Electronic Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION

Efficient dynamic kinetic resolution of racemic secondary alcohols by a chemoenzymatic system using bifunctional iridium complexes with C-N chelate amido ligands

Yasuhiro Sato, Yoshihito Kayaki and Takao Ikariya

Department of Applied Chemistry, Graduate School of Science and Engineering, Tokyo Institute of Technology, O-okayama 2-12-1-E4-1, Meguro-ku, Tokyo 152-8552, Japan

CONTENTS

General information. Toluene was purchased from Kanto Chemical and was used after drying over sodium benzophenone ketyl and the following distillation under argon. Synthesis of the C-N chelate Ir complexes, Cp*Ir[κ^2(*N*,*C*)-{NHC(CH_3)$_2$-2-C_6H_4}] (**3a**) and Cp*Ir[κ^2(*N*,*C*)-{NHC(C_6H_5)$_2$-2-C_6H_4}] (**3b**), was presented in our previous paper.[1] Other reagents were used as delivered. The ^{1}H, and ^{13}C 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. Analytical gas chromatography was performed with a Shimadzu GC-17A gas chromatograph equipped with a DB-1 capillary column (0.25 mm × 30 m) purchased from Agilent Technologies. Recycling preparative HPLC was performed on a Japan Analytical Industry LC-918 system connected to RI and UV detectors. According to the reported methods, analytical chiral HPLC was performed on a Chiralcel OD column (4.6 mm × 25 cm), a Chiralcel OJ-H column (4.6 mm × 25 cm) and a Chiralcel AD-H column (4.6 mm × 25 cm) with hexane/2-propanol as the eluent where baseline separation was obtained.

General Procedure for Racemization of (*R*)-1-Phenylethanol Promoted by Amido Complexes.

The Ir complex (10 μmol) was dissolved in toluene (2.0 mL) and (*R*)-1-phenylethanol (1.0 mmol) was added under an argon atmosphere. The solution was stirred at 30 ºC and monitored over a period by taking aliquots (10 μL) that were filtered over a short pad of Florizil (eluent: toluene), and analyzed by HPLC equipped with a Chiralcel OD column.

Screening Experiments of Dynamic Kinetic Resolution of 1-Phenylethanol.

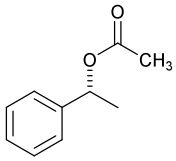
A 20-mL Schlenk flask was charged with catalyst (50 μmol), CALB (7.0 mg), and toluene (5.0 mL) under Ar atmosphere. (*R*)-1-phenylethanol (1 mmol) and acyl donor (1.0 mmol) were added and the mixture was stirred at 30 ^{o}C for 6 h. After durene (11.2 mg, 0.08 mmol; an internal standard) was added, the reaction mixture was filtered through a PTFE filter (0.45 μm). Product yield was determined by GC analysis and optical yield was determined by HPLC equipped with a Chiralcel OJ-H column.

General Procedure for Dynamic Kinetic Resolution of Secondary Alcohols Catalyzed by 1a.

A 20-mL Schlenk flask was charged with **1a** (10 μmol), CALB (7 mg), and toluene(1 mL) under Ar atmosphere. Secondary alcohol (1 mmol) and phenyl acetate (1.05 mmol) were added. After the reaction was carried out at 30 ^{o}C for 12 h, the product was purified by flash column chromatography on silica gel (ethyl acetate) and further chromatographed with a recycling preparative HPLC apparatus with JAIGEL-1H and JAIGEL-2H columns (polystyrene gels) using chloroform as an eluent. Optical yield was determined by HPLC equipped with a Chiralcel OJ-H column or a Chiralcel AD-H column.

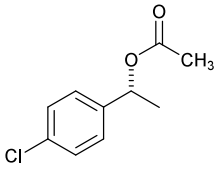
Characterization Data for the Isolated products.

