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Efficient iridium and rhodium-catalyzed asymmetric transfer hydrogenation using 9-amino(9-deoxy) *cinchona* alkaloids as chiral ligands

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9-Amino (9-deoxy) *cinchona* alkaloids, derived from natural *cinchona* alkaloids, were applied in asymmetric transfer hydrogenation in both iridium and rhodium catalytic systems using *i*-propanol as the hydrogen source. A series of aromatic ketones was examined, and good to excellent conversions and enantioselectivities were observed. The best results were achieved using 9-amino(9-deoxy) epicinchonine 2a as the ligand and $[Ir(COD)Cl]_2$ as the metal precursor, and for the isobutylphenone, the conversion and enantioselectivity were obtained in 90 and 97% e.e. respectively. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: asymmetric transfer hydrogenation; chiral ligands; iridium catalysis; rhodium catalysis; *cinchona* alkaloids

INTRODUCTION

In the past 30 years, the natural *cinchona* alkaloids have been widely applied as versatile chiral basic catalysts, ligands, chromatographic selectors and NMR discriminating agents in asymmetric synthesis.[1] As catalysts or promoters, *cinchona* alkaloids can be used directly in many important reactions, such as Aldol,[2] Darzens,[3] Baylis–Hillmann,[4] Michael addition,[5] Diels–Alder[6] and Claisen rearrangement reactions.[7] As a metal ion ligand, its application in osmium (IV)-catalyzed asymmetric dihydroxylation (AD)[8] and asymmetric aminohydroxylation (AA)[9] is also remarkably successful. However up until now, only a few studies on *cinchona* alkaloids and their derivatives used as ligands coordinated with other transition metals have been reported.[10,11]

On the other hand, the asymmetric hydrogenation of prochiral ketones is an important approach to obtaining optically active alcohols, and its investigation has received much attention in recent years.[12–15] In view of the low cost of the reducing agent and operational simplicity, metal-catalyzed transfer hydrogenation reaction using *iso*-propanol (*i*-PrOH) as a hydrogen source appears to be a safe and attractive supplement to catalytic hydrogenation with H_2. In the last decade, some chiral diamine ligands and chiral P,N ligands have been used to coordinate metals such as Ru, Rh, Ir, Al and Sm in asymmetric transfer hydrogenation.[16–19] Since this reaction has great significance in enantioselective homogeneously catalyzed industrial processes, the development of new easily obtained, stable and recoverable catalysts that provide high activity and enantioselectivity remains a challenge of high importance. As part of a program aimed at developing efficient chiral ligands derived from *cinchona* alkaloids,[20,21] we report herein the results of our studies on iridium and rhodium catalytic asymmetric transfer hydrogenation reaction using 9-amino(9-deoxy) *cinchona* alkaloids **2a–d** as ligands, which have the classic 1,2-diamine moiety in their structures. To the best of our knowledge, this class of compounds derived from *cinchona* alkaloids has not previously been described as ligands in asymmetric transfer hydrogenation.

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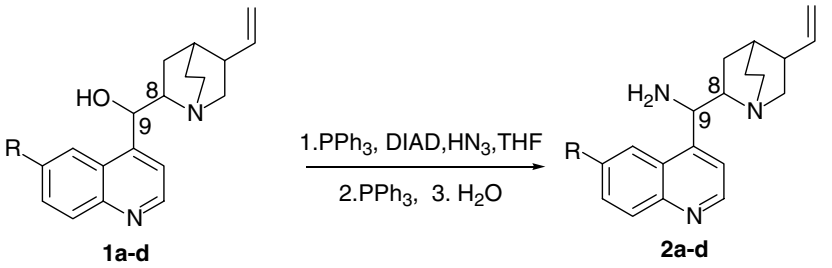
RESULTS AND DISCUSSION

Synthesis of 9-amino(9-deoxy) *cinchona* alkaloids 2a–d

The general approach to synthesizing 9-amino(9-deoxy) *cinchona* alkaloids derivatives is outlined in Scheme 1. According to the procedure of Brunner,[22,23] ligands can



1a-d

1a Cinchonine (8R, 9S, R= H)
1b Cinchonidine (8S, 9R, R= H)
1c Quinine (8S, 9R, R=OCH_3)
1d Quinidine (8R, 9S, R=OCH_3)

2a-d

2a (8R, 9R, R= H)
2b (8S, 9S, R= H)
2c (8S, 9S, R=OCH_3)
2d (8R, 9R, R=OCH_3)

Scheme 1. Synthesis of the chiral ligands **2a–d**.

