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Asymmetric transfer hydrogenation of acetophenone derivatives using 2-benzyl-tethered ruthenium (II)/TsDPEN complexes bearing η^6-(*p*-OR) (R = H, ^{i}Pr, Bn, Ph) ligands

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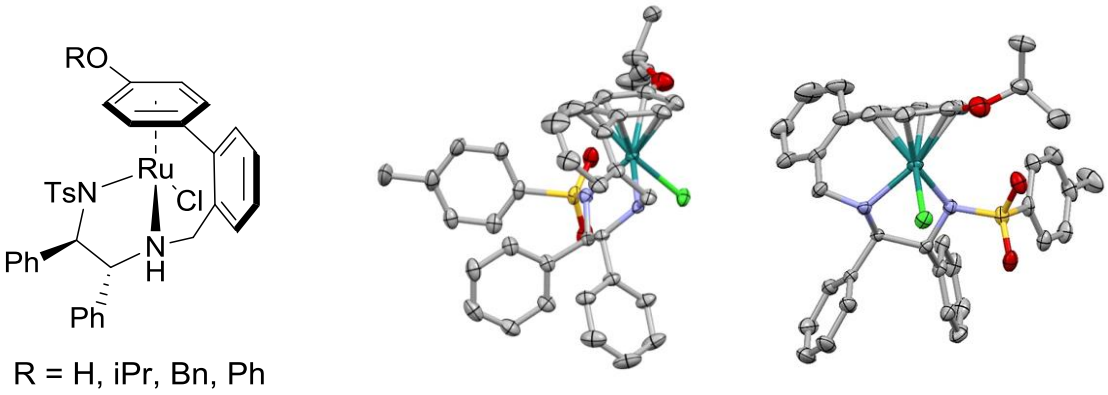
TOC graphic



Abstract

A series of 4'-OR (R = H, iPr, Bn, Ph) substituted ruthenium (II) biphenyl TsDPEN complexes are described; the complexes are accessed *via* an operationally simple and reliable two-step ligand synthesis followed by ligation to the ruthenium (II) centre. We report the preliminary asymmetric transfer hydrogenation (ATH) results on a range of primarily acetophenone derivatives with these new complexes using FA/TEA (5:2) as a reducing agent; the results confirm that these catalysts are capable of reducing the substrates within 48 hours with excellent enantioselectivities.

Keywords: asymmetric transfer hydrogenation; enantioselective ketone reduction; benzyl tethered; ruthenium catalyst; arene-exchange.

Highlights:

- A series of 'OR (R=H, iPr, Bn, Ph) 2-benzyl-tethered Ru(II) catalysts have been prepared through an 'arene-exchange' route.
- The new catalysts are effective in the asymmetric transfer hydrogenation of ketones to form enantiomerically-enriched alcohols in high ee.
- The new catalysts are prepared via an operationally simple procedure.

1 Introduction

The use of asymmetric transfer hydrogenation (ATH) to synthesise enantiopure and enantioenriched compounds is a long-standing and diverse area of chemistry.[1] The area was pioneered by Noyori and co-workers who first synthesised ruthenium-arene TsDPEN complexes for ATH of ketones to the corresponding asymmetric alcohols.[2] Further iterations of complexes of this type, first by ourselves[3] and later by others,[4] have employed a saturated covalent tether between the arene and diamine moieties, imparting increased selectivity and stability compared to their first generation untethered analogues.[5] The enantioselectivity of reduction using these catalysts in the reduction of aryl-substituted substrates relies on favourable CH-π interactions between the catalyst and the substrate (Fig. 1) combined with destabilisation of the transition state leading to the minor product by a repulsive SO_2—arene interaction (not illustrated).[6]

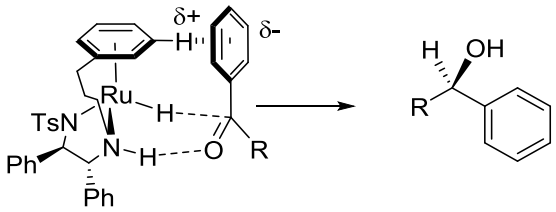


Fig. 1: Asymmetric reduction of aryl-ketones by a tethered Ru(arene)(TsDPEN) catalyst.[6]

A drawback of these saturated-tether complexes with respect to their simpler congeners is their more complex ligand synthesis, which typically requires the use of a Birch reduction to create an hexadiene intermediate for the complexation step with ruthenium trichloride.[2,3,4] This has partially been ameliorated with the introduction of an alternative approach in which an arene ring in the catalyst precursor ligand directly substitutes another arene in an existing η^6-arene complex.[7] This approach has recently been demonstrated to significantly simplify the synthesis of 2-benzyl-tethered complexes which are unsubstituted at the η^6-arene ring and which contain a p-OMe substituent on this ring,[7b] by reducing the synthetic complexity of the ligand and allowing more benign reaction conditions to be used compared to the original 1,4-hexadiene route.[8] In one example that we have reported, it was noted that a 4'-OMe substituted 2-benzyl-tethered catalyst exhibited excellent selectivity in ATH reactions,[7b] which we hypothesise to be the result of increased catalyst-substrate interactions which drive enhanced selectivity. In this report we expand on this work and describe an extended series of 2-benzyl-tethered 4'-OR (R = H, iPr, Bn, Ph) catalysts **1-4** (Fig.

