Novel hydrido-ruthenium(II) complexes with histidine derivatives and their application in the hydrogenation of ketones

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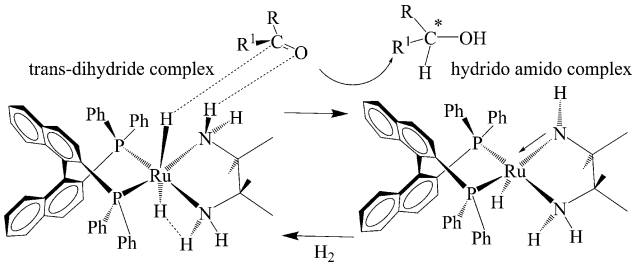
The complexes RuHCl((*R*)-binap)(L-NH_2) with L-NH_2 = (*S*)-histidine-Me-ester (**1**), histamine (**3**), (*S*)-histidinol (**4**) or 1-Me-(*S*)-histidine-Me-ester (**5**), and RuHCl((*S*)-binap)(L-NH_2) with L-NH_2 = (*S*)-histidine-Me-ester (**2**) have been prepared in 60–81% overall yields in a one-pot, three-step procedure from the precursor $RuCl_2(PPh_3)_3$. Their octahedral structures with hydride *trans* to chloride were deduced from their NMR spectra and confirmed by the results of a single crystal X-ray diffraction study for complex **3**. Under H_2 and in the presence of KO*t*Bu, complexes **1–5** in 2-propanol form moderately active catalyst precursors for the asymmetric hydrogenation of acetophenone to 1-phenylethanol. Complex **5** is more active and enantioselective than complexes **1–4**, allowing complete conversion to 1-phenylethanol in 46% e.e. (*R*) in 72 h at 20 °C under 1 MPa of H_2 with substrate : catalyst : base = 2000 : 1 : 30. Complex **5**, when activated, also catalyzes the hydrogenation of *trans*-4-phenyl-3-buten-2-one to exclusively the allyl alcohol 4-phenyl-3-buten-2-ol under 2.7 MPa of H_2 at 50 °C in 2-propanol. This selectivity for C=O *versus* C=C hydrogenation is consistent with a mechanism involving the outer sphere transfer of hydride and proton to the polar bond. Further extensions to complexes with peptides with N-terminal histidine groups appear feasible on the basis of the current work.

Introduction

Certain ruthenium complexes containing both primary or secondary amine, and phosphine or β-aminophosphine ligands, are excellent catalysts for the hydrogenation of unsaturated polar bonds such as ketones[1,2] and imines,[1,3,4] to give valuable alcohols or amines. Amine-donor complexes containing the binap ligand or its analogues are of much current interest in the asymmetric hydrogenation of ketones.[1,2,5–20] Mechanistic studies have demonstrated that these reactions involved transfer of hydride (from Ru–H) and a proton (from the amine NH) to the substrate in an outer sphere mechanism (Scheme 1).[21–23] Ruthenium complexes containing the amino-methylpyridine ligand (ampy)[24–28] or its derivatives[29] have proven to be particularly active precatalysts. We wondered whether derivatives of the amino acid histidine would provide imidazole and amine donors to ruthenium in the same fashion that ampy provides pyridyl and amino donors and thus produce the same activating effect.

The matching of the chirality of the diphosphine ligand and the amine donor (L-NH_2) in the precatalysts RuXY(diphosphine)(L-NH_2) is key to obtaining high enantioselectivity in the hydrogenation of prochiral ketones.[1,6,30–36] Therefore we were interested to test both enantiomers of binap with L-histidine and its derivatives in the asymmetric hydrogenation of ketones. Histidine and its derivatives are known to coordinate to ruthenium (see below) *via* the amino and/or imidazole nitrogen and also *via* the carboxylate oxygen.[37–39] Histidine complexes of copper are of interest for their use in the treatment of Menke's disease.[40] In this example, the histidine is bound in a tridentate fashion through the amino, imidazole and carboxylate groups (Fig. 1). In our case, carboxylate coordination is predicted to inhibit catalyst activity and so we will utilize the methyl ester of derivatives of histidine.



Scheme 1 The outer-sphere H^-/H^+ transfer mechanism of catalyst action.

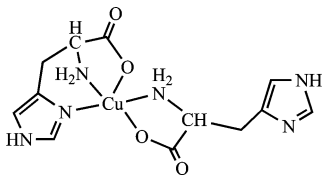


Fig. 1 Histidine copper complex used in the treatment of Menke's disease.[40]

Results and discussion

Synthesis and characterization

The hydrido-ruthenium(II) complexes RuHCl(binap)(L-NH_2) (L-NH_2 = (*S*)-histidine-Me-ester (**1–2**); histamine (**3**); (*S*)-histidinol

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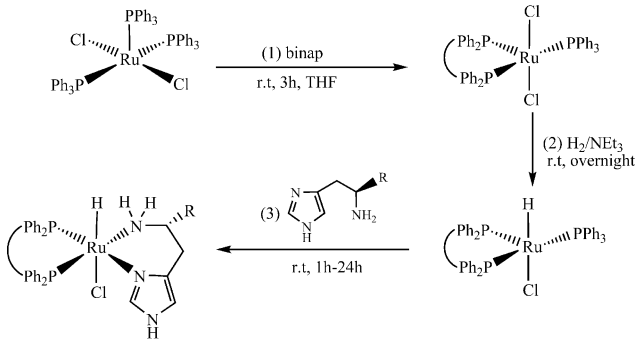
(**4**)) have been prepared in a one-pot, three-step procedure from the precursor $RuCl_2(PPh_3)_3$ (Scheme 2). The first step involved the reaction of $RuCl_2(PPh_3)_3$ with one equiv. of the binap ((*R*)- or (*S*)-) ligand in THF to give the enantiomerically pure intermediate $RuCl_2$(binap)(PPh_3). This was directly followed by a second reaction under H_2 in the presence of an excess of NEt_3 to produce the deep red intermediate RuHCl(binap)(PPh_3) that was then reacted *in situ* with the histidine derivative to produce the desired *trans*-RuHCl(binap)(L-NH_2) complexes as yellow solids, in 60–81% overall yields.