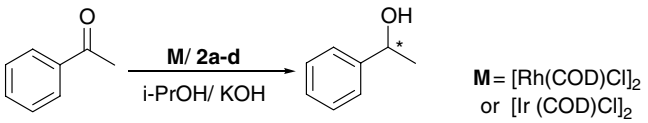
be prepared conveniently. The key step is a Mitsunobu reaction that leads to the C9-azido compound by an S_N2 mechanism. The reduction is performed *in situ* by adding triphenylphosphane (Staudinger reaction). Hydrolysis of the intermediate aminophosphorane yields the free amine. Here, one point should be mentioned is that 9-amino(9-deoxy) epicinchonidine **2b** has not been documented so far. It was also prepared by this route with some modifications. In the first step, small amounts of chloroform were added to the reaction mixture due to the poor solubility of cinchonidine in THF, and the Mitsunobu reaction was carried out at 50 °C (10 °C higher than the general procedure). The formation of the intermediate azides was monitored by IR-spectroscope, which exhibited the N_3-vibration at 2099 cm^{-1}. The reduction and hydrolysis were performed in a one pot reaction. The crude product was purified by chromatography using Et_2O–MeOH–Et_3N (10 : 1 : 0.5) as eluent, and afforded the compound **2b** in 70% overall yield. The structures of all the 9-amino(9-deoxy) *cinchona* alkaloids were established by FTIR, ^1H NMR and mass spectroscopy.

Asymmetric transfer hydrogenation of aromatic ketones

Asymmetric transfer hydrogenation of acetophenone

The Rh(I) or Ir(I) catalyst was generated *in situ* by mixing 9-amino(9-deoxy) *cinchona* alkaloids **2a–d** with $[Rh(COD)Cl]_2$ or $[Ir(COD)Cl]_2$ (2 : 1) in *i*-propanol at room temperature under argon for 0.5 h. Transfer hydrogenation occurred at certain temperatures when KOH and ketones were added to the above catalyst solution. Initial studies were performed using acetophenone **3a** as a model substrate under different conditions (Scheme 2).

For the transfer hydrogenation reaction of acetophenone **3a**, the absolute configuration of the product was highly dependent upon both the C8-position and C9-position configuration in the chiral ligands. The results are summarized in Table 1. It is not surprising that **2a** and **2b**, as well as **2c** and **2d**, acting as diastereomeric pairs, led to the products with different absolute configurations. **2a** and **2d**, as well as **2b** and **2c**, which have the same configurations in the C8-position and C9-position, also offered the same absolute configurations of products. Notably, **2c** and **2d**, with the additional methoxy group, give only slightly lower e.e. than **2a** and **2b.**



Scheme 2. The asymmetric transfer hydrogenation of acetophenone.

Table 1. Influence of Ir(I)–**2a–d** complexes on the configuration of products in the catalytic reduction of acetophenone[a]

Entry	Ligand	Catalyst (%)	Time (h)	Yield (%)[b]	e.e. (%)[c]	Configuration[d]
1	**2a**	5	48	75	75	*S*
2	**2b**	5	48	70	74	*R*
3	**2c**	5	48	80	72	*R*
4	**2d**	5	48	60	70	*S*

[a] Conditions: reactions were carried out using a 0.05 M solution of acetophenone (1 mmol) in *i*-propanol; ketone–Ir–ligand–KOH = 100 : 2.5 : 5 : 10; 0–16 °C, 48 h. [b] Isolated yield. [c] Determined by chiral CP-Cyclodex B-236 M column. [d] Assigned by comparison with the sign of the specific rotation of the known compounds.

When using different catalyst precursors, we found different catalytic activities. Table 2 demonstrates clearly that $[Ir(COD)Cl]_2$ is superior to $[Rh(COD)Cl]_2$, as far as conversion and enantiomeric excess are concerned.

