Published in Green Chemistry, issue 9, 391-397, 2007
which should be used for any reference to this work

Water-soluble arene ruthenium catalysts containing sulfonated diamine ligands for asymmetric transfer hydrogenation of α-aryl ketones and imines in aqueous solution

Jérôme Canivet and Georg Süss-Fink*

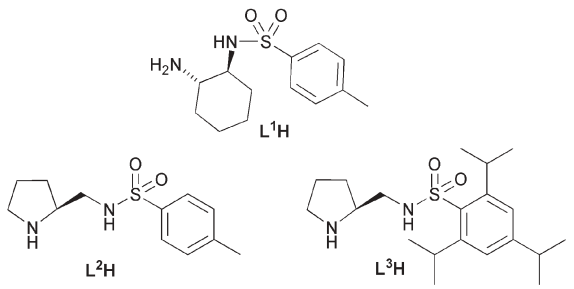
A new family of nine cationic organometallic aqua complexes of the type $[(arene)Ru(RSO_2N\cap NH_2)(OH_2)]^+$ (**1–9**), containing chiral *N*,*N*-chelating ligands, has been synthesised and isolated as the tetrafluoroborate salts, which are water-soluble and stable to hydrolysis. The enantiopure complexes **1–9** catalyse the transfer hydrogenation of prochiral aryl ketones and imines in aqueous solution to give the corresponding alcohols and amines with good conversion and enantioselectivity. This method gives an environmentally friendly access, for instance, to isoquinoline alkaloids by asymmetric catalysis in water.

Introduction

Water-soluble organometallic complexes attract continuously growing interest for applications in catalysis, because of environmentally friendly processing, simple product separation and pH dependent selectivity in aqueous media. The chemistry of organometallic aqua ions was comprehensively reviewed by Koelle.[1] Related reviews deal with water-soluble organometallics complexed by hydrophilic ligands,[2] metal-mediated organic synthesis in water[3] and catalysis by water-soluble organometallic complexes in biphasic systems.[4] In particular, the transfer hydrogenation of ketones and imines in organic solvents is a powerful tool for asymmetric synthesis which was pioneered by Noyori,[5–7] Morris,[8] Bullock[9] and Bäckvall.[10] Several recent reports deal with asymmetric transfer hydrogenation of ketones with formate in aqueous media using active catalytic systems based on *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine and derivatives,[11–16] or on aromatic proline amides derivatives.[17] These catalytic systems show good activities and enantioselectivities, but the catalysts are formed *in situ* from precursors and have not been isolated.

Recently we reported the synthesis of arene ruthenium chloro complexes, $[(arene)Ru(\mathbf{L^1})Cl]$ ($\mathbf{L^1H}$ = (*R*,*R*)-*N*-(*p*-toluenesulfonyl)diaminocyclohexane), which catalyse the transfer hydrogenation of acetophenone in aqueous solution using formate as the hydrogen source, with a TOF of 43 h^{-1} and enantiomeric excess of 93%.[18] Moreover, the known 2-*S*-(*p*-toluenesulfonylamino)methylpyrrolidine ($\mathbf{L^2H}$) and 2-*S*-(2,4,6-triisopropyl-benzenesulfonylamino)methylpyrrolidine ($\mathbf{L^3H}$) ligands show, in combination with *p*-cymene ruthenium dichloro dimer, a slight activity and selectivity for the same reaction in isopropanol.[19]

Whereas the enantioselective transfer hydrogenation of C=O double bonds is well-known, the same reaction for the C=N double bonds is much less studied. There are several reports on the enantioselective transfer hydrogenation of imines, particularly of derivatives of 3,4-dihydroisoquinoline, using catalytic systems based on *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine and derivatives in combination with ruthenium or rhodium precursors in azeotropic formic acid–triethylamine to give the corresponding chiral amine, with TOFs between 20 and 30 h^{-1} and more than 95% for enantiomeric excess.[20–23] More recently, Wu *et al.* reported, for the same reaction, similar catalytic systems involving a surfactant in aqueous solution, with sodium formate as the hydrogen source, with enantiomeric excesses greater than 96%.[24]



Herein, we report the synthesis of water-soluble arene ruthenium complexes containing enantiopure chiral monosulfonated diamine ligands, including the new ligand *S*-2-(*S*-camphor-10-sulfonylamino)methylpyrrolidine, and their catalytic potential for the asymmetric transfer hydrogenation of aromatic ketones and imines in aqueous solution using sodium formate as the hydrogen source.

Results

Synthesis of cationic arene ruthenium complexes containing chiral sulfonated diamine ligands

The arene ruthenium chloro complexes $[(arene)Ru(\mathbf{L^1})Cl]$, containing a chiral bidentate ligand derived from $\mathbf{L^1H}$ = *N*-tosyl-*trans*-1,2-diaminocyclohexane, which have been

Institut de Chimie, Université de Neuchâtel, Case Postale 158, Neuchâtel, CH-2009, Switzerland. E-mail: georg.suess-fink@unine.ch; Fax: 0041 32 718 25 11; Tel: 0041 32 718 24 00

reported recently,[18] react in aqueous solution with silver sulfate to give, with precipitation of silver chloride, the corresponding cationic aqua complexes $[(arene)Ru(\mathbf{L^1})(OH_2)]^+$ (**1**: arene = C_6H_6, **2**: arene = *p*-$MeC_6H_4{}^iPr$, **3**: arene = C_6Me_6), which can be isolated from the filtered solution, upon addition of $NaBF_4$, as the tetrafluoroborate salts (eqn (1)).

$$[(arene)Ru(\mathbf{L^1})Cl] + Ag^+ + H_2O \rightarrow [(arene)Ru(\mathbf{L^1})(OH_2)]^+ + AgCl \quad (1)$$

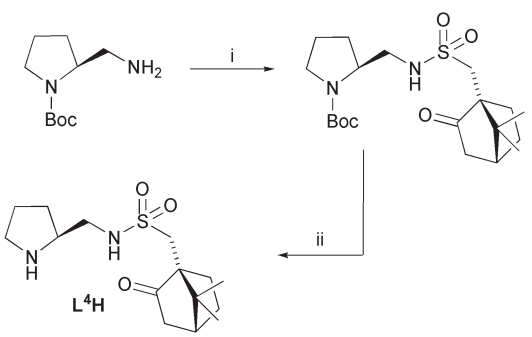
On the other hand, the $\mathbf{L^2}$ and $\mathbf{L^3}$ analogues $[(arene)Ru(\mathbf{L^2})(OH_2)]^+$ (**4**: arene = C_6H_6, **5**: arene = *p*-$MeC_6H_4{}^iPr$, **6**: arene = C_6Me_6) and $[(arene)Ru(\mathbf{L^3})(OH_2)]^+$ (**7**: arene = C_6Me_6) are accessible from the corresponding arene ruthenium triaqua complexes and $\mathbf{L^2H}$ and $\mathbf{L^3H}$, according to eqn (2). All cationic aqua complexes can be isolated from the filtered solution, upon addition of $NaBF_4$, as the stable tetrafluoroborate salts.

