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SUPPORTING INFORMATION

Advantageous asymmetric ketone reduction with competitive hydrogenation/transfer hydrogenation system using chiral bifunctional iridium catalysts

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CONTENTS

General information. All manipulation of oxygen and moisture-sesitive materials were conducted under purified argon atmosphere using standard Schlenk techniques. Solvents were purchased from Kanto Chemical Co., Inc. or Nacalai Tesque, Inc. and dehydrated and distilled by the standard dehydration procedure before use. Acetophenone and 4'-methylacetophenone purchased from Tokyo Chemical Industries Co., Ltd. were freshly distilled under argon before use. Special-grade H_2 (99.999% purity) was used as received from commercial suppliers. Ir complexes, [Cp*Ir(*S*,*S*)-Msdpen][1] and [Cp*Ir(*S*,*S*)-Tsdpen][2] were synthesized according to the reported preparative methods. The ^1H, and ^2H NMR spectra were acquired on JEOL JNM-LA300 and JNM-ECX400 spectrometers. NMR chemical shifts were referenced to $SiMe_4$ by using residual proton impurities in the deuterated solvent. High performance liquid chromatography (HPLC) analysis was performed using a system comprised of a JASCO column oven: CO-1565, an ary 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-3 column (4.6 mm × 25 cm) to determine the ee of **5**, with hexane/2-propanol as the eluent where baseline separation was obtained. Gas chromatographic analyses for chiral alcohol products from 1,3- or 1,4-diacetylbenzene were performed on a Shimadzu GC-17A equipped with a CP-Chirasil-Dex CB column capillary column (0.25 mm × 30 m) purchased from Agilent Technologies. The identification of the absolute configurations was performed by comparison of their retention times with those of reference compounds.

Experimental procedures for reaction of amidoiridium complexes 2 with H_2.

(a) Reaction of 2b and H_2 (1 atm).

A solution of **2b** (22.6 mg, 32.7 μmol) in THF-d_8 (1.5 mL) was stirred with H_2 bubbling at room temperature for 1 h. Then, the reaction mixure was analyzed by ^{1}H NMR to determine the yield of **3b**.

(b) Reaction of 2a or 2b and H_2 (30 atm).

High-pressure ^{1}H NMR spectra were recorded with a 300 MHz NMR spectrometer (JEOL LA-300) operating at a proton frequency of 300.5 MHz. The experimental setup is presented in our previous report.[3] The high-pressure cell assembly consisted of a non-magnetic Ti–Al alloy valve and a zirconia tube with a inner volume of 3.4 mL. The valves are attachable to the top of the zirconia tube and fixed with Kalrez® perfluoroelastomer O-rings. H_2 gas can be introduced through stainless steel capillaries to the cell controlled by a syringe pump (ISCO model 260D). The pressure of the system was maintained with a back-pressure regulator (JASCO model 880-81).

Before the NMR spectra were recorded, a solution of **2a** or **2b** (20.2–23.5 mg, 32.8–34.0 μmol) in THF-d_8 (1.0 mL) (12.1 μL, 0.117 mmol) was placed in the high-pressure cell and degassed via freeze-pump-thaw cycles at –78 °C. After the introduction of H_2 at 25 °C, the assembly was operated under H_2 (30 atm) in a non-spinning mode.

Reaction of Amido–Ir Complexes 2 and CD_3OD.

An NMR tube equipped with a J-Young valve was charged with **2a**–**2b** (3.5–3.9 mg, 5.6–5.7 μmol) and CD_3OD (0.5 mL) at room temperature for 10 min. Deuterated **3a**–**3b** were formed in 95–99% yield. The H/D ratios on Ir*H* and NH_2 protons of **3a** were determined to be 100%D (Ir*H*, *δ*/ppm: –10.85 ppm) and 90%D (NH_2, *δ*/ppm: 4.57, 4.93),

according to ^{1}H NMR (399.78 MHz, CD_3OD) and ^{2}H NMR (297.60 MHz, THF) analysis. Similarly, The H/D ratios on Ir*H* and NH_2 protons of **3b** were determined to be 100%D (Ir*H*, δ/ppm: –10.95 ppm) and 95%D (NH_2, δ/ppm: 4.34, 4.72).

General Procedure for Hydrogenation with Amido Complexes 2.

Catalyst (0.010 mmol), triphenylmethane (an internal standard) and substrates (1.0 mmol) were placed in a stainless steel autoclave equipped with a pressure gauge and a gas displacement tube. The solvent (1 mL) was added to the mixture under argon atmosphere. Then, hydrogen gas (30 atm) was introduced into the autoclave. The reaction mixture was stirred at 30 °C for 24 h. After carefully venting hydrogen, the reaction mixture was analyzed by ^{1}H NMR and HPLC to determine yields and enantiomeric excesses.

(*S*)- or (*R*)-4'-Methyl-1-phenylethanol (5)

^{1}H NMR (399.78 MHz, $CDCl_3$, rt, δ/ppm): 1.47 (d, 3H, CH_3CHOH, J = 6.7 Hz), 2.34 (s, 3H, CH_3C$_6$H$_4$), 4.75 (q, 1H, C*H*, J = 6.7 Hz), 7.10 (d, 2H, C$_6H_4$, J = 7.9 Hz), 7.21 (d, 2H, C$_6H_4$, J = 7.9 Hz). HPLC (column, Chiralcel OD-3; eluent, 2-propanol/hexane 5:95; temp, rt; flow rate, 1.0 mL/min; UV detection, 220 nm); t_R (*S*) = 7.93 min; t_R (*R*) = 8.62 min.

(*S,S*)-1,4-bis(1-hydroxyethyl)benzene

^{1}H NMR (399.78 MHz, $CDCl_3$, rt, δ/ppm): 1.42 (d, 6H, CH_3CHOH, J = 6.4 Hz), 4.79 (q, 2H, C*H*, J = 6.5 Hz), 7.31 (s, 4H, C$_6H_4$). GC (column, CP-Chirasil-Dex CB; 250 °C injection temperature, 160 °C column temperature); t_R (*R,R*) = 8.53 min; t_R (*meso*) = 8.99 min; t_R (*S,S*) = 11.54 min.

(*S*)-1-acetyl-4-(1-hydroxyethyl)benzene

^{1}H NMR (399.78 MHz, $CDCl_3$, rt, δ/ppm): 1.47 (d, 3H, CH_3CHOH, J = 6.4 Hz), 2.55 (s, 3H, CH_3COC$_6$H$_4$), 4.92 (q, 1H, CH, J = 6.2 Hz), 7.43 (d, 2H, C$_6H_4$, J = 8.2 Hz), 7.89 (d, 2H, C$_6H_4$, J = 8.2 Hz). GC (column, CP-Chirasil-Dex CB; 250 °C injection temperature, 160 °C column temperature); t_R (*R*) = 8.46 min; t_R (*S*) = 8.82 min.

(*S*,*S*)-1,3-bis(1-hydroxyethyl)benzene

^{1}H NMR (399.78 MHz, $CDCl_3$, rt, δ/ppm): 1.42 (d, 6H, CH_3CHOH, J = 6.7 Hz), 4.78 (q, 2H, CH, J = 6.7 Hz), 7.15–7.35 (m, 4H, C$_6H_4$). GC (column, CP-Chirasil-Dex CB; 250 °C injection temperature, 160 °C column temperature); t_R (*R*,*R*) = 6.96 min; t_R (*meso*) = 7.09 min; t_R (*S*,*S*) = 9.94 min.

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