The amount of catalyst was also found to influence the reaction dramatically. As shown in Table 3, when the ratio of catalyst increased from 1 to 10%, the conversion and enantioselectivity increased respectively from 65 to 90%, and 58 to 95% e.e. (entries 1–6). When 1% catalyst was used, the reaction did not occur until the temperature was raised to 0 °C. In contrast, when 10% catalyst (or more) was used, the reaction occurred at −20 °C, even with less time (entries 7

Table 2. Influence of catalytic precursor in the reduction of acetophenone[a]

Entry	Ligand	Catalyst precursor	Catalyst (%)	Temperature (°C)	Yield (%)[b]	e.e. (%)[c]	Configuration[d]
1	**2a**	[Rh (COD) Cl]$_2$	5	0	60	60	*S*
2	**2a**	[Ir (COD) Cl]$_2$	5	0	87	72	*S*
3	**2a**	[Rh (COD) Cl]$_2$	10	0	83	78	*S*
4	**2a**	[Ir (COD) Cl]$_2$	10	0	87	82	*S*
5	**2c**	[Rh (COD) Cl]$_2$	5	0	65	57	*R*
6	**2c**	[Ir (COD) Cl]$_2$	5	0	80	62	*R*

[a] Conditions: reactions were carried out using a 0.05 M solution of acetophenone (1 mmol) in *i*-propanol; M–ligand–KOH = 1 : 2 : 4; 48 h. [b] Isolated yields. [c] Enantiomeric excess was determined by chiral CP-Cyclodex B-236 M column. [d] Configurations were assigned by comparison with the sign of the specific rotation of the known compounds.

Table 3. Influence of the ratio of catalyst to substrate on the reduction of acetophenone catalyzed by Ir(I)–**2a** complex[a]

Entry	Catalyst (%)	Temperature (°C)	Time (h)	Yield (%)[b]	e.e. (%)[c]
1	1	−20	48	0	0
2	1	0–25	48	65	58
3	3	0–25	48	83	62
4	5	−20–0	48	70	83
5	10	−20–0	48	90	88
6	**10**	**−20**	**48**	**86**	**95**
7	20	−20	22	70	91
8	25	−20	20	76	92
9	25	−20	48	92	89

[a] Conditions: reactions were carried out using a 0.05 M solution of acetophenone (1 mmol) in *i*-propanol; M–ligand–KOH = 1 : 2 : 4. [b] Isolated yield. [c] Determined by chiral CP-Cyclodex B-236 M column.

and 8). The effect of temperature on the enantioselectivity of the reaction was also found to be a significant variable. The enantioselectivity increased constantly as the temperature was lowered, although the rate of reaction was reduced (entries 6 vs 5). Extension of the ratio of catalyst from 10 to 25% enhanced the rate of the conversion, but resulted in slight erosion of the asymmetric induction (entries 9 vs 6). The highest enantiomeric excess (up to 95% e.e.) was achieved at −20 °C with 10% catalyst (entry 6).

We have also studied the effect of base co-catalyst on the reduction of acetophenone (Table 4). It is well known that the base can activate the catalyst markedly.[24] As in previous reports, base was used to deprotonate *i*-PrOH, allowing the complexation of the metal and isopropoxide ion, followed by formation of the nonracemic metal hydride and elimination of acetone. Lemaire[25] has shown that their catalytic system, [Rh(COD)Cl]$_2$–chiral 1,2-diamine complex was inactive without the base.

NaOH, *i*-PrONa, and KOH were tested in the reduction of acetophenone. Table 4 shows both conversion and enantioselectivity were the best using KOH as co-catalyst (entries 1–3). When the molar ratio of M–ligand–KOH was lower, the chemical yield and enantioselectivity decreased dramaticly. On the other hand, when we sequentially increased the amount of base, the enantioselectivity went down slightly (entries 5 and 6 vs 2).