$$[(arene)Ru(OH_2)_3]^{2+} + LH \rightarrow [(arene)Ru(L)(OH_2)]^+ + H_3O^+ + H_2O \quad (2)$$

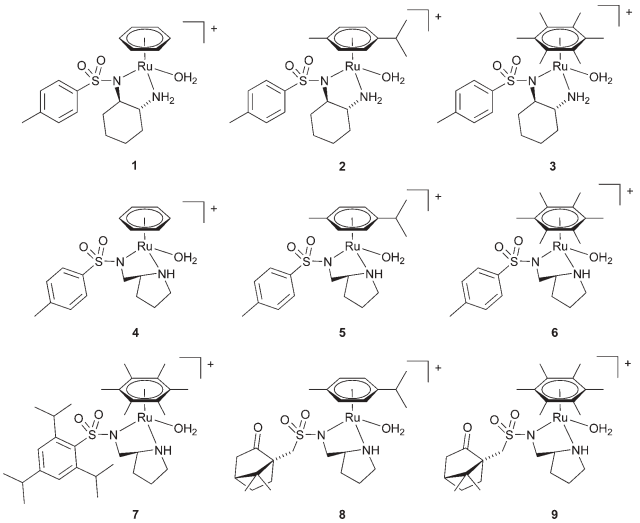
Moreover, we synthesised a new representative of the series of chiral (sulfonylamino)methylpyrrolidine ligands, which contains a second chiral centre in the sulfonyl moiety: Thus, 2-*S*-(*S*-camphor-10-sulfonylamino)methylpyrrolidine ($\mathbf{L^4H}$) was obtained by reacting the *N*-Boc protected *S*-2-aminomethylpyrrolidine (Boc = *t*-butyl carbonate) with *S*-Camphor-10-sulfonyl chloride, followed by deprotection with trifluoroacetic acid. (Scheme 1)

The new enantiopure $\mathbf{L^4H}$ reacts in the same way (eqn (2)) as $\mathbf{L^2H}$ or $\mathbf{L^3H}$ with arene ruthenium triaqua complexes $[(arene)Ru(OH_2)_3]^{2+}$ to give the cations $[(arene)Ru(\mathbf{L^4})(OH_2)]^+$ (**8**: arene = *p*-$MeC_6H_4{}^iPr$, **9**: arene = C_6Me_6), which precipitate from the aqueous solution as tetrafluoroborate salts upon saturation with $NaBF_4$.

All compounds $[(arene)Ru(L)(OH_2)][BF_4]$ (containing cations **1–9**), are air-stable, orange-yellow and water-soluble powders, which have been fully characterised by ^1H and ^{13}C NMR spectroscopy, mass spectroscopy and elemental analysis (see Experimental). The systematic variation of the substituents in both the arene and the sulfonated diamine ligands allows us to study in detail the steric and electronic influence on the catalytic activities and selectivities of these complexes for transfer hydrogenation reactions.



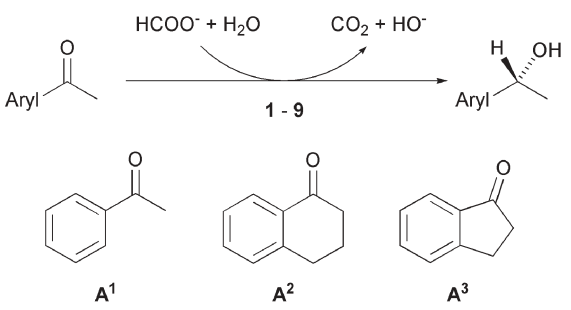
Scheme 1 (i) *S*-Camphor-10-sulfonyl chloride, Et_3N. (ii) CF_3COOH.



Enantioselective transfer hydrogenation of aryl ketones in water

The synthesis of chiral alcohols from the corresponding prochiral ketones by enantioselective transfer hydrogenation has a great potential, particularly if the reaction can be carried out in water using sodium formate as the hydrogen source.[11,14,18,25–27] Recently we found the chloro complexes $[(arene)Ru(\mathbf{L^1})Cl]$ were able to catalyse the transfer hydrogenation of acetophenone to give enantioselectively phenylethanol; in the case of arene = C_6Me_6, the aqua complex $[(arene)Ru(\mathbf{L^1})(OH_2)]^+$ (**3**) could be identified as a catalytically active species.[18] As expected, all aqua complexes **1–9** are active catalysts for the enantioselective transfer hydrogenation of various prochiral aryl ketones ($\mathbf{A^1}$ = acetophenone, $\mathbf{A^2}$ = α-tetralone, $\mathbf{A^3}$ = 1-indanone, see Scheme 2) to give the corresponding chiral aryl alcohols with enantioselectivities up to 94% (Table 1). All reactions are found to be quantitative (TON > 99) after 2 to 5 h.

As Table 1 reveals, the best results, as far as both catalytic activity and enantioselectivity are concerned, have been obtained with the aqua complex **3** as the catalyst, the turnover frequencies varying from 25 to 44 h^{-1} and the enantiomeric excess attaining 93 to 94% (entries 3, 12 and 20). For the hydrogenation of $\mathbf{A^1}$ (entries 1–9), the diaminocyclohexane complexes **1** to **3** show a more than two times better enantioselectivity than the 2-methylaminopyrrolidine complexes **4** to **9**, which contain less rigid ligands. This difference



Scheme 2 Enantioselective transfer hydrogenation of aryl ketones $\mathbf{A^1}$, $\mathbf{A^2}$ and $\mathbf{A^3}$ catalysed by aqua complexes **1–9** in water.

Table 1 Enantioselective transfer hydrogenation of aryl ketones $\mathbf{A^1}$, $\mathbf{A^2}$ and $\mathbf{A^3}$ by aqua complexes **1–9** in water[a]

Entry	Catalyst	Substrate	TOF/h^{-1} [b,c]	ee (%)[b]
1	**1**	$\mathbf{A^1}$	48	51
2	**2**	$\mathbf{A^1}$	45	83
3	**3**	$\mathbf{A^1}$	44	93
4	**4**	$\mathbf{A^1}$	34	25
5	**5**	$\mathbf{A^1}$	37	23
6	**6**	$\mathbf{A^1}$	43	39
7	**7**	$\mathbf{A^1}$	40	38
8	**8**	$\mathbf{A^1}$	39	44
9	**9**	$\mathbf{A^1}$	38	30
10	**1**	$\mathbf{A^2}$	15	91
11	**2**	$\mathbf{A^2}$	37	84
12	**3**	$\mathbf{A^2}$	25	94
13	**4**	$\mathbf{A^2}$	15	48
14	**5**	$\mathbf{A^2}$	24	23
15	**6**	$\mathbf{A^2}$	19	13
16	**7**	$\mathbf{A^2}$	25	11
17	**8**	$\mathbf{A^2}$	28	21
18	**9**	$\mathbf{A^2}$	25	14
19	**2**	$\mathbf{A^3}$	35	70
20	**3**	$\mathbf{A^3}$	35	93
21	**5**	$\mathbf{A^3}$	21	30
22	**6**	$\mathbf{A^3}$	28	13