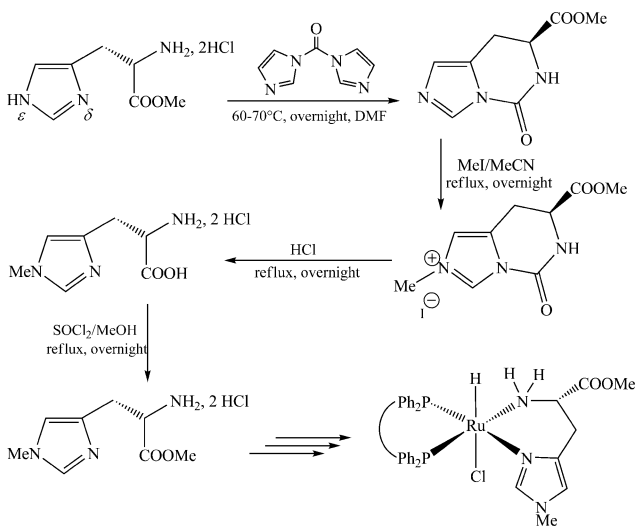


1. R=COOMe: RuHCl((*R*)-binap)((*S*)-histidine-Me-ester)
2. R=COOMe: RuHCl((*S*)-binap)((*S*)-histidine-Me-ester)
3. R=H: RuHCl((*R*)-binap)(histamine)
4. R=CH_2OH: RuHCl((*R*)-binap)((*S*)-histidinol)

Scheme 2 One-pot three-step procedure.

This synthetic route constitutes an effective "one-pot" procedure in high yield for the preparation of *trans*-RuHCl(diphosphine)(diamine) complexes, which are usually obtained after isolation of the different intermediates in lower combined yields based on $RuCl_2(PPh_3)_3$.[3,21,41,42]

Complexes **1–4** have an acidic N–H proton on the imidazole ring that will be deprotonated under the basic catalytic conditions. In order to probe the influence of this deprotonation reaction on catalytic activity we have also prepared the *N*-methyl histidine derivative RuHCl((*R*)-binap)(1-Me-(*S*)-histidine-Me-ester),



Scheme 3 Preparation of 1-Me-(*S*)-histidine-Me-ester and its ruthenium complex **5**.

(**5**) according to Scheme 3. Regioselective methylation at the *N*-ε position of (*S*)-histidine was obtained as described by Jain *et al.*[43] after selective protection of the δ-*N* with carbonyldiimidazole. Alkylation with methyl iodide in refluxing acetonitrile and deprotection in dilute HCl provide then the 1-Me-(*S*)-histidine.[43] Esterification of the latter using thionyl chloride in methanol gave the 1-Me-(*S*)-histidine-Me-ester.[44] Its ruthenium complex **5** was finally prepared in a one-pot reaction from $RuCl_2(PPh_3)_2$ in the same way as complexes **1–4** (*vide supra*).

Complexes **1–4** were isolated in a pure form but the purification of **5** was not successful because of its greater solubility in common solvents, including hexanes. The complexes are yellow solids that are air sensitive both in the solid-state and in solution. Their structures were deduced from their NMR spectra and confirmed by the results of elemental analyses and a single crystal X-ray diffraction study for complex **3**. The NMR spectra supported the *trans* geometry proposed in Schemes 2–3, with the hydride ligand *trans* to the chloride, as described below. The $^{31}P\{^1H\}$ NMR spectra showed AB doublets at *ca.* 68 and 73 ppm ($J_{AB} \sim 40$ Hz), and the hydride region of the ^1H NMR consists of a triplet centred at −17 ppm. The magnitude of the $^2J_{H-P}$ coupling constant (26 Hz) is characteristic of the hydride ligand *cis* to the two phosphorus atoms of the binap on ruthenium.[9,21,41] The proton resonance of the N–H on the imidazole ring appears as a sharp singlet at *ca.* 11 ppm.

A single-crystal X-ray diffraction study of RuHCl((*R*)-binap)(histamine) (**3**) confirmed the proposed octahedral *trans* geometry (Fig. 2). Various attempts at obtaining X-ray quality crystals of the other complexes were unsuccessful. However, their structures are expected to be similar to that of **3** on the basis of their similar NMR spectra. Crystals of **3**, as THF solvate, were grown from a concentrated THF/hexanes solution. Although no