Asymmetric transfer hydrogenation of different ketone substrates

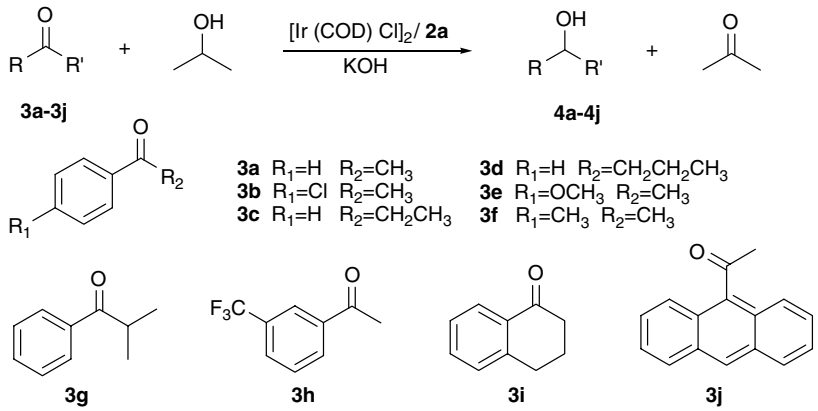
For exploring the scope and limitations of the reaction catalyzed by 9-amino(9-deoxy) *cinchona* alkaloids **2a–d**, a variety of aromatic ketones (Scheme 3) were applied in asymmetric transfer hydrogenation with *i*-propanol using ligand **2a** under the optimized conditions. In general, good to excellent conversion and enantioselectivity were achieved (Table 5).

The conversion and enantioselectivity of the reaction were affected by the steric and electronic properties

Table 4. Influence of the basic co-catalyst on the enantioselectivity of the reduction using Ir(I)–**2a** complex[a]

Entry	Base	Molar ratio of M–ligand–base	Temperature (°C)	Time (h)	Yield[b] (%)	e.e.[c] (%)
1	*i*-PrONa	1 : 2 : 4	−20–0–25	72	50	72
2	KOH	1 : 2 : 4	−20	48	86	95
3	NaOH	1 : 2 : 4	−20	48	67	83
4	KOH	1 : 2 : 2	−20	48	25	61
5	KOH	1 : 2 : 6	−20	48	83	91
6	KOH	1 : 2 : 10	−20	48	84	89

[a] Conditions: reactions were carried out using a 0.05 M solution of acetophenone (1 mmol) in *i*-propanol. Ketone–M–ligand = 100 : 5 : 10. [b] Isolated yield. [c] Determined by chiral CP-Cyclodex B-236 M column.



Scheme 3. Different ketones used in the asymmetric transfer hydrogenation.

Table 5. Asymmetric transfer hydrogenation of different ketones catalyzed by Ir(I)–**2a** complex[a]

Entry	Ketone	Temperature (°C)	Time (h)	Yield (%)[b]	Ee (%)[c]
1	**3a**	−20	48	86	95
2	**3b**	−20	48	50	72
3	**3c**	−20	48	70	94
4	**3d**	−20	24	70	96
5	**3e**	−20	48	85	97
6	**3f**	−20	48	85	95
7	**3g**	−20	48	90	97
8	**3g**	0–25	22	88	95
9	**3h**	−20	22	90	75
10	**3i**	−20	48	67	65
11	**3j**	−20	48	50	60

[a] Conditions: reactions were carried out using a 0.05 M solution of acetophenone (1 mmol) in 2-propanol; ketone–Ir–ligand–KOH = 100 : 5 : 10 : 20. [b] Isolated yields. [c] Determined by chiral CP-Cyclodex B-236 M column and chiral HPLC.

of the substrates. Substitution at the phenyl ring of acetophenone with an electron-donating group gave yields and enantioselectivities that were similar to those obtained with acetophenone (Table 5, entries 5 and 6 vs 1). Introduction of an electron-drawing group, however, led to lower enantioselectivities (entries 2 and 9), although the yield of the 3-trifluoromethylphenyl ethanol increased (entry 9). Increasing the steric bulk of the aryl group in the starting ketone from phenyl to anthracenyl had a negative effect on the enantioselectivity (entry 11). The cyclic substrate 1-tetralone was also converted under the same conditions to the corresponding alcohols in 65% e.e. (entry 10). Interestingly, the bulk of the R_2 group in the ketone demonstrated a slight positive effect on the yields (entries 3, 4 and 7 vs 1). Furthermore, isobutylphenone, among the most notorious substrates in asymmetric transfer hydrogenation, converts to the corresponding optically active alcohol in 97% e.e. and 90% yield (entry 7), presenting a significant improvement on the result in previous literature, even in the condition of increasing temperature (entry 8).