[a] Conditions: H_2O (5 mL), A (1 mmol), ratio catalyst/substrate/formate = 1/100/500, 60 °C, pH = 9, 2 h. [b] Determined by chiral HPLC analysis. [c] Turnover frequencies determined after 30 minutes and expressed in mol of product/(mol of Ru × h).

increases with the backbone rigidity of the substrate, as found for $\mathbf{A^2}$ (entries 12 and 15) and $\mathbf{A^3}$ (entries 20 and 22). As far as catalytic activity is concerned, all aqua complexes **1–9** show comparable TOF values for one given substrate. However, the catalytic activities differ substantially with changing substrate: the more rigid substrates $\mathbf{A^2}$ and $\mathbf{A^3}$ are hydrogenated slower than the more flexible $\mathbf{A^1}$. The substitution pattern of the chiral ligand L or an additional chiral centre in **1–9** has no significant influence on the catalytic activity.

The pH dependence of both, catalytic activity and enantioselectivity of the transfer hydrogenation reaction has been studied in the case of substrate $\mathbf{A^1}$ and catalyst **6**. Fig. 1 shows the conversion and ee profiles in the pH range from 5 to 10. While enantioselectivity is almost independent of the pH, the highest activity was found for pH = 9.

Enantioselective transfer hydrogenation of aryl imines in water

The aqua complexes $[(arene)Ru(L)(OH_2)]^+$ (**1–9**) are also found to catalyse the enantioselective transfer hydrogenation of aryl imines in aqueous solution, using sodium formate as the hydrogen source. This catalytic reaction, so far much less studied than the transfer hydrogenation of ketones, works with **1–9** for the prochiral substrates phenyl-*N*-(1-phenylethylidene) methanamine ($\mathbf{A^4}$), 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline ($\mathbf{A^5}$) and 1-(5-chloro-2-nitrophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline ($\mathbf{A^6}$), see Scheme 3. This is particularly interesting in the case of $\mathbf{A^5}$, because the product *R*-salsolidine and its derivatives are valuable intermediates in the synthesis of alkaloid drugs showing antibacterial effects[28,29] or being active in neurodisease treatment.[30]

The results are compiled in Table 2. In all cases, the best results are obtained with the *p*-cymene and hexamethylbenzene

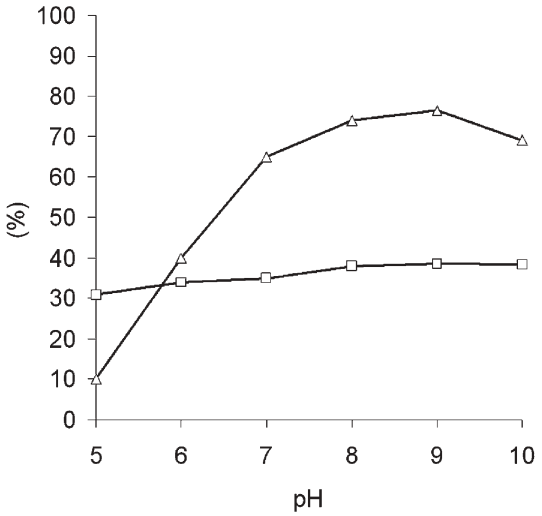


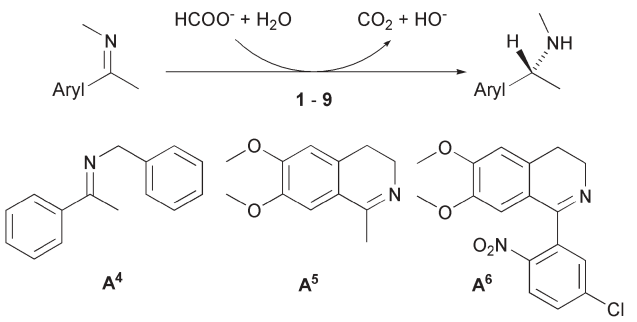
Fig. 1 pH-dependent profile of conversion (△) and enantiomeric excess (□) for the transfer hydrogenation of acetophenone $\mathbf{A^1}$ (1 mmol) using **6** as catalyst and HCOONa as hydrogen donor in water (5 mL), at 60 °C, for 2 h, the catalyst/substrate/formate ratio being 1/100/500.

complexes containing the chiral ligand $\mathbf{L^1}$ (**2** and **3**); while the differences in the catalytic activities are less pronounced, the enantioselectivities differ more markedly. All reactions are found to be quantitative (TON > 99) after 2 to 5 h.

The pH-dependence of catalytic activity and enantioselectivity, studied in the case of substrate $\mathbf{A^5}$ and catalyst **5**, in the pH range from 7 to 12 (Fig. 2), also shows an activity maximum at pH = 9, while the enantioselectivity is almost not influenced by the pH, in line with the findings for aryl ketones.

Discussion

In all catalytic reactions reported herein, the transfer hydrogenation of aryl ketones or of aryl imines in aqueous solution using sodium formate as hydrogen source, the catalytically active aqua complexes $[(arene)Ru(L)(OH_2)]^+$ can be recovered unchanged after the catalytic run as tetrafluoroborate salts. Based on the observation of an intermediary hydrido complex in the case of the transfer hydrogenation of acetophenone catalysed by the non-chiral ortho-phenanthroline (phen) complex $[(C_6Me_6)Ru(phen)(OH_2)]^{2+}$,[31] and the X-ray-crystallographic characterisation of the bipyridine (bipy) analogue



Scheme 3 Enantioselective transfer hydrogenation of aryl imines $\mathbf{A^4}$, $\mathbf{A^5}$ and $\mathbf{A^6}$ catalysed by aqua complexes **1–9** in water.

