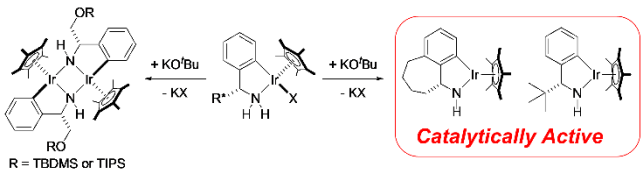

Hunting the Actual Catalyst: Mono- and di-nuclear chiral amidoiridium complexes were specifically synthesized by changing the substituents on the C–N chelating ligand. The isolated mononuclear amido complex based on (*R*)-1-phenyl-2,2-dimethylpropylamine was easily accessible to the hydrido(amine) complex in 2-propanol with excellent diastereoselectivity and served as an efficient catalyst for the asymmetric transfer hydrogenation of acetophenone.

Yasuhiro Sato, Yoshihito Kayaki and Takao Ikariya**

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Comparative Study of Bifunctional Mononuclear and Dinuclear Amidoiridium Complexes with Chiral C–N Chelating Ligands for the Asymmetric Transfer Hydrogenation of Ketones