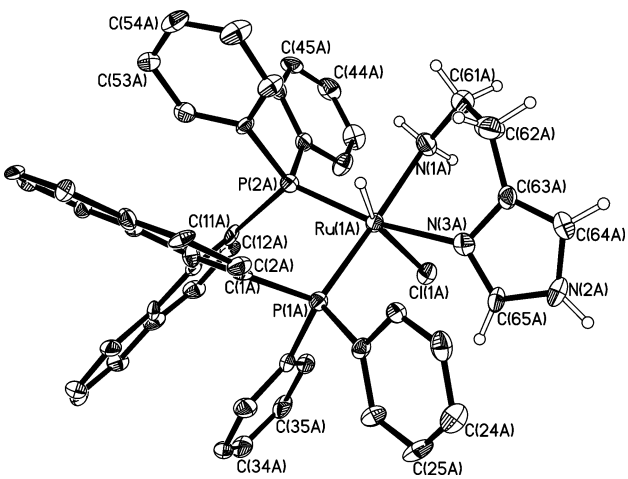


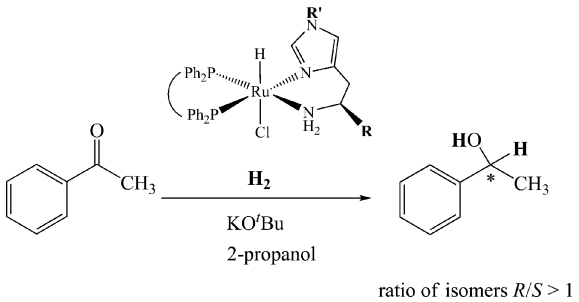
Fig. 2 X-Ray structure of RuHCl((*R*)-binap)(histamine), (**3**). Thermal ellipsoids are shown at 30% probability and the solvent molecule and the hydrogen atoms of the ((*R*)-binap) are omitted for clarity. Selected bond distances (Å) and angles (°): Ru(1A)–H = 1.65(8); Ru(1A)–Cl(1A) = 2.634(3); Ru(1A)–N(1A) = 2.208(7); Ru(1A)–N(3A) = 2.148(8); Ru(1A)–P(1A) = 2.236(3); Ru(1A)–P(2A) = 2.245(3); N(1A)–Ru(1A)–N(3A) = 81.8(3); P(1A)–Ru(1A)–P(2A) = 89.6(1); P(2A)–Ru(1A)–N(1A) = 90.3(2); P(1A)–Ru(1A)–N(3A) = 97.7(2); H–Ru(1A)–N(1A) = 89(3); Cl(1A)–Ru(1A)–N(1A) = 81.4(3); Cl(1A)–Ru(1A)–N(3A) = 80.7(2); Cl(1A)–Ru(1A)–P(1A) = 102.81(9); Cl(1A)–Ru(1A)–P(2A) = 105.5(1).

histamine complexes of ruthenium have been crystallographically characterized there are structures for four ruthenium histidine complexes: two with tridentate ligands (chloro(L-histidinato-*N*,*N*′,*O*)(η²,η²-norbornadiene)ruthenium(II)[37] and chloro(D,L-histidinato-*N*,*N*′,*O*)bis(triphenylphosphine)ruthenium(II)),[37] one with a bidentate ligand as in complex **3** (chloro(η⁶-benzene)-(L-histidinato methyl ester-*N*,*N*′)ruthenium(II) chloride) (**A**),[38] and one monodentate through the imidazole ring ((L-histidinato)-pentaammine-ruthenium(II) trichloride).[39] The ruthenium–nitrogen distances in **3** (Ru–N1 = 2.208(7); Ru–N3 = 2.148(8) Å) are longer than corresponding distances in complex **A** (Ru–NH_2 2.141(3); Ru–N(imidazole) 2.062(3) Å), presumably due to the steric crowding imposed by the binap ligand in complex **3**. The N1–Ru–N3 angles are similar (N1–Ru–N3 = 81.8(3)° in **3** *vs* N–Ru–N = 80.3° in **A**). The histamine ligand forms a similar twist–boat six membered ring with the metal in each complex so that one N1–H group can form a hydrogen-bonding interaction with the adjacent chloride ligand (2.7 Å in **3** *vs* 3.0 Å in **A**). The RuH–HN distances of 3.1–3.5 Å are too long for significant hydrogen bonding. In other respects the structure of **3** (Ru–Cl = 2.634(3), Ru–P1 = 2.236(3), Ru–P2 = 2.245(3), P1–Ru–P2 = 89.6(1), Ru–NH_2 = 2.208(7), RuCl···HN 2.7 Å) is similar to those of the other RuHCl(binap)(L–NH_2) structures,[1,3,10,21,41] particularly RuHCl((*R*)-binap)($PPh_2CH_2CH_2NH_2$)[1] (Ru–Cl = 2.580(2) Ru–P1(binap) = 2.255(2), Ru–P2(binap) = 2.307(2), P(1)–Ru–P(2) = 90.67(6), Ru–NH_2 2.195(5) RuCl···HN 2.6 Å). This latter complex is a very active ketone hydrogenation catalyst and so the lower catalytic activity of complex **3** (see below) is not apparent from the geometry.

Hydrogenation of ketones

Complexes **1–5** were tested as catalyst precursors for the hydrogenation of acetophenone to 1-phenylethanol (Scheme 4, Table 1). Under H_2 and in the presence of KO*t*Bu, they constitute moderately active pre-catalysts with a modest enantioselectivity.

The comparable runs in Table 1 indicate that complex **5** (entry 8) is significantly more active and enantioselective than complexes **1–4** (entries 1–2 and 5–6). Using **5**, full conversion of acetophenone in 1-phenylethanol with an e.e. of 46% (*R*) was achieved in 72 h at 20 °C under 1 MPa of H_2 with substrate : catalyst : base = 2000 : 1 : 30. Under more severe conditions (2.7 MPa, 50 °C), complexes **1–4** showed lower conversions (23–96%) and e.e. values (0–34% (*R*)). This suggests that the deprotonation of the imidazole ring might be deactivating. However the system with catalyst **4** and one equivalent of base is less active than with 30 equivalents of base (entry 7), presumably without imidazole deprotonation.