Table 2 Enantioselective transfer hydrogenation of aryl imines $\mathbf{A}^4$, $\mathbf{A}^5$ and $\mathbf{A}^6$ by aqua complexes **1–9** in water[a]

Entry	Catalyst	Substrate	TOF/h^{-1} [b,c]	ee (%)[b]
1	**1**	$\mathbf{A}^4$	54	48
2	**2**	$\mathbf{A}^4$	49	74
3	**3**	$\mathbf{A}^4$	51	91
4	**4**	$\mathbf{A}^4$	37	21
5	**5**	$\mathbf{A}^4$	40	48
6	**6**	$\mathbf{A}^4$	38	35
7	**7**	$\mathbf{A}^4$	32	29
8	**8**	$\mathbf{A}^4$	35	44
9	**9**	$\mathbf{A}^4$	29	32
10	**1**	$\mathbf{A}^5$	46	46
11	**2**	$\mathbf{A}^5$	50	88
12	**3**	$\mathbf{A}^5$	44	51
13	**4**	$\mathbf{A}^5$	46	21
14	**5**	$\mathbf{A}^5$	45	47
15	**6**	$\mathbf{A}^5$	45	44
16	**7**	$\mathbf{A}^5$	38	41
17	**8**	$\mathbf{A}^5$	41	45
18	**9**	$\mathbf{A}^5$	40	42
19	**2**	$\mathbf{A}^6$	24	61
20	**3**	$\mathbf{A}^6$	22	50
21	**5**	$\mathbf{A}^6$	18	25
22	**6**	$\mathbf{A}^6$	12	18

[a] Conditions: H_2O (5 mL), A (1 mmol), ratio catalyst/substrate/formate = 1/100/500, 60 °C, pH = 9, 2 h. [b] Determined by chiral HPLC analysis. [c] Turnover frequencies determined after 30 minutes and expressed in mol of product/(mol of Ru × h).

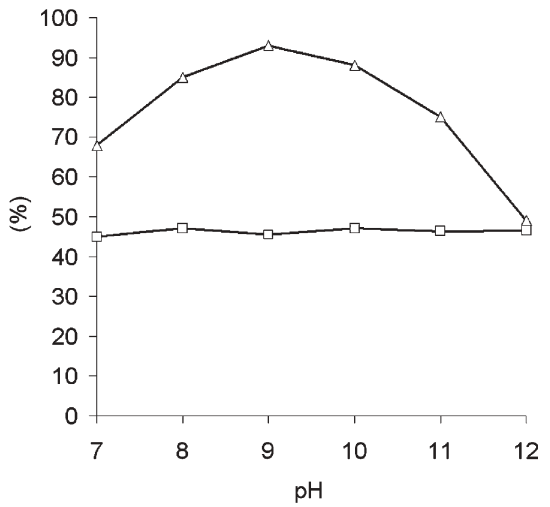
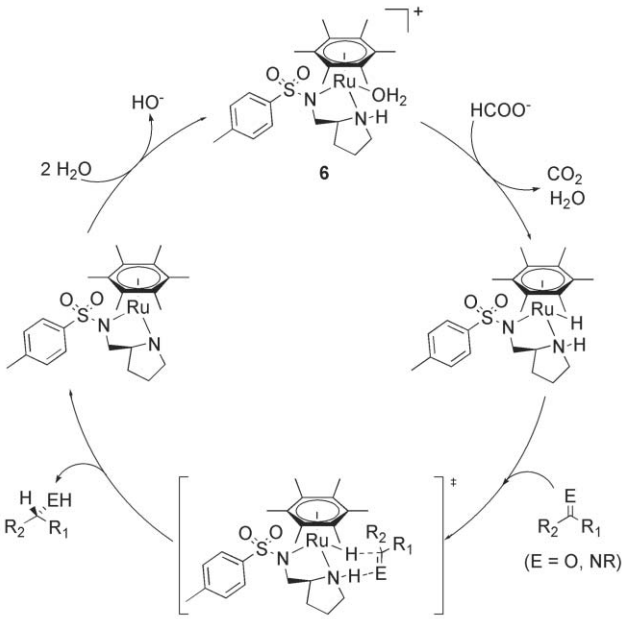


Fig. 2 pH-dependent profile of conversion (△) and enantiomeric excess (□) for the transfer hydrogenation of acetophenone $\mathbf{A}^5$ (1 mmol) using **5** as catalyst and HCOONa as hydrogen donor in water (5 mL), at 60 °C, for 2 h, the catalyst/substrate/formate ratio being 1/100/500.

$[(C_6Me_6)Ru(bipy)H][CF_3SO_3]$,[32] and based on the pioneering mechanistic work of Noyori, with [(arene)Ru(TsNCHPhCHPhNH$_2$)Cl],[6,7,33,34] Morris,[8] and Wills,[35] we propose the catalytic cycle outlined in Scheme 4 (for the example of complex **6**) as a mechanistic description of the catalytic action of the aqua complexes **1–9** in the transfer hydrogenation of aryl ketones and imines.

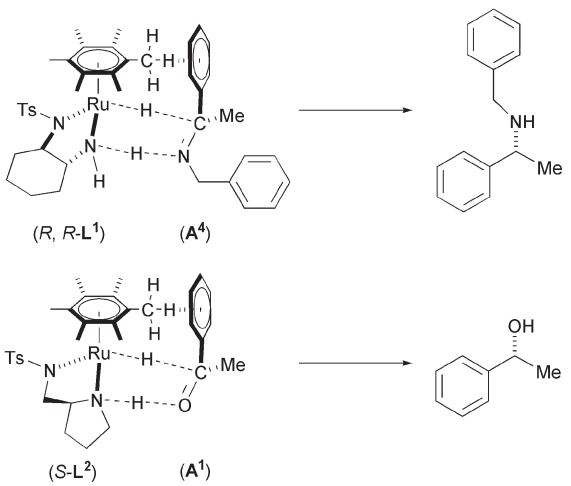
Interestingly, we observed that all prochiral aryl ketones and imines preferentially yield, with **1–9**, the *R* enantiomer of the corresponding chiral alcohols or amines, although the configuration of the chiral ligands is not the same: *R*,*R*-$\mathbf{L}^1$ in **1–3**, *S*-$\mathbf{L}^2$ in **4–6**, *S*-$\mathbf{L}^3$ in **7** and *S*,*S*-$\mathbf{L}^4$ in **8** and **9**. This can be rationalised in terms of CH/π interactions[36] between the hydrogen atoms of the arene ligand of the ruthenium complex and the aryl substituent of the substrate in the hydrogen bridged transition state (see Scheme 4, bottom). In all cases, the chiral ligand L (*R*, *R*-$\mathbf{L}^1$, *S*-$\mathbf{L}^2$, *S*-$\mathbf{L}^3$, *S*, *S*-$\mathbf{L}^4$) orients the *Si* face of the prochiral carbon atom of the substrate towards the ruthenium centre (Scheme 5).



Scheme 4 Postulated catalytic cycle for the enantioselective transfer hydrogenation of imines using [**6**]BF_4 as catalyst and sodium formate as hydrogen source in aqueous solution.

Conclusion

In conclusion, we report herein the synthesis of nine water-soluble chiral arene ruthenium aqua complexes containing



Scheme 5 CH/π interaction postulated between the arene ligand of the ruthenium complexes and the aryl substituent of the prochiral substrate, exemplified for two different cases.