(*R*)- 1-Phenylethyl acetate (2a)[2]



Isolated yield: 92% yield. ^{1}H NMR (399.8 MHz, $CDCl_3$, rt, δ /ppm): 1.54 (d, 3H, $^{3}J_{HH}$ = 6.7 Hz; $C_6H_5CHCH_3$), 2.08 (s, 3H; CH_3COO), 5.89 (q, 1H, $^{3}J_{HH}$ = 6.7 Hz; $C_6H_5CHCH_3$), 7.28-7.36 (m, 5H; $C_6H_5CHCH_3$). $^{13}C\{^{1}H\}$ NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 21.3, 22.1, 72.2, 126.0, 127.8, 128.4, 141.6, 170.2. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel OJ-H; eluent, 0.8:99.2 2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *R* isomer, 21.3 min; t_R of *S* isomer, 27.6 min.

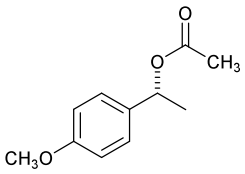
(*R*)-1-(4-Chlorophenyl)ethyl acetate (2b)[2]



Isolated yield: 89% yield. ^{1}H NMR (399.8 MHz, $CDCl_3$, rt, δ /ppm): 1.51 (d, 3H, $^{3}J_{HH}$ = 6.7 Hz; $C_6H_4ClCHCH_3$), 2.07 (s, 3H; CH_3COO), 5.84 (q, 1H, $^{3}J_{HH}$ = 6.7 Hz; $C_6H_4ClCHCH_3$), 7.27-7.33 (m, 4H; $C_6H_4ClCHCH_3$). $^{13}C\{^{1}H\}$ NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 21.2, 22.1, 71.5, 127.4, 128.6, 133.5, 140.1, 170.1. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel OJ-H; eluent, 1:99

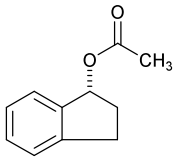
2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *R* isomer, 15.1 min; t_R of *S* isomer, 18.8 min.

(*R*)-1-(4-Methoxyphenyl)ethyl acetate (2c)[2]



Isolated yield: 72% yield. ^{1}H NMR (399.8 MHz, CDCl3, rt, δ /ppm): 1.53 (d, 3H, $^{3}J_{HH}$ = 6.7 Hz; $C_6H_4OCH_3CHCH_3$), 2.05 (s, 3H; CH_3COO), 3.80 (s, 3H; $C_6H_4OCH_3CHCH_3$), 5.85 (q, 1H, $^{3}J_{HH}$ = 6.7 Hz; $C_6H_4OCH_3CHCH_3$), 6.86-7.32 (m, 4H; $C_6H_4OCH_3CHCH_3$). ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 21.3, 21.8, 55.2, 71.9, 113.8, 127.5, 133.7, 159.2, 170.3. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel OJ-H; eluent, 1:99 2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *R* isomer, 36.4 min; t_R of *S* isomer, 44.4 min.

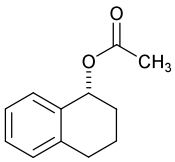
(*R*)-2,3-Dihydro-1H-inden-1-yl acetate (2d)[2]



Isolated yield: 93% yield. ^{1}H NMR (399.8 MHz, $CDCl_3$, rt, δ /ppm): 2.07 (s, 3H; CH_3COO), 2.08-3.16 (m, 4H; $C_6H_4CH(CH_2)_2$), 6.19-6.22 (m, 1H; $C_6H_4CH(CH_2)_2$), 7.21-7.43 (m, 4H; $C_6H_4CH(CH_2)_2$). ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 21.3, 30.1, 32.2, 78.3, 124.7, 125.5, 126.6, 128.9, 141.0, 144.4, 171.0. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel OJ-H; eluent, 1:99

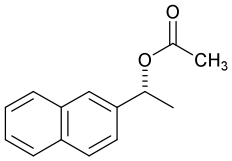
2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *S* isomer, 12.8 min; t_R of *R* isomer, 17.0 min.

(*R*)-1,2,3,4-Tetrahydronaphthalen-1-yl acetate (2e)[2]



Isolated yield: 81% yield. ^{1}H NMR (399.8 MHz, $CDCl_3$, rt, δ /ppm): 1.82-2.90 (m, 6H; $C_6H_4CH(CH_2)_3$), 2.09 (s, 3H; CH_3COO), 6.00-6.02 (m, 1H; $C_6H_4CH(CH_2)_3$), 7.12-7.29 (m, 4H; $C_6H_4CH(CH_2)_3$). ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 18.7, 21.4, 28.9, 29.0, 69.9, 126.0, 128.0, 129.0, 129.4, 134.5, 137.9, 170.7. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel OJ-H; eluent, 1:99 2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *S* isomer, 12.3 min; t_R of *R* isomer, 14.6 min.