CONCLUSIONS

In conclusion, this work examined the use of the *cinchona* alkaloids derivatives, 9-amino(9-deoxy) *cinchona* alkaloids as ligands in both iridium and rhodium system in asymmetric transfer hydrogenation. Acetophenone was initially used as a model substrate to test the feasibility of the reaction, and the complex of $[Ir(COD)Cl]_2$ and 9-amino (9-deoxy) epicinchonine **2a** was found to be the most efficient catalyst system. For a variety of aromatic ketones, moderate to excellent enantioselectivities were observed. This is the first case using *cinchona* alkaloids skeleton in the iridium-catalyzed asymmetric reactions. Moreover, except for osmium-catalyzed Sharpless AD and AA, these are the best enantioselectivities reported using the intact quinine skeleton as a ligand in metal-catalyzed asymmetric reactions.[10,11] Since all the ligands are alkaloids, it is easy to separate them from reaction products and recover them effectively by base–acid conversion.

EXPERIMENTAL

Materials

Quinine, quinidine, cinchonine and cinchonidine were purchased from Fluka. Diisopropyl azodicarboxylate was purchased from Alfa Asesar. Hydrazoic acid-chloroform (3.65%) was prepared starting from sodium azide and sulfuric acid in our laboratory. All other regents were purchased from TianjinChemical Reagent Co. Inc. Acetophenone was distilled from $KMnO_4$ prior to use. Tetrahydrofuran was freshly distilled under nitrogen from a deep-blue solution of sodium-benzophenone. *i*-Propanol was treated with sodium and degassed. Other chemicals were used as received.

NMR analyses

^{1}H NMR was performed in $CDCl_3$ and recorded on a Varian INOVA 400 MHz spectrometer, and ^{1}H NMR spectra were collected at 400.0 MHz using a 10 000 Hz spectral width, a relaxation delay of 1.0 s, and tetramethylsilane (0.0 ppm) as the internal reference.

Analytical thin-layer chromatography

All thin-layer chromatography (TLC) analyses were performed with precoated glass-backed plates (silica gel 60-GF 254).

Flash column chromatography

Flash column chromatography was performed on silica gel 60 (300–400 mesh).

Chiral chromatography analyses

Gas chromatography analyses were performed on a chiral CP-Cyclodex-β-236 M column (25 m × 0.32 mm) on Varian CP-3800. Chiral high-performance liquid chromatography analyses were performed on a Waters–Breeze system equipped with 1525 HPLC pump, 2487 UV detector, Daicel Chiralcel OJ-H (length 250 mm × i.d. 4.6 mm × 5 μm), OB-H (length 250 mm × i.d. 4.6 mm × 5 μm) column and hexane–*i*-PrOH (v/v) as solvent.

Optical rotations analyses

All optical rotations ($[\alpha]^{25}_D$) analyses were performed on a Perkin–Elmer 343 polarimeter. Optical rotations are measured at the wavelength of the sodium D-line (589.3 nm) at a temperature of 25 °C, with reference to a layer 1 dm thick of a solution containing 1 g of the substance per milliliter.

Synthesis of ligands-9-amino(9-deoxy) *cinchona* alkaloids

*Synthesis of ligand **2b***

A well stirred mixture of cinchonidine (2.94 g, 10 mmol) **1b** and triphenylphosphine (3.15 g, 12 mmol) in 50 ml absolute THF and 10 ml chloroform was cooled to 0 °C, and hydrazoic acid-chloroform (3.65%, 12 mmol) was added. Then, DIAD (diisopropyl azodicarboxylate; 2.16 ml, 11 mmol) in 10 ml absolute THF was added slowly. The mixture was heated to 50 °C and a yellow transparent solution was obtained. The reaction was stirred for 3 h at 50 °C. Then triphenylphosphine (2.62 g, 10 mmol) in 10 ml of absolute THF was added in one portion and the solution was stirred at 40 °C until gas evolution ceased. Water (1 ml) was added and the solution was stirred overnight. Solvents were removed *in vacuo* and the residue was dissolved in CH_2C1_2 and poured into 2 M hydrochloric acid (1 : 1, 100 ml). The aqueous phase was washed with CH_2Cl_2 (3 × 30 ml). Then 2 M NaOH was added until pH >10. The mixture was extracted with diethyl ether (3 × 60 ml) and the combined organic phase was washed with saturated Na_2CO_3 aqueous solution (3 × 60 mL) and dried with Na_2CO_3. The solvent was removed and the product **2b** was obtained by purified on silica gel (eluent: Et_2O–MeOH–Et_3N = 10 : 1 : 0.5).