R,*R*-*N*-(*p*-toluenesulfonyl)diaminocyclohexane or *S*-2-(sulfonyl-amino)methylpyrrolidine derivatives as chelating ligands. All these complexes are found to effectively catalyse the transfer hydrogenation of α-aryl ketones and α-aryl imines in aqueous solution using formate as the hydrogen source, without any additional surfactant. These catalytic reactions involve CH/π interactions between the arene ligand of the catalyst and the aryl substituent of the substrate, previously reported by Noyori.[36] Moreover, the transfer hydrogenation of 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline (**A**[5]) to *R*-salsolidine with a TOF of 50 h^{-1} and ee of 88% using water-soluble complexes give an environmentally friendly access to isoquinoline alkaloids by asymmetric catalysis in aqueous solution.

Experimental

General remarks

All manipulations were carried out in an inert atmosphere using standard Schlenk techniques and freshly distilled solvents saturated with nitrogen prior to use. The starting dimers $[(arene)RuCl_2]_2$[37] and the *N*-Boc-*S*-2-aminomethylpyrrolidine, the *S*-2-[*N*-(4-toluenesulfonyl)aminomethyl]pyrrolidine (**L**[2]**H**) and the *S*-2-[(*N*-(2,4,6-triisopropylbenzensulfonyl)amino-methyl]pyrrolidine (**L**[3]**H**) were prepared according to the published methods.[19] The arene ruthenium chloro complexes, [(arene)Ru(**L**[1])Cl], were synthesised as previously reported.[18] All other reagents were commercially available and were used without further purification. NMR spectra were recorded on a Bruker 400 MHz spectrometer. Electro-spray mass spectra were obtained in positive- or negative-ion mode with an LCQ Finnigan mass spectrometer. Microanalyses were carried out by the Laboratoire de Chimie Pharmaceutique, Université de Genève (Switzerland).

Synthesis of L[4]H

***S*-*tert*-butyl-2-(*S*-camphor-10-sulfonylamino)methylpyrrolidine-1-carboxylate.** To a solution of *S*-*tert*-butyl-2-amino-methylpyrrolidine-1-carboxylate (350 mg, 1.84 mmol) in pyridine (20 mL) was added 1.5 equivalents of the *S*-camphor-10-sulfonyl chloride (693 mg, 2.8 mmol) at 0 °C. After 6 hours, Et_2O (100 mL) was added and the organic layer was washed with HCl 10% (2 × 30 mL), saturated $NaHCO_3$ (2 × 30 mL) and saturated NaCl (30 mL). The resulting yellowish oil was purified on a silica gel column (pentane–ethylacetate = 3 : 1) to obtain the pure product as colourless oil. (Yield: 65%, 485 mg). ^{1}H NMR δ (400 MHz, $CDCl_3$, 21 °C): 0.85 (s, 3H), 1.02 (s, 3H), 1.21 (b, 1H), 1.43 (s, 9H), 1.82–2.13 (b, 9H), 2.84–2.91 (d, J = 15 Hz, 1H), 3.27–3.34 (b, 4H), 3.92 (b, 1H) ppm. ^{13}C NMR δ (200 MHz, $CDCl_3$, 21 °C): 19.39 (CH_3), 19.93 (CH_3), 25.52 (CH_2), 26.94 (CH_2), 27.00 (CH_2), 27.55 ((CH_3)$_3$), 28.81 (CH_2), 31.58 (CH), 42.75 (C*(CH$_3$)$_2$*), 42.92 (CH_2*CO*), 46.15 (CH_2), 46.72 (CH_2), 49.80 (CH_2*SO$_2$*), 58.06 (CH), 59.29 (C*CH$_2$*), 79.88 (C*(CH$_3$)$_3$*), 170.65 (CO*O^{t}Bu*), 217.05 (CO) ppm. *m*/*z* (ESI, negative ion) 413.6 [$C_{20}H_{33}N_2O_5S^-$]. (Found: C, 57.88; H, 8.24; N,6.71. $C_{20}H_{34}N_2O_5S$ requires C, 57.94; H, 8.27; N, 6.76).

***S*-2-(*S*-camphor-10-sulfonylamino)methylpyrrolidine (L[4]H).** To a solution of *S*-*tert*-butyl-2-(*S*-camphor-10-sulfonylamino) methyl-pyrrolidine-1-carboxylate (284 mg, 0.7 mmol) in dry CH_2Cl_2 were added 10 equivalents of trifluoroacetic acid (0.6 mL) at room temperature to give a dark yellowish solution. After 8 hours, the organic layer was washed with saturated $NaHCO_3$ (2 × 50 mL) and saturated NaCl (2 × 30 mL). After evaporation, the residue was purified on silica gel column (pentane–ethylacetate = 3 : 1) to give the desired product **L**[4]**H** as colourless oil. (Yield: 60%, 130 mg). ^{1}H NMR δ (400 MHz, $CDCl_3$, 21 °C) = 0.91 (s, 3H), 1.05 (s, 3H), 1.25 (b, 1H), 1.72–2.07 (b, 9H), 2.78–2.86 (d, J = 16 Hz, 1H), 3.29–3.32 (b, 4H), 3.91 (b, 1H) ppm. ^{13}C NMR δ (200 MHz, $CDCl_3$, 21 °C) = 19.37 (CH_3), 19.93 (CH_3), 25.51 (CH_2), 26.94 (CH_2), 27.04 (CH_2), 28.81 (CH_2), 31.58 (CH), 42.75 (C*(CH$_3$)$_2$*), 42.88 (CH_2*CO*), 46.17 (CH_2), 46.70 (CH_2), 49.84 (CH_2*SO$_2$*), 58.01 (CH), 59.32 (C*CH$_2$*), 217.12 (CO) ppm. *m*/*z* (ESI, negative ion) 313.2 [$C_{15}H_{25}N_2O_3S^-$]. (Found: C, 57.38; H, 8.38; N, 9.08. $C_{15}H_{26}N_2O_3S$ requires C, 57.30; H, 8.33; N, 8.91).

Preparation of arene ruthenium aqua complexes 1–9

Method A for complexes 1 to 3. To a suspension of the appropriate chloro complex [(arene)Ru(**L**[1])Cl][18] (0.3 mmol) in deionised water was added 2 equivalents of silver sulfate (0.6 mmol, 187 mg). After stirring at room temperature in the dark for 2 hours, the resulting orange solution was filtered over celite. Then solid $NaBF_4$ was added until saturation of the solution, visible by the appearance of a yellow precipitate. Then the suspension was centrifuged, the solid was dissolved in 10 ml of dry acetonitrile and filtered over celite to eliminate the excess of $NaBF_4$. After evaporation of the solvent, the tetrafluoroborate salt was obtained as an orange-yellow powder in good yields.