2), with the aim of varying the steric bulk and electronic properties and to thus augment the existing CH-π interactions in simpler, unsubstituted Ru(II) catalysts.

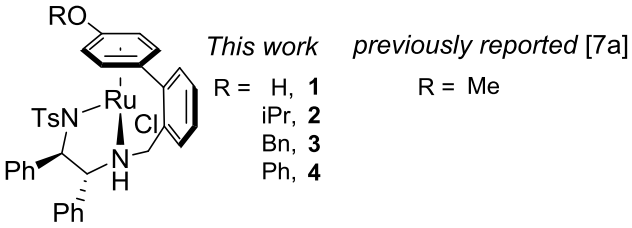
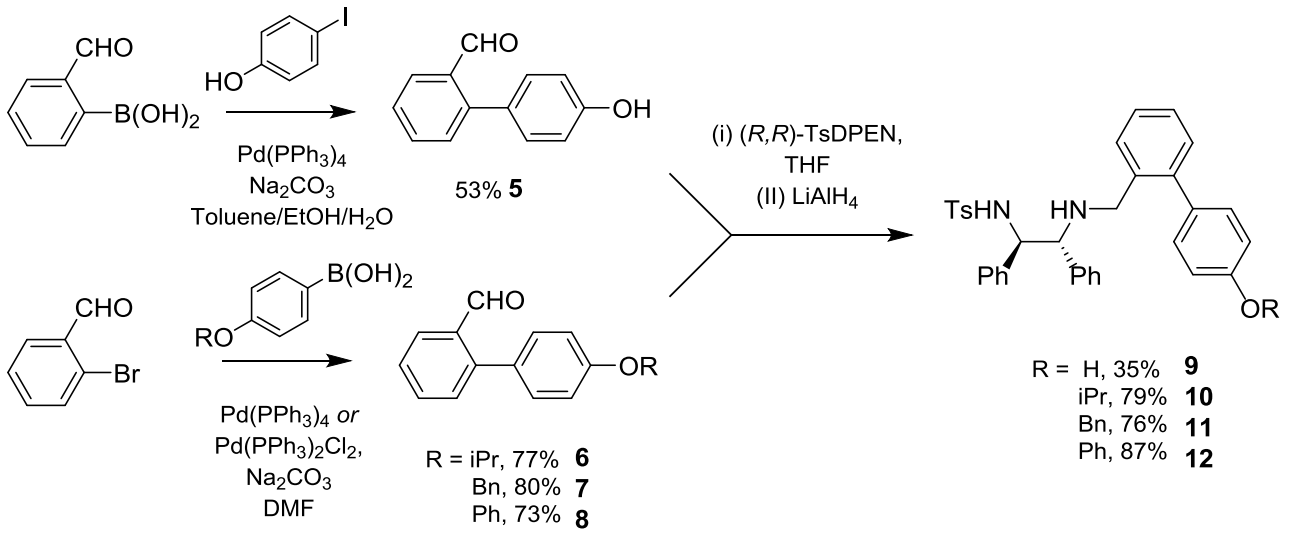


Fig. 1: 4'-OR-substituted 2-benzyl-tethered Ru(arene)((*R,R*)TsDPEN) catalysts prepared in this project