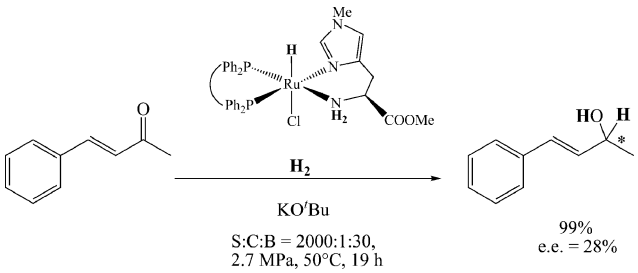
ratio of isomers *R*/*S* > 1

Scheme 4 Hydrogenation of acetophenone.

The correct matching of binap chirality with amine chirality is often crucial in obtaining an elevated e.e. value in such complexes.[10,31] This matching effect is apparent to a limited degree in comparison of the enantioselectivity of complexes **1** and **2**, diastereomers containing binap in opposite configurations. The (*R*)-binap/(*S*)-histidine isomer **1** gives an alcohol of higher e.e. than that produced by the (*S*)-binap/(*S*)-histidine isomer **2** under identical conditions (entries 1 and 2).

Moreover, under base-free conditions (entry 4), it appears that complex **2** can also produce 1-phenylethanol in 15% after 18 h, with a slight improvement in the e.e. (32%). It was hoped that the alcohol group of the histidinol ligand in **4** would assist in the H_2 splitting reaction in an intramolecular fashion by positioning the OH group to act as a proton relay from H_2 to amido nitrogen and therefore increase the rate of hydrogenation. Alcohol solvents are suspected to assist in the splitting of dihydrogen in a variety of reactions.[2,45–47] But in our case there is no observable effect, possibly because of the large excess of 2-propanol used as the solvent.

Complex **5** also hydrogenates *trans*-4-phenyl-3-buten-2-one to exclusively the allyl alcohol 4-phenyl-3-buten-2-ol under 2.7 MPa of H_2 at 50 °C in 2-propanol (Scheme 5). This selectivity for C=O *versus* C=C hydrogenation is consistent with an outer sphere



Scheme 5 Hydrogenation of *trans*-4-phenyl-3-buten-2-one.

Table 1 The hydrogenation of acetophenone to 1-phenylethanol (*R* form in excess) catalyzed by complexes **1–5**

Entry	Cat.	S : C : B	Solvent	*T*/°C	pH_2/MPa	Time/h	Conv. (%)	e.e. (%)
1	**1**	2000 : 1 : 30	2-PrOH	50	2.7	19	67	23
2	**2**	2000 : 1 : 30	2-PrOH	50	2.7	29	91	0
3	**2**	500 : 1 : 2	2-PrOH	50	2.7	16	99	0
4	**2**	500 : 1 : 0	2-PrOH	50	2.7	18	15	32
5	**3**	500 : 1 : 30	2-PrOH	50	2.7	18	23	18
6	**4**	500 : 1 : 30	2-PrOH	50	2.7	18	96	34
7	**4**	500 : 1 : 1	2-PrOH	50	2.7	19	34	18
8	**5**	2000 : 1 : 30	2-PrOH	20	1.0	72	98	46
9	**5**	500 : 1 : 1	2-PrOH	20	1.0	48	99	7

mechanism with the transfer of H^+/H^- only to the polar bond.[21–23] This is generally observed for the hydrogenation of polar bonds by the catalyst system RuHCl(diphosphine)(diamine)/base.[21,41,48]

Conclusions

A variety of potential catalyst precursors RuHCl(binap)(L-NH_2) (L-NH_2 = (*S*)-histidine-Me-ester (**1–2**); histamine (**3**); (*S*)-histidinol (**4**); (*S*)-1-Me-histidine-Me-ester (**5**)) have been prepared by an effective one-pot three-step procedure in high yield. Proving that such complexes are active catalysts for H_2-hydrogenation of ketones opens the door to the coordination chemistry of polypeptides with N-terminal histidine groups and their use in asymmetric catalysis. Dipeptides have been used in transfer hydrogenation catalysis[49–52] but not in ketone H_2-hydrogenation. His-his complexes of zinc have been reported as models for zinc finger proteins[53] and his-his complexes of vanadyl are known.[54]

Experimental

General comments

All preparations and manipulations were carried out under an argon, nitrogen, or hydrogen atmosphere using standard Schlenk, vacuum-line, and glove-box techniques. Dry, oxygen-free solvents were prepared by distillation from appropriate drying agents and employed throughout. The synthesis of 1-methyl-(*S*)-histidine dihydrochloride has been reported previously.[43] The 1-methyl-(*S*)-histidine methyl ester dihydrochloride has been prepared by esterification of 1-methyl-(*S*)-histidine dihydrochloride according to the general procedure described by Mancilla *et al.* for esterification of α-amino acid.[44] $RuCl_2(PPh_3)_3$ was prepared by a slight modification of the published procedure.[55] All other reagents used in the experiments were obtained from commercial sources and used as received. The elemental analyses were performed at the University of Toronto, on samples handled under argon. Varian Gemini 400 MHz and 300 MHz spectrometers were employed for recording ^1H (400 MHz and 300 MHz), $^{13}C\{^1H\}$ (100 MHz and 75 MHz), and $^{31}P\{^1H\}$ (161 MHz and 121 MHz) NMR spectra at ambient temperature. The ^1H and ^{13}C NMR spectra were referenced to solvent resonances, as follows: 7.26 and 77.16 ppm for $CHCl_3$ and $CDCl_3$, 7.16 and 128.06 ppm for C_6D_5H and C_6D_6, 1.85 and 25.62 ppm for THF-d_8. The ^{31}P NMR spectra were referenced to 85% H_3PO_4 (0 ppm). Gas chromatography was carried out on a Perkin Elmer Autosystem XL.