[(C_6H_6)Ru(L[1])(OH_2)](BF_4) ([1]BF_4). (Yield: 70%, 116 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 0.94(m, CH_2), 1.23 (m, 2 CH_2), 1.44 (m, CH), 1.58 (m, CH_2), 1.86 (m, CH), 2.32 (s, *p*-(CH_3)$C_6H_4SO_2$), 5.81 (s, C_6H_6), 7.15 (d, J = 7.1 Hz, *p*-(CH_3)$C_6H_4SO_2$), 7.72 (d, J = 7.0 Hz, *p*-(CH_3)$C_6H_4SO_2$) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 21.9 (*p*-(*C*H$_3$)$C_6H_4SO_2$), 23.8 (CH_2), 25.2 (CH_2), 32.2 (CH_2), 32.7 (CH_2), 59.1 (CH), 60.5 (CH), 83.8 (C_6H_6), 127.8 (2 CH), 128.4 (2 CH), 138.1 (*p*-(CH_3)*C*$_6H_4SO_2$), 143.5 (*p*-(CH_3)*C*$_6H_4SO_2$) ppm. *m*/*z* (ESI, positive ion) 465.1 [$C_{19}H_{27}N_2O_3RuS^+$]. (Found: C, 41.43; H, 5.08; N, 4.98. $C_{19}H_{27}BF_4N_2O_3RuS$ requires C, 41.39; H, 4.94; N, 5.08).

[(*p*-MeC_6H_4*^{i}*Pr)Ru(L[1])(OH_2)](BF_4) ([2]BF_4). (Yield: 73%, 133 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.11 (m, CH_2), 1.22 (m, 2 CH_2), 1.30 (d, J = 7.2 Hz, (C*H*$_3$)$_2$CH), 1.55 (m, CH), 1.74 (m, CH_2), 2.08 (m, CH), 2.34 (s, *p*-(C*H*$_3$)$C_6H_4SO_2$), 2.92 (m, J = 7 Hz, (CH_3)$_2$C*H*), 5.62 (d, J = 6.2Hz, C_6H_4), 5.78 (d, J = 6.3Hz, C_6H_4), 7.21 (d, J = 8 Hz, *p*-(CH_3)$C_6H_4SO_2$), 7.75 (d, J = 8 Hz, *p*-(CH_3)$C_6H_4SO_2$) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 18.1 (CH_3), 21.6 (CH(*C*H$_3$)$_2$), 22.1 (*p*-(*C*H$_3$)$C_6H_4SO_2$), 24.2 (CH_2), 24.5 (CH_2), 31.8 (*C*H(CH$_3$)$_2$), 33.4 (CH_2), 34.1 (CH_2), 57.8 (CH), 60.5 (CH), 87.2 (C_6H_4), 104.5 (C_6H_4), 108.3 (C_6H_4), 126.5

(*p*-(CH_3)$C_6H_4SO_2$), 129.4 (*p*-(CH_3)$C_6H_4SO_2$), 138.8 (*p*-(CH_3)$C_6H_4SO_2$), 143.5 (*p*-(CH_3)$C_6H_4SO_2$) ppm. *m/z* (ESI, positive ion) 521.1 [$C_{23}H_{35}N_2O_3RuS^+$]. (Found: C, 45.51; H, 5.98; N, 4.58. $C_{23}H_{35}BF_4N_2O_3RuS$ requires C, 45.47; H, 5.81; N, 4.61).

[(C_6Me_6)Ru(L^1)(OH_2)][BF_4] ([3][BF_4]). (Yield: 97%, 185 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.12 (m, 2 CH_2), 1.28 (m, CH_2), 1.31 (m, CH), 1.45 (m, CH_2), 1.82 (m, CH), 2.24 (s, $C_6(CH_3)_6$), 2.51 (s, CH_3), 7.34 (d, J = 7.3 Hz, C_6H_4), 7.84 (d, J = 7.6 Hz, C_6H_4). ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 16.8 ($C_6(CH_3)_6$), 21.7 (*p*-(CH_3)$C_6H_4SO_2$), 24.3 (CH_2), 34.1 (CH_2), 34.8 (CH_2), 57.5 (CH), 59.3 (CH), 91.7 (C_6Me_6), 127.4 (*p*-(CH_3)$C_6H_4SO_2$), 127.8 (*p*-(CH_3)$C_6H_4SO_2$), 138.1 (*p*-(CH_3)$C_6H_4SO_2$), 142.8 (*p*-(CH_3)$C_6H_4SO_2$). *m/z* (ESI, positive ion) 549.2 [$C_{25}H_{39}N_2O_3RuS^+$]. (Found: C, 47.41; H, 6.31; N, 4.32. $C_{25}H_{39}BF_4N_2O_3RuS$ requires C, 47.25; H, 6.19; N, 4.41).

Method B for complexes 4 to 9. To a suspension of the appropriate dimer [(arene)$RuCl_2$]$_2$ (0.15 mmol) in deionised water was added 2 equivalents of silver sulfate (0.6 mmol, 187 mg). After stirring at room temperature in the dark for 2 hours, the resulting yellow solution was filtered and then added to 0.4 mmol of **L^2H**, **L^3H** or **L^4H** under inert atmosphere. Then the solution was allowed to react at room temperature for 2 hours, during this time the solution darkened. Then solid $NaBF_4$ was added until saturation of the solution, which led to a yellow precipitate. Then the suspension was centrifuged, the solid was dissolved in 10 ml of dry acetonitrile, and filtered on celite to eliminate the excess of $NaBF_4$. After evaporation of the solvent, the tetrafluoroborate salt was obtained as an orange-yellow powder.

[(C_6H_6)Ru(L^2)(OH_2)][BF_4] ([4][BF_4]). (Yield: 60%, 97 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.32–1.45 (m, 1H), 1.51–1.62 (m, 2H), 2.27 (s, 3H), 2.62 (m, 2H), 2.88–2.91 (m, 1H), 3.14–3.21 (m, 1H), 5.62 (s, 6H), 7.21 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 21.32 (CH_3), 25.42 (CH_2), 28.56 (CH_2), 46.11 (CH_2), 46.56 (CH_2), 58.21 (CH), 83.36 (C_6H_6), 127.18 ($CH_{arom.}$), 129.78 ($CH_{arom.}$), 137.06 ($C_{arom.}$), 143.21 ($C_{arom.}$) ppm. *m/z* (ESI, positive ion) 451 [$C_{18}H_{25}N_2O_3RuS^+$]. (Found: C, 40.31; H, 4.73; N, 5.26. $C_{18}H_{25}BF_4N_2O_3RuS$ requires C, 40.23; H, 4.69; N, 5.21).