2b colorless oil, yield 70%. $[\alpha]^{25}_D - 51$ (*c* 0.5 in $CHCl_3$). IR(KBr)ν_{max}/cm^{-1}: 3370, 3293, 2936, 2869, 1622, 1589, 1508, 759. ^{1}H NMR (400M, $CDCl_3$): δ 0.85–1.09(m, 2H), 1.49–1.57 (m, 3H), 2.15 (s, 2H), 2.24 (m, 1H), 2.92–3.03 (m, 5H), 4.74 (s, br, 1H), 5.05 (m, 2H), 5.84 (m, 1H), 7.55–8.35 (m, 5H), 8.88 (d, J = 4.4 Hz, 1H). MS: m/z 293 M^+, 157, 136, 108, 95. Anal. calcd for $C_{19}H_{23}N_3$: C, 77.78; H, 7.90; N, 14.32. Found: C, 77.80; H, 7.87; N, 14.31.

2a, 2c, 2d were synthesized by similar procedure

2a colorless oil, yield 64%. $[\alpha]^{25}_D + 103$ (*c* 1.5 in $CHCl_3$) [literature,[22] yield 61%. $[\alpha]^{25}_D + 105$ (*c* 1.0 in $CHCl_3$)]. IR(KBr)ν_{max}/cm^{-1}: 3380, 3290, 2940, 2875, 1590, 1570, 1510. ^{1}H NMR (400M, $CDCl_3$): δ 0.86–1.58 (m, 5H), 2.11 (s, 2H), 2.23 (m, 1H), 3.05 (m, 5H), 4.79 (d, J = 10.1 Hz, 1H), 5.06 (m, 2H), 5.87 (m, 1H), 7.54–8.36 (m, 5H), 8.91 (d, J = 4.6 Hz, 1H). MS: m/z 293 M^+, 157, 136, 108.

2c slightly yellow oil, yield 56%. $[\alpha]^{25}_D + 83$ (*c* 0.5 in $CHCl_3$) [literature,[22] $[\alpha]^{25}_D + 80$ (*c* 1.1 in $CHCl_3$)]. IR(KBr) δ_{max}/cm^{-1}: 3380, 3290, 2080, 2940, 2860, 1625, 1600, 1515. ^{1}H NMR (400M, $CDCl_3$), 0.80 (m, 1H), 1.26–1.63 (m, 4H), 2.08 (S, 2H), 2.27 (m, 1H), 2.77 (m, 2H), 3.02–3.34 (m, 3H), 3.97 (s, 3H), 4.57 (d, J = 10.4 Hz, 1H), 4.97 (m, 2H), 5.79 (m, 1H), 7.36–8.05 (m, 4H), 8.75 (d, J = 4.6 Hz, 1H). MS: m/z 323 M^+, 207, 188, 136.

2d slightly yellow oil, yield 51%. $[\alpha]^{25}_D + 70$ (*c* 1.5 in $CHCl_3$) [literature,[23] yield 46%. $[\alpha]^{22}_D = +69$ (*c* 2.51 in $CHCl_3$)]. IR(KBr) ν_{max}/cm^{-1}: 3370, 3290, 2940, 2860, 1625, 1600, 1515. ^{1}H NMR (400M, $CDCl_3$), 0.78–0.96 (m, 1H), 1.14–1.32 (m, 1H), 1.46–1.56(m, 3H), 2.16 (S, 2H), 2.28 (m, 1H), 2.79–3.01 (m, 5H), 3.97 (s, 3H), 4.67 (d, J = 9.9 Hz, 1H), 5.09 (m, 2H), 5.79–5.87 (m, 1H), 7.35 (m, 1H), 7.55(d, J = 4.6 Hz, 1H), 7.64–8.14(m, 2H), 8.75 (d, J = 4.3 Hz, 1H). MS: m/z 323 M^+, 207, 188, 136.