Preparations

RuHCl[(*R*)-binap][(*S*)-histidine-Me-ester] (1). Dry THF (20 cm^3) was added to $RuCl_2(PPh_3)_3$ (400 mg, 0.42 mmol) and (*R*)-binap (260 mg, 0.42 mmol). The dark brown suspension was stirred under an Ar atmosphere for 7 h. After addition of triethylamine (174 mm^3, 1.2 mmol), the reaction flask was stirred under a H_2 atmosphere overnight. The resulting red solution was purged with Ar and then (*S*)-histidine-Me-ester dihydrochloride (101 mg, 0.42 mmol) was added. After stirring for 2.5 h, the resulting orange solution was filtered through a small pad of Celite, concentrated to a small volume (*ca.* 2 cm^3) and 10 cm^3 of Et_2O were added. A yellow powder precipitated and was isolated by filtration, washed with Et_2O and vacuum-dried. **1**: Yield: 260 mg, 67%. (Found: C, 66.37; H, 5.13; N, 4.79%. $C_{51}H_{44}P_2N_3Cl_1Ru_1O_2$ requires C, 65.91; H, 4.77; N, 4.52%); δ_H (300 MHz; C_6D_6) −17.5 (1 H, t, *J* 26.1, Ru*H*), 2.19–2.24 (2 H, m, NH_2), 2.63 (1 H, d, *J* 14.1, C*H*), 2.71–2.75 (2 H, m, NH_2), 3.00 (3 H, s, CO_2Me), 3.51–3.63 (2 H, m, CH_2) 6.06–8.65 (32 H, m, Ph, naphthyl and =C*H*–NH protons), 11.5 (1 H, s, N*H*); δ_C (75 MHz; THF-d_8) 33.3 (s, CH_2), 53.3 (s, CO_2Me), 55.1 (s, *C*H), 113.24 (s, =*C*–NH), 125.88–142.58 (m, Ph, naphthyl and =*C*H–NH carbons), 175.06 (s, *C*O); δ_P (121 MHz; C_6D_6) 69.8 (d, J_{AB} 41.5), 73.5 (d, J_{AB} 41.5).

RuHCl[(*S*)-binap][(*S*)-histidine-Me-ester], (2). Dry THF (20 cm^3) was added to $RuCl_2(PPh_3)_3$ (500 mg, 0.52 mmol) and (*S*)-binap (325 mg, 0.52 mmol). The dark brown suspension was stirred under an N_2 atmosphere for 5 h. After addition of triethylamine (218 mm^3, 1.6 mmol), the reaction flask was stirred under an H_2 atmosphere overnight. The resulting red solution was purged with Ar and then (*S*)-histidine-Me-ester dihydrochloride (126 mg, 0.52 mmol) was added. After stirring for 2 h, the resulting orange solution was filtered through a small pad of Celite, concentrated to a small volume (*ca.* 5 cm^3) and 10 cm^3 of Et_2O were added. A yellow powder precipitated and was isolated by filtration, washed with Et_2O and vacuum-dried. **2**: Yield: 285 mg, 60%. (Found: C, 65.91; H, 4.91; N, 4.30%. $C_{51}H_{44}P_2N_3Cl_1Ru_1O_2$ requires C, 65.91; H, 4.77; N, 4.52%); δ_H (300 MHz; C_6D_6) −17.50 (1 H, t, *J* 26.1, Ru*H*), 2.63–2.79 (3 H, m, C*H* and NH_2), 2.82 (2 H, m, NH_2), 2.93 (3 H, s, CO_2Me), 3.11–3.27 (2 H, m, CH_2) 5.98–8.64 (32 H, m, Ph, naphthyl and =C*H*–NH protons), 11.2 (1 H, s, N*H*); δ_P (121 MHz; C_6D_6) 68.9 (d, J_{AB} 41.1), 72.5 (d, J_{AB} 41.1).

RuHCl[(*R*)-binap][histamine], (3). Dry THF (60 cm^3) was added to $RuCl_2(PPh_3)_3$ (1.2 g, 1.25 mmol) and (*R*)-binap (780 mg, 1.25 mmol). The dark brown suspension was stirred under an Ar atmosphere for 3 h. After addition of triethylamine (522 mm^3, 3.75 mmol), the reaction flask was stirred under an H_2 atmosphere overnight. The resulting red solution was purged with Ar and then histamine (138 mg, 1.25 mmol) was added. After stirring for 1 h, the resulting orange solution was filtered through a small pad of Celite, concentrated to a small volume (*ca.* 5 cm^3) and 20 cm^3 of Et_2O were added. A yellow powder precipitated and was isolated by filtration, washed with Et_2O and vacuum-dried. **3**: Yield: 880 mg, 81%. (Found: C, 67.18; H, 5.34; N, 4.52%. $C_{49}H_{42}P_2N_3Cl_1Ru_1$ requires C, 67.54; H, 4.86; N, 4.82%); δ_H (400 MHz; C_6D_6) −17.59 (1 H, t, *J* 26.8, Ru*H*), 1.71–1.98, 2.41–2.43, 3.02–3.05 (6 H, m, CH_2 and NH_2), 5.87–8.57 (32 H, m, Ph, naphthyl and =C*H*–NH protons), 11.5 (1 H, s, N*H*); δ_C (75 MHz; THF-d_8) 33.3 (s, CH_2), 53.3 (s, CO_2Me), 55.1 (s, *C*H), 113.24 (s, =*C*–NH), 125.88–142.58 (m, Ph, naphthyl and =*C*H–NH carbons), 175.06 (s, *C*O); δ_C (100 MHz; C_6D_6) 28.7 (s, CH_2CH_2), 40.3 (s, CH_2NH_2), 109.97 (s, =*C*–NH), 124.59–142.73 (m, Ph, naphthyl and =*C*H–NH carbons); δ_P (121 MHz; C_6D_6) 68.5 (d, J_{AB} 39.4), 72.9 (d, J_{AB} 39.4).