[(*p*-$MeC_6H_4{}^iPr$)Ru(L^2)(OH_2)][BF_4] ([5][BF_4]). (Yield: 58%, 107 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.12 (d, J = 6.8 Hz, 6H), 1.29–1.37 (m, 1H), 1.54–1.61 (m, 2H), 1.97 (s, 3H), 2.32 (s, 3H), 2.52 (m, 2H), 2.63 (m, 1H), 2.92–2.99 (m, 1H), 3.15–3.23 (m, 1H), 5.61(d, J = 6.2 Hz, 2H), 5.78 (d, J = 6.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 19.04 (CH_3), 21.32 (CH_3), 22.44 ((CH_3)$_2$), 25.42 (CH_2), 27.38 (CH), 28.56 (CH_2), 46.11 (CH_2), 46.56 (CH_2), 58.21 (CH), 86.31 ($CH_{arom.}$), 88.28 ($CH_{arom.}$), 106.13 ($C_{arom.}$), 107.08 ($C_{arom.}$), 127.05 ($CH_{arom.}$), 129.85 ($CH_{arom.}$), 137.12 ($C_{arom.}$), 143.18 ($C_{arom.}$) ppm. *m/z* (ESI, positive ion) 507.1 [$C_{22}H_{33}N_2O_3RuS^+$]. (Found: C, 44.45; H, 5.71; N, 4.57. $C_{22}H_{33}BF_4N_2O_3RuS$ requires C, 44.53; H, 5.60; N, 4.72).

[(C_6Me_6)Ru(L^2)(OH_2)][BF_4] ([6][BF_4]). (Yield: 61%, 112 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.33–1.42 (m, 1H), 1.57–1.64 (m, 2H), 1.98 (s, 18H), 2.28 (s, 3H), 2.57 (dd, J = 5.1 Hz, J = 5.8 Hz, 2H), 2.91–2.96 (m, 1H), 3.17–3.28 (m, 1H), 7.26 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.2 Hz, 2H) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 15.18 ($C_6(CH_3)_6$), 21.32 (CH_3), 25.42 (CH_2), 28.56 (CH_2), 46.11 (CH_2), 46.56 (CH_2), 58.21 (CH), 92.05 ($C_6(CH_3)_6$), 127.18 ($CH_{arom.}$), 129.78 ($CH_{arom.}$), 137.06 ($C_{arom.}$), 143.21 ($C_{arom.}$) ppm. *m/z* (ESI, positive ion) 535.2 [$C_{24}H_{37}N_2O_3RuS^+$]. (Found: C, 46.41; H, 6.08; N, 4.48. $C_{24}H_{37}BF_4N_2O_3RuS$ requires C, 46.38; H, 6.00; N, 4.51).

[(C_6Me_6)Ru(L^3)(OH_2)][BF_4] ([7][BF_4]). (Yield: 59%, 132 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.18 (s, 6H), 1.20 (s, 3H), 1.23 (s, 9H), 1.25 (m, 1H), 1.44 (m, 2H), 1.87 (s, 18H), 2.48 (m, 2H), 2.82 (m, 2H), 2.89 (m, 1H), 3.16–3.21 (m, 1H), 3.31 (m, 1H), 7.10 (s, 2H) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 15.03 ($C_6(CH_3)_6$), 23.31 (CH_3), 25.42 (CH_2), 25.78 (CH_3), 28.56 (CH_2), 29.56 (CH), 34.15 (CH), 46.11 (CH_2), 46.56 (CH_2), 58.21 (CH), 92.12 ($C_6(CH_3)_6$), 123.56 ($CH_{arom.}$), 134.25 ($CH_{arom.}$), 150.15 ($C_{arom.}$), 152.32 ($C_{arom.}$) ppm. *m/z* (ESI, positive ion) 647.3 [$C_{32}H_{53}N_2O_3RuS^+$]. (Found: C, 52.21; H, 7.39; N, 3.78. $C_{32}H_{53}BF_4N_2O_3RuS$ requires C, 52.38; H, 7.28; N, 3.82).

[(*p*-$MeC_6H_4{}^iPr$)Ru(L^4)(OH_2)][BF_4] ([8][BF_4]). (Yield: 60%, 118 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.02 (s, 3H), 1.11 (s, 3H), 1.12 (d, J = 6.8 Hz, 6H), 1.21 (b, 1H), 1.67–1.99 (b, 9H), 1.97 (s, 3H), 2.63 (m, 1H), 2.71–2.79 (b, 1H), 3.26–3.30 (b, 4H), 3.84 (b, 1H), 5.61(d, J = 6.2 Hz, 2H), 5.78 (d, J = 6.2 Hz, 2H) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 19.04 (CH_3), 19.28 (CH_3), 19.89 (CH_3), 22.44 ((CH_3)$_2$), 25.48 (CH_2), 27.01 (CH_2), 27.10 (CH_2), 27.38 (CH), 28.79 (CH_2), 31.62 (CH), 42.71 ($C(CH_3)_2$), 42.85 (CH_2CO), 46.12 (CH_2), 46.53 (CH_2), 49.88 (CH_2SO_2), 57.96 (CH), 59.27 (CCH_2), 86.31 ($CH_{arom.}$), 88.28 ($CH_{arom.}$), 106.13 ($C_{arom.}$), 107.08 ($C_{arom.}$), 217.03 (CO) ppm. *m/z* (ESI, positive ion): = 567.2 [$C_{25}H_{41}N_2O_4RuS^+$]. (Found: C, 45.81; H, 6.40; N, 4.32. $C_{25}H_{41}BF_4N_2O_4RuS$ requires C, 45.94; H, 6.32; N, 4.29).

[(C_6Me_6)Ru(L^4)(OH_2)][BF_4] ([9][BF_4]). (Yield: 62%, 122 mg). ^{1}H NMR δ (400 MHz, D_2O, 21 °C) = 1.02 (s, 3H), 1.11 (s, 3H), 1.21 (b, 1H), 1.67–1.99 (b, 9H), 2.01 (s, 18H), 2.71–2.79 (b, 1H), 3.26–3.30 (b, 4H), 3.84 (b, 1H) ppm. ^{13}C NMR δ (200 MHz, D_2O, 21 °C) = 15.15 ($C_6(CH_3)_6$), 19.28 (CH_3), 19.89 (CH_3), 25.48 (CH_2), 27.01 (CH_2), 27.10 (CH_2), 28.79 (CH_2), 31.62 (CH), 42.71 ($C(CH_3)_2$), 42.85 (CH_2CO), 46.12 (CH_2), 46.53 (CH_2), 49.88 (CH_2SO_2), 57.96 (CH), 59.27 (CCH_2), 92.11 ($C_6(CH_3)_6$), 217.03 (CO) ppm. *m/z* (ESI, positive ion) 595.2 [$C_{27}H_{45}N_2O_4RuS^+$]. (Found: C, 47.46; H, 6.54; N, 4.13. $C_{27}H_{45}BF_4N_2O_4RuS$ requires C, 47.58; H, 6.65; N, 4.11).