Typical procedure for the asymmetric transfer hydrogenation

An appropriate amount of ligand was added to an appropriate amount of the catalyst precursor in dry degassed *i*-propanol and stirred at room temperature for 30 min under argon. A solution of KOH in 4 ml of *i*-propanol was added and the reaction mixture was stirred for another 10 min. The ketone was then added in portion (0.05 M) and the reduction was conducted at given temperature for the time indicated (monitored by TLC). After completion of the reaction, the resulting solution was neutralized with 1 M HCl, and then extracted with Et_2O. The organic phase was dried over $MgSO_4$ and the solvent was evaporated to give the corresponding alcohol, which was purified by flash chromatography on silica gel. The enantiomeric excess was determined by GC or HPLC analysis according to literature.

*(S)-(−)-1-phenylethanol (**4a**)*

Table 5, entry 1; 95% e.e. (*S*), $[\alpha]^{25}_D = -48.0$ (*c* 1.0, CH_2Cl_2) [literature[16] $[\alpha]^{25}_D = -50.0$ (*c* 1.0, CH_2Cl_2)]. ^{1}H NMR: δ 7.25–7.40 (5H, m), 4.90 (1H, d, J = 6.5 Hz), 1.85 (1H,

br s), 1.50 (3H, d, $J = 6.6$ Hz). HPLC Daicel Chiralcel OJ-H, hexane–*i*-PrOH = 95 : 5 (0.7 ml min^{-1}), $t_S = 17.9$ min (major), $t_R = 15.7$ min (minor).

*(S)-(−)-1-p-Chlorophenylethanol (**4b**)*

Table 5, entry 2; 72% e.e. (*S*), $[\alpha]^{25}_D = -36.0$ (*c* 1.0, Et_2O) [literature[16] $[\alpha]^{25}_D = -46.3$ (*c* 2.05, Et_2O)]. ^{1}H NMR: δ 7.29 (4H, m), 4.87 (1H, d, $J = 6.5$ Hz), 2.09 (1H, s), 1.49 (3H, d, $J = 6.3$ Hz). GLC: CP-Cyclodex-β-236 M, 150 °C, He (2.0 kg/cm^2), $t_S = 15.1$ min (major), $t_R = 14.8$ min (minor).

*(S)-(−)-1-phenyl-1-propanol (**4c**)*

Table 5, entry 3; 94% e.e. (*S*), $[\alpha]^{25}_D = -33.1$ (*c* 1.0, EtOH) [literature[16] $[\alpha]^{23}_D = -34.0$ (*c* 5.03, EtOH)]. ^{1}H NMR: δ 7.25–7.36 (5H, m), 4.61 (1H, d, $J = 6.4$ Hz), 1.71–1.89 (2H, m), 1.59 (1H, s), 1.09 (3H, t). HPLC Daicel Chiralcel OJ-H, hexane–*i*-PrOH = 95 : 5 (0.7 ml min^{-1}), $t_S = 13.1$ min (major), $t_R = 15.0$ min (minor).

*(S)-(−)-1-phenyl-1-butanol (**4d**)*

Table 5, entry 4; 96% e.e. (*S*), $[\alpha]^{25}_D = -43.5$ (*c* 1.0, $CHCl_3$) [literature[26] $[\alpha]^{23}_D = -45.0$ (*c* 1.0, $CHCl_3$)]. ^{1}H NMR: δ 7.21–7.48 (5H, m), 4.67 (1H, d, $J = 7.5$ Hz), 1.91–1.87 (2H, m), 1.79 (1H, s), 1.31–1.23 (2H, m), 0.95 (3H, t). HPLC Daicel Chiralcel OB-H, hexane–*i*-PrOH = 90 : 10 (0.7 ml min^{-1}), $t_S =$ 16.7 min (major), $t_R = 17.4$ min (minor).

*(S)-(−)-1-p-methoxylphenylethanol (**4e**)*

Table 5, entry 5; 97% e.e. (*S*), $[\alpha]^{25}_D = -52.1$ (*c* 1.0, $CHCl_3$) [literature[16] $[\alpha]^{23}_D = -51.9$ (*c* 1.04, $CHCl_3$)]. ^{1}H NMR: δ 7.23–7.33 (2H, m), 6.85–6.91 (2H, m), 4.83 (1H, d, $J =$ 6.5 Hz), 3.90 (3H, s), 1.85 (1H, br s), 1.49 (3H, d, $J =$ 6.7 Hz). HPLC Daicel Chiralcel OB-H, hexane–*i*-PrOH = 90 : 10 (0.5 ml min^{-1}), $t_S = 24.5$ min (major), $t_R = 30.3$ min (minor).