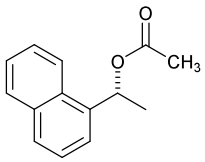
(*R*)-1-(2-Naphthyl)ethyl acetate (2f)[2]



Isolated yield: 81% yield. ^{1}H NMR (399.8 MHz, $CDCl_3$, rt, δ /ppm): 1.63 (d, 3H, $^{3}J_{HH}$ = 6.5 Hz; $C_{10}H_7CHCH_3$), 2.11 (s, 3H; CH_3COO), 6.06 (q, 1H, $^{3}J_{HH}$ = 6.5 Hz; $C_{10}H_7CHCH_3$), 7.47-7.86 (m, 7H; $C_{10}H_7CHCH_3$). ^{13}C{^{1}H} NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 21.3, 22.1, 72.4, 124.0, 124.9, 126.0, 126.1, 127.6, 127.9, 128.3, 132.9, 133.1, 138.9, 170.3. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel

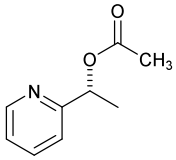
OJ-H; eluent, 1:99 2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *R* isomer, 37.8 min; t_R of *S* isomer, 48.3 min.

(*R*)-1-(1-Naphthyl)ethyl acetate (2g)[2]



Isolated yield: 92% yield. ^{1}H NMR (399.8 MHz, CDCl3, rt, δ /ppm): 1.71 (d, 3H, $^{3}J_{HH}$ = 6.7 Hz; $C_{10}H_7CHCH_3$), 2.13 (s, 3H; CH_3COO), 6.66 (q, 1H, $^{3}J_{HH}$ = 6.7 Hz; $C_{10}H_7CHCH_3$), 7.46-8.10 (m, 7H; $C_{10}H_7CHCH_3$). $^{13}C\{^{1}H\}$ NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 21.3, 21.6, 69.4, 123.08, 123.12, 125.3, 125.6, 126.2, 128.4, 128.8, 130.2, 133.7, 137.3, 170.3. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel AD-H; eluent, 1 : 99 2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *R* isomer, 15.2 min; t_R of *S* isomer, 16.3 min.

(*R*)-1-(2-Pyridyl)ethyl acetate (2h)[3]



Isolated yield: 92% yield. ^{1}H NMR (399.8 MHz, $CDCl_3$, rt, δ /ppm): 1.58 (d, 3H, $^{3}J_{HH}$ = 6.7 Hz; $C_5H_4NCH_3CHCH_3$), 2.11 (s, 3H; CH_3COO), 5.90 (q, 1H, $^{3}J_{HH}$ = 6.7 Hz; $C_5H_4NCHCH_3$), 7.17-8.58 (m, 4H; $C_5H_4NCHCH_3$). $^{13}C\{^{1}H\}$ NMR (100.5 MHz, $CDCl_3$, rt, d/ppm): 20.6, 21.2, 72.9, 120.4, 122.6, 136.7, 149.2, 160.2, 170.2. The ee determined by chiral HPLC analysis was 99%: column, Chiralcel OJ-H; eluent, 0.7:99.3

2-propanol-hexane; temp, 30 ^{o}C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of *R* isomer, 24.2 min; t_R of *S* isomer, 26.3 min.

References

1. S.Arita, T. Koike, Y. Kayaki and T. Ikariya, *Organometallics*, 2008, **27**, 2795.

2 M. Päiviö, D. Mavrynsky, R. Leino and L. T. Kanerva, *Eur. J. Org. Chem*, 2011, 1452.

3 T. Itoh, Y. Matsushita, Y. Abe, S. Han, S. Wada, S. Hayase, M. Kawatsura, S. Takai, M. Morimoto and Y. Hirose, *Chem. —Eur. J.*, 2006, **12**, 9228.