Transfer hydrogenation catalysis

The transfer hydrogenation reactions of aryl ketones **A^1** to **A^3** and aryl imines **A^4** to **A^6** (1 mmol), using **1** to **9** as tetrafluoroborate salts (10 μmol) as catalyst and HCOONa (5 mmol) as hydrogen source, were carried out in water (5 mL) under inert atmosphere. In a typical experiment, the solution

was heated for 2 hours at 60 °C, then the reaction was quenched by cooling to 0 °C. The organic products were extracted by Et_2O and identified after filtration through silica gel by HPLC on Chiracel OB-H capillary column for aryl ketones $\mathbf{A^1}$ to $\mathbf{A^3}$ (hexane–isopropanol = 92 : 8, 0.7 mL min^{-1}, 215 nm) and on Chiracel OD-H capillary column for aryl imines $\mathbf{A^4}$ to $\mathbf{A^6}$ (hexane–isopropanol–diethylamine = 90 : 10 : 0.1, 1 mL min^{-1}, 230 nm). Conversion and enantioselectivity were determined by integration of the signals. The pH was monitored using a pH meter (Mettler Toledo InLab® 413) and adjusted using HNO_3 (for pH = 4 to 9) or NaOH (for pH = 10).

Acknowledgements

Financial support of this work by the Swiss National Science Foundation and a generous loan of ruthenium(III) chloride hydrate from the Johnson Matthey Research Centre are gratefully acknowledged.

References

1 U. Koelle, *Coord. Chem. Rev.*, 1994, **135**, 623–650.
2 M. Barton and J. D. Atwood, *J. Coord. Chem.*, 1991, **24**, 43–67.
3 A. G. Samuelson, *Curr. Sci.*, 1992, **63**, 547–550.
4 W. A. Herrmann and C. W. Kohlpaintner, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1524–1544.
5 R. Noyori, *Angew. Chem., Int. Ed.*, 2002, **41**, 2008–2022.
6 T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. Sandoval and R. Noyori, *J. Am. Chem. Soc.*, 2006, **128**, 8724–8725.
7 T. Ikariya, K. Murata and R. Noyori, *Org. Biomol. Chem.*, 2006, **4**, 393–406.
8 V. Rautenstrauch, X. Hoang-Cong, R. Churlaud, K. Abdur-Rashid and R. H. Morris, *Chem.–Eur. J.*, 2003, **9**, 4954–4967.
9 R. M. Bullock, *Chem.–Eur. J.*, 2004, **10**, 2366–2374.
10 J. S. M. Samec, J. E. Backvall, P. G. Andersson and P. Brandt, *Chem. Soc. Rev.*, 2006, **35**, 237–248.
11 P. N. Liu, J. G. Deng, Y. Q. Tu and S. H. Wang, *Chem. Commun.*, 2004, 2070–2071.
12 Y. P. Ma, H. Liu, L. Chen, X. Cui, J. Zhu and J. E. Deng, *Org. Lett.*, 2003, **5**, 2103–2106.
13 F. Wang, H. Liu, L. F. Cun, J. Zhu, J. G. Deng and Y. Z. Jiang, *J. Org. Chem.*, 2005, **70**, 9424–9429.
14 X. F. Wu, X. G. Li, F. King and J. L. Xiao, *Angew. Chem., Int. Ed.*, 2005, **44**, 3407–3411.
15 J. Xiao, X. Wu, A. Zanotti-Gerosa and F. Hancock, *Chim. Oggi*, 2005, **23**, 50–55.
16 X. F. Wu, X. G. Li, W. Hems, F. King and J. L. Xiao, *Org. Biomol. Chem.*, 2004, **2**, 1818–1821.
17 H. Y. Rhyoo, H. J. Park and Y. K. Chung, *Chem. Commun.*, 2001, 2064–2065.
18 J. Canivet, G. Labat, H. Stoeckli-Evans and G. Suss-Fink, *Eur. J. Inorg. Chem.*, 2005, 4493–4500.
19 N. Dahlin, A. Bogevig and H. Adolfsson, *Adv. Synth. Catal.*, 2004, **346**, 1101–1105.
20 J. M. Mao and D. C. Baker, *Org. Lett.*, 1999, **1**, 841–843.
21 N. Uematsu, A. Fujii, S. Hashiguchi, T. Ikariya and R. Noyori, *J. Am. Chem. Soc.*, 1996, **118**, 4916–4917.
22 E. Vedejs, *J. Org. Chem.*, 2004, **69**, 5159–5167.
23 D. G. Blackmond, M. Ropic and M. Stefinovic, *Org. Process Res. Dev.*, 2006, **10**, 457–463.
24 J. S. Wu, F. Wang, Y. P. Ma, X. C. Cui, L. F. Cun, J. Zhu, J. G. Deng and B. L. Yu, *Chem. Commun.*, 2006, 1766–1768.
25 X. F. Wu, D. Vinci, T. Ikariya and J. L. Xiao, *Chem. Commun.*, 2005, 4447–4449.
26 X. G. Li, X. F. Wu, W. P. Chen, F. E. Hancock, F. King and J. L. Xiao, *Org. Lett.*, 2004, **6**, 3321–3324.
27 H. Y. Rhyoo, H. J. Park, W. H. Suh and Y. K. Chung, *Tetrahedron Lett.*, 2002, **43**, 269–272.
28 V. A. Zagorevsky, E. A. Bendikov, R. S. Mirzoyan, D. A. Zykov, V. V. Shavyrina, T. S. Ganshina and Z. D. Kirsanova, *Khim.-Farm. Zh.*, 1982, **16**, 815–817.
29 P. C. Wyss, P. Gerber, P. G. Hartman, C. Hubschwerlen, H. Locher, H. P. Marty and M. Stahl, *J. Med. Chem.*, 2003, **46**, 2304–2312.
30 M. Gao, D. Y. Kong, A. Clearfield and Q. H. Zheng, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 2229–2233.
31 J. Canivet, L. Karmazin-Brelot and G. Suss-Fink, *J. Organomet. Chem.*, 2005, **690**, 3202–3211.
32 S. Ogo, K. Uehara, T. Abura, Y. Watanabe and S. Fukuzumi, *Organometallics*, 2004, **23**, 3047–3052.
33 R. Noyori, M. Yamakawa and S. Hashiguchi, *J. Org. Chem.*, 2001, **66**, 7931–7944.
34 C. A. Sandoval, T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata and R. Noyori, *Chem. Asian J.*, 2006, **1-2**, 102–110.
35 P. Peach, D. J. Cross, J. A. Kenny, I. Mann, I. Houson, L. Campbell, T. Walsgrove and M. Wills, *Tetrahedron*, 2006, **62**, 1864–1876.
36 M. Yamakawa, I. Yamada and R. Noyori, *Angew. Chem., Int. Ed.*, 2001, **40**, 2818–2821.
37 M. A. Bennett, T. N. Huang, T. W. Matheson and A. K. Smith, *Inorg. Synth.*, 1982, **21**, 74–78.