RuHCl[(*R*)-binap][(*S*)-histidinol], (4). Dry THF (25 cm^3) was added to $RuCl_2(PPh_3)_3$ (700 mg, 0.73 mmol) and (*R*)-binap (455 mg, 0.73 mmol). The dark brown suspension was stirred under an Ar atmosphere for 5 h. After addition of triethylamine (300 mm^3, 2.2 mmol), the reaction flask was stirred under an H_2 atmosphere overnight. The resulting red solution was purged with

Ar and then (*S*)-histidinol dihydrochloride (157 mg, 0.73 mmol) was added. After stirring overnight, the resulting orange solution was filtered through a small pad of Celite, concentrated to a small volume (*ca.* 5 cm^3) and 15 cm^3 of Et_2O were added. A yellow powder precipitated and was isolated by filtration, washed with Et_2O and vacuum-dried. **4**: Yield: 450 mg, 68%. (Found: C, 66.57; H, 4.66; N, 4.55%. $C_{50}H_{44}P_2N_3Cl_1Ru_1O_1$ requires C, 66.62; H, 4.92; N, 4.66%); δ_H (300 MHz; C_6D_6) −17.89 (1 H, t, *J* 26.4, Ru*H*), 2.17–2.21, 2.34–2.36, 2.70–2.79, 3.06–3.21 (5 H, m, C*H*, CH_2 and NH_2), 6.11–8.52 (32 H, m, Ph, naphthyl and =C*H*–NH protons), 11.1 (1 H, s, N*H*); δ_C (100 MHz; $CDCl_3$) 29.7 (s, CH_2), 50.6 (s, *C*H), 63.7 (s, CH_2OH), 111.7 (s, =*C*–NH), 124.4–141.7 (m, Ph, naphthyl and =*C*H–NH carbons); δ_P (121 MHz; C_6D_6) 67.9 (d, J_{AB} 39.0), 72.7 (d, J_{AB} 39.0).

RuHCl[(*R*)-binap][1-Me-(*S*)-histidine-Me-ester], (5). Dry THF (25 cm^3) was added to $RuCl_2(PPh_3)_3$ (520 mg, 0.54 mmol) and (*R*)-binap (338 mg, 0.54 mmol). The dark brown suspension was stirred under an N_2 atmosphere for 5 h. After addition of triethylamine (250 mm^3, 1.6 mmol), the reaction flask was stirred under an H_2 atmosphere overnight. The resulting red solution was purged with N_2 and then 1-Me-(*S*)-histidine-Me-ester dihydrochloride (140 mg, 0.54 mmol) was added. After stirring for 5 h, the resulting orange solution was filtered through a small pad of Celite, concentrated to a small volume (*ca.* 5 cm^3) and 15 cm^3 of Et_2O were added. A yellow powder precipitated and was isolated by filtration, washed with Et_2O and vacuum-dried. **5**: Crude yield: 270 mg, 53% (the product contains free PPh_3 and (*R*)-binap). δ_H (300 MHz; C_6D_6) −16.47 (1 H, t, *J* 26.9, Ru*H*), 1.94 (3 H, s, N*Me*) 2.10–2.40, 2.8–3.8 (m, 5H, C*H*, CH_2 and NH_2), 3.06 (3 H, s, CO_2Me), 6.53–8.8 (32 H, m, Ph, naphthyl and =C*H*–NH protons); δ_P (121 MHz; C_6D_6) 69.8 (d, J_{AB} 41.5), 73.5 (d, J_{AB} 41.5).

General procedure for the hydrogenation of acetophenone

In the Ar glovebox, the ruthenium complex (5.0×10^{-3} mmol) and acetophenone (500–2000 equiv.) were dissolved in 2 cm^3 of the 2-propanol and stirred for 2 min. The solution of base was prepared by dissolution of potassium *tert*-butoxide (1–30 equiv) in 3 cm^3 of 2-propanol. The solution containing the substrate and the precatalyst, followed by the solution of base were injected into a 50 cm^3 Parr hydrogenator reactor at the desired pressure and temperature, maintained by use of a Fischer Scientific Isotemp 1016D water bath. The conversion and enantiomeric excess of the products were determined with GC analysis using a chiral column (CP Chirasil-Dex CB 25 m × 2.5 mm) utilizing an H_2 carrier gas at a column pressure of 5 psi, an oven temperature of 130 °C, an injector temperature of 250 °C, and a FID of 275 °C. The retention times were acetophenone 5.0 min, (*R*)-1-phenylethanol 8.5 min, (*S*)-1-phenylethanol 9.1 min.