*(S)-(−)-1-p-methylphenylethanol (**4f**)*

Table 5, entry 6; 95% e.e. (*S*), $[\alpha]^{25}_D = -41.3$ (*c* 2.0, MeOH) [literature[27] $[\alpha]^{27}_D = -22.3$ (*c* 3.79, MeOH)]. ^{1}H NMR: δ 7.15–7.31 (4H, m), 4.85 (1H, d, $J = 6.3$ Hz), 2.36 (3H, s), 1.83 (1H, br s), 1.53 (3H, d, $J = 6.2$ Hz). HPLC Daicel Chiralcel OB-H, hexane–*i*-PrOH = 90 : 10 (0.7 ml min^{-1}), $t_S = 21.3$ min (major), $t_R = 27.8$ min (minor).

*(S)-(−)-2-methyl-1-phenyl-1-propanol (**4g**)*

Table 5, entry 7; 97% e.e. (*S*), $[\alpha]^{25}_D = -48.5$ (*c* 1.0, Et_2O) [literature[28] 20 $[\alpha]^{23}_D = -45.7$ (*c* 0.06, Et_2O)]. ^{1}H NMR: δ 7.19–7.35 (5H, m), 4.37 (1H, dd, $J = 2.8, 7.1$ Hz), 1.96 (1H, d, $J = 6.7$ Hz), 1.85 (1H, d, $J = 3.5$ Hz), 1.00 (3H, m), 0.83 (3H, brs). HPLC Daicel Chiralcel OB-H, hexane–*i*-PrOH = 90 : 10 (0.7 ml min^{-1}), $t_S = 21.3$ min (major), $t_R = 27.8$ min (minor).

*(S)-(−)-1-m-trifluoromethylphenylethanol (**4h**)*

Table 5, entry 9; 75% ee (*S*), $[\alpha]^{25}_D = -21.7$ (*c* 1.5, MeOH) [literature[27] $[\alpha]^{24}_D = -17.1$ (*c* 2.92, MeOH)]. ^{1}H NMR: δ 7.25–7.56 (4H, m), 4.93 (1H, d, $J = 5.5$ Hz), 2.03 (1H, br s), 1.53 (3H, d, $J = 7.2$ Hz). GLC: CP-Cyclodex-β-236 M, 120 °C, He (2.0 kg cm^{-2}), $t_S = 9.5$ min (major), $t_R = 9.1$ min (minor).

*(S)-(+)-1-tetralol (**4i**)*

Table 5, entry 10; 65% e.e. (*S*), $[\alpha]^{25}_D = +21.5$ (*c* 1.5, $CHCl_3$) [literature[16] $[\alpha]^{23}_D = +32.7$ (*c* 2.46, $CHCl_3$)]. ^{1}H NMR: δ 7.10–6.85 (4H, m), 4.59 (1H, d, $J = 4.5$ Hz), 2.83 (2H, m), 2.00 (1H, br s), 1.55–1.83 (4H, m). HPLC Daicel Chiralcel OB-H, hexane–*i*-PrOH = 95 : 5 (0.7 ml min^{-1}), $t_S = 15.3$ min (major), $t_R = 10.8$ min (minor).

*(S)-(−)-1-(9-anthryl)ethanol (**4j**)*

Table 5, entry 11; 60% e.e. (*S*), $[\alpha]^{25}_D = -9.30$ (*c* 1.0, THF) [literature[29] $[\alpha]^{22}_D = +11.47$ (*c* 0.91, THF)]. ^{1}H NMR: δ 8.7–7.7 (5H, m), 7.6–7.1 (4H, m), 6.35 (1H, d, $J = 6.3$ Hz), 2.09 (1H, br s), 1.79 (3H, d, $J = 5.6$ Hz). HPLC Daicel Chiralcel OJ-H, hexane–*i*-PrOH = 95 : 5 (0.5 ml min^{-1}), $t_S = 27.3$ min (major), $t_R = 25.6$ min (minor).

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