Hydrogenation of *trans*-4-phenyl-3-buten-2-one

The hydrogenation reactions and the GC analysis were conducted as above, except that for the GC conditions the oven temperature was 140 °C. The retention times were *trans*-4-phenyl-3-buten-2-one 13.4 min, *trans*-(*R*)-4-phenyl-3-buten-2-ol 15.9 min, *trans*-(*S*)-4-phenyl-3-buten-2-ol 16.2 min. The product was also identified by ^{1}H NMR spectroscopy and the data obtained matched literature values.[56]

Table 2 Summary of crystal data, details of intensity collection and least-squares refinement parameters for **3**

3	
Empirical Formula	$C_{49}H_{42}N_3P_2ClRu{\cdot}C_4H_8O$
Formula weight	943.42
Crystal size/mm	0.12 × 0.14 × 0.16
Crystal class	Orthorhombic
Space group	$P\,2_12_12_1$
T/K	150.0
a/Å	19.3194(9)
b/Å	20.3567(9)
c/Å	22.6289(8)
α/°	90
β/°	90
γ/°	90
V/Å^3	8899.5(7)
Z	8
ρ_{calc}/Mg m^{-3}	1.408
μ(Mo-Kα)/mm^{-1}	0.528
F(000)	3904
Range *θ* collected/°	2.69 to 25.07
No. of reflections	38283
Independent reflections	15602
$R_1(I > 2\sigma(I))$	0.0694
wR_2 (all data)	0.1681
Goodness of fit	0.971
Parameters refined	1105
Maximum peak in final Δ*F* map/e Å^{-3}	0.721

Definition of *R* indices: $R_1 = \Sigma(F_o - F_c)/\Sigma(F_o)$ $wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$

X-Ray crystal structure determination of complex 3

X-Ray crystallographic data for **3** were collected on a Bruker-Nonius Kappa-CCD diffractometer using monochromated Mo-Kα radiation and were measured using a combination of *ϕ* scans and *ω* scans with *κ* offsets, to fill the Ewald sphere. The data were processed using the Denzo-SMN package. Absorption corrections were carried out using SORTAV. The structure was solved and refined using SHELXTL V6.1 for full-matrix least-squares refinement that was based on F^2. The hydride position was refined. All other H atoms were included in calculated positions and allowed to refine in riding-motion approximation with U_{iso} tied to the carrier atom. Crystallographic data for the compounds is given in Table 2. The structural parameters for the two independent molecules in the unit cell of **3** were quite similar and only details for one of them have been reported (Fig. 2).

CCDC reference number 633747.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b702803b

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References

1 K. Abdur-Rashid, R. W. Guo, A. J. Lough, R. H. Morris and D. Song, *Adv. Synth. Catal.*, 2005, **347**, 571–579.
2 C. A. Sandoval, T. Ohkuma, K. Muñiz and R. Noyori, *J. Am. Chem. Soc.*, 2003, **125**, 13490–13503.
3 K. Abdur-Rashid, A. J. Lough and R. H. Morris, *Organometallics*, 2001, **20**, 1047–1049.
4 C. J. Cobley and J. P. Henschke, *Adv. Synth. Catal.*, 2003, **345**, 195–201.
5 R. J. Hamilton and S. H. Bergens, *J. Am. Chem. Soc.*, 2006, **128**, 13700–13701.
6 H. L. Ngo and W. Lin, *J. Org. Chem.*, 2005, **70**, 1177–1187.
7 Q. Jing, X. Zhang, H. Sun and K. L. Ding, *Adv. Synth. Catal.*, 2005, **347**, 1193–1197.
8 R. J. Hamilton, C. G. Leong, G. Bigam, M. Miskolzie and S. H. Bergens, *J. Am. Chem. Soc.*, 2005, **127**, 4152–4153.
9 R. Guo, R. H. Morris and D. Song, *J. Am. Chem. Soc.*, 2005, **127**, 516–517.
10 R. Guo, A. J. Lough, R. H. Morris and D. Song, *Organometallics*, 2004, **23**, 5524–5529.
11 M. Berthod, C. Saluzzo, G. Mignani and M. Lemaire, *Tetrahedron: Asymmetry*, 2004, **15**, 639–645.
12 T. Ohkuma, T. Hattori, H. Ooka, T. Inoue and R. Noyori, *Org. Lett.*, 2004, **6**, 2681–2683.
13 A. Hu, H. L. Ngo and W. Lin, *Org. Lett.*, 2004, **6**, 2937–2940.
14 D. G. Genov and D. J. Ager, *Angew. Chem., Int. Ed.*, 2004, 2816–2819.
15 G. J. Deng, Q. H. Fan, X. M. Chen and G. H. Liu, *J. Mol. Catal. A: Chem.*, 2003, **193**, 21–25.
16 K. Mikami, T. Korenaga, Y. Yusa and M. Yamanaka, *Adv. Synth. Catal.*, 2003, **345**, 246–254.
17 A. Hu, H. L. Ngo and W. Lin, *J. Am. Chem. Soc.*, 2003, **125**, 11490–11491.
18 T. Ohkuma, M. Koizumi, K. Muniz, G. Hilt, C. Kabuto and R. Noyori, *J. Am. Chem. Soc.*, 2002, **124**, 6508–6509.
19 R. Noyori, *Angew. Chem., Int. Ed.*, 2002, **41**, 2008–2022.
20 J. Wu, H. Chen, W. Kwok, K. Lam, Z. Zhou, C. Yeung and A. Chan, *Tetrahedron Lett.*, 2002, **43**, 1539–1543.
21 K. Abdur-Rashid, S. E. Clapham, A. Hadzovic, J. N. Harvey, A. J. Lough and R. H. Morris, *J. Am. Chem. Soc.*, 2002, **124**, 15104–15118.
22 S. E. Clapham, A. Hadzovic and R. H. Morris, *Coord. Chem. Rev.*, 2004, **248**, 2201–2237.
23 R. Noyori, M. Yamanaka and S. Hashiguchi, *J. Org. Chem.*, 2001, **66**, 7931–7944.
24 K. Abdur-Rashid, R. Abbel, A. Hadzovic, A. J. Lough and R. H. Morris, *Inorg. Chem.*, 2005, **44**, 2483–2492.
25 T. Ohkuma, C. A. Sandoval, R. Srinivasan, Q. Lin, Y. Wei, K. Muniz and R. Noyori, *J. Am. Chem. Soc.*, 2005, **127**, 8288–8289.
26 W. Baratta, J. Schutz, E. Herdtweck, W. A. Herrmann and P. Rigo, *J. Organomet. Chem.*, 2005, **690**, 5570–5575.
27 W. Baratta, G. Chelucci, S. Gladiali, K. Siega, M. Toniutti, M. Zanette, E. Zangrando and P. Rigo, *Angew. Chem., Int. Ed.*, 2005, **44**, 6214–6219.
28 W. Baratta, E. Herdtweck, K. Siega, M. Toniutti and P. Rigo, *Organometallics*, 2005, 1660–1669.
29 A. Hadzovic, C. M. MacLaughlin, D. Song, and R. H. Morris, in preparation.
30 T. Ohkuma, H. Ooka, S. Hashiguchi, T. Ikariya and R. Noyori, *J. Am. Chem. Soc.*, 1995, **117**, 2675–2676.
31 R. Noyori and T. Ohkuma, *Angew. Chem., Int. Ed.*, 2001, **40**, 40–73.
32 M. J. Burk, W. Hems, D. Herzberg, C. Malan and A. Zanotti-Gerosa, *Org. Lett.*, 2000, **2**, 4173–4176.
33 J. Wu, H. Chen, W. Kwok, R. Guo, Z. Zhou, C. Yeung and A. S. C. Chan, *J. Org. Chem.*, 2002, **67**, 7908–7910.
34 J. P. Henschke, A. Zanotti-Gerosa, P. Moran, P. Harrison, B. Mullen, G. Casy and I. C. Lennon, *Tetrahedron Lett.*, 2003, **44**, 4379–4383.
35 H. U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner and M. Studer, *Adv. Synth. Catal.*, 2003, **345**, 103–151.
36 G. A. Grasa, A. Zanotti-Gerosa and W. P. Hems, *J. Organomet. Chem.*, 2006, **691**, 2332–2334.
37 W. S. Sheldrick and R. Exner, *Inorg. Chim. Acta*, 1992, **195**, 1–9.
38 W. S. Sheldrick and S. Heeb, *J. Organomet. Chem.*, 1989, **377**, 357–366.
39 K. Krogh-Jespersen, J. D. Westbrook, J. A. Potenza and H. J. Schugar, *J. Am. Chem. Soc.*, 1987, **109**, 7025–7031.
40 P. Deschamps, P. P. Kulkarni and B. Sarkar, *Inorg. Chem.*, 2004, **43**, 3338–3340.
41 K. Abdur-Rashid, M. Faatz, A. J. Lough and R. H. Morris, *J. Am. Chem. Soc.*, 2001, **123**, 7473–7474.
42 R. Guo, C. Elpelt and R. H. Morris, *Chem. Commun.*, 2005, 3050–3052.
43 R. Jain and L. A. Cohen, *Tetrahedron*, 1996, **52**, 5363–5370.
44 T. Mancilla, L. Carrillo, L. S. Zamudio-Rivera, H. I. Beltran and N. Farfan, *Org. Prep. Proced. Int.*, 2001, **22**, 341–349.
45 M. Ito, M. Hirakawa, K. Murata and T. Ikariya, *Organometallics*, 2001, **20**, 379–381.
46 C. Hedberg, K. Kallstrom, P. I. Arvidsson, P. Brandt and P. G. Andersson, *J. Am. Chem. Soc.*, 2005, **127**, 15083–15090.
47 C. P. Casey, J. B. Johnson, S. W. Singer and Q. Cui, *J. Am. Chem. Soc.*, 2005, **127**, 3100–3109.
48 R. Abbel, K. Abdur-Rashid, M. Faatz, A. Hadzovic, A. J. Lough and R. H. Morris, *J. Am. Chem. Soc.*, 2005, **127**, 1870–1882.
49 I. M. Pastor, P. Vastila and H. Adolfsson, *Chem. Commun.*, 2002, **80**, 2046–2047.
50 I. M. Pastor, P. Västilä and H. Adolfsson, *Chem.–Eur. J.*, 2003, **9**, 4031–4045.
51 J. Wettergren, A. Bogevig, M. Portier and H. Adolfsson, *Adv. Synth. Catal.*, 2006, **348**, 1277–1282.
52 P. Vastila, A. B. Zaitsev, J. Wettergren, T. Privalov and H. Adolfsson, *Chem.–Eur. J.*, 2006, **12**, 3218–3225.
53 R. Vogler and H. Vahrenkamp, *Eur. J. Inorg. Chem.*, 2002, **17**, 761–766.
54 E. Garribba, G. Micera, A. Panzanelli, E. Lodyga-Chruscinska and D. Sanna, *Eur. J. Inorg. Chem.*, 2005, 1369–1382.
55 P. A. Hollan, T. A. Stephenson and G. Wilkinson, *Inorg. Synth.*, 1970, **12**, 237.
56 P. D. de Koning, M. Jackson and I. C. Lennon, *Org. Process Res. Dev.*, 2006, **10**, 1054–1058.