2 Results and Discussion

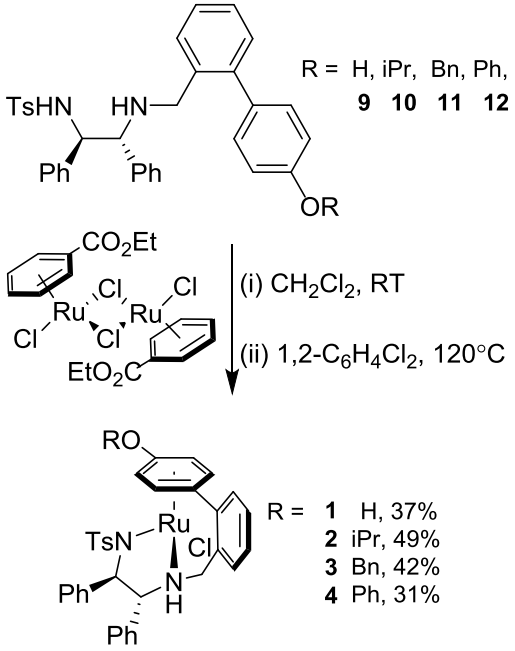
The ligands were synthesised *via* a simple two-step procedure utilising ubiquitous palladium catalysed C-C coupling reactions and operationally simple reductive aminations (Scheme 1). The aldehyde precursors were formed by Suzuki coupling commercial aryl-boronic acids with the corresponding aryl halide.[9] Catalysis by $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ with Na_2CO_3 as a base afforded precursors **5** – **8** in high yield (53 – 80%). These aldehydes were reacted in anhydrous THF with (*R,R*)-TsDPEN to form the prerequisite imine which was subsequently reduced using lithium aluminium hydride, furnishing the desired diamine ligands (**9** – **12**) in reasonable yields (35 – 87%). This synthetic route enabled the isolation of all four target (*R,R*)-TsDPEN-biphenyl-4'-OR ligands in good overall yield from cheap and readily-available commercially available starting materials.



Scheme 1: Synthesis of 2-benzyl-linked OR substituted (*R,R*)-TsDPEN ligands **9** – **12**(DOUBLE LINE SCHEME)

In order to form the envisaged catalysts, the ligands were reacted with a ruthenium (II) dimer, $[(C_6H_5CO_2Et)RuCl_2]_2$ (Scheme 2). Complex formation of this type is achieved through a well-established arene-exchange procedure which has been developed in our laboratory.[7a,b] The ligand and metal starting precursor were first mixed in CH_2Cl_2 to enable coordination of the diamine moiety of the ligand to the ruthenium centre. The solvent was then removed and replaced with chlorobenzene,[10] and heated at 120 °C

to facilitate displacement of the electron poor ethyl benzoate ligand by the more electron-rich pendant biphenyl of the coordinated diamine. In the case of the hydroxyl and isopropoxy functionalised catalysts, **1** and **2**, complex formation proceeded as expected under established reaction conditions (120 °C, 4 hr, *ca.* 100 mM). In the presence of 4Å molecular sieves,[7b] complex **2** was isolated in a lower yield of 42%. The formation of the complex with the free OH group, i.e. **1**, with the potential for further functionalisation, was particularly pleasing as it was initially thought that this group might hinder the attempts at complexation. However, using these reaction conditions for the synthesis of benzyloxy and phenoxy ligands (**3** and **4**) resulted in complex, intractable mixtures or product formation in very low yields. We postulated that this was due to the presence of 4'-OR arene substituents that were also capable of ligation to the ruthenium (II) centre. Due to the conformational rigidity of the biphenyl ligand system, it seemed likely that this process would be intermolecular i.e. between two different ruthenium centres. As such, these reactions were repeated at lower concentrations to reduce this potential side-reaction. Pleasingly, conducting the arene displacement at *ca.* 25 mM enabled the isolation of the target compounds **3** and **4**. The isolated yields of the diastereomerically pure compounds are moderate but broadly in-line with previously reported isolated complexes.[7a,b]



Scheme 2: Synthesis of 2-benzyl-linked OR substituted (*R,R*)-TsDPEN RuCl catalysts (SINGLE LINE SCHEME)

In order to study the structure of the complexes further, X-ray diffraction quality crystals were obtained for the O^{i}Pr and OBn appended catalysts **2** and **3** (Fig. 3).[11] The single-crystal X-ray structures for the two catalysts reveal very similar topology; the expected η^6 coordination of the biphenyl arene with a tethered chelating diamine ligand with an *S*-configuration at the metal centre. The 4'-OBn catalyst **3** co-crystallises with a chloroform solvate but the structures of **2** (*P 2yb*) and **3** (*P 2ac 2ab*) are otherwise unremarkable. Examination of the metrics again highlights the similarity of the two structures (Table 1). They exhibit very similar ruthenium-aryl (Ru – Cnt_{Ar}) distances; 1.667 Å and 1.675 Å for **2** and **3** respectively. This similarity is

also reflected in the Ru – N bond distances, *d*(Ru27 – N11) = **2**; 2.108 Å, **3**; 2.122 Å, and *d*(Ru27 – N26) = **2**; 2.122 Å, **3**; 2.127 Å, implying that variation of the OR substituent does not significantly affect the first coordination sphere of the ruthenium centre. Based on the solid-state X-ray crystallography results, catalysts **2** and **3** would therefore be expected to exhibit similar catalytic activity and enantioselectivities in ketone reduction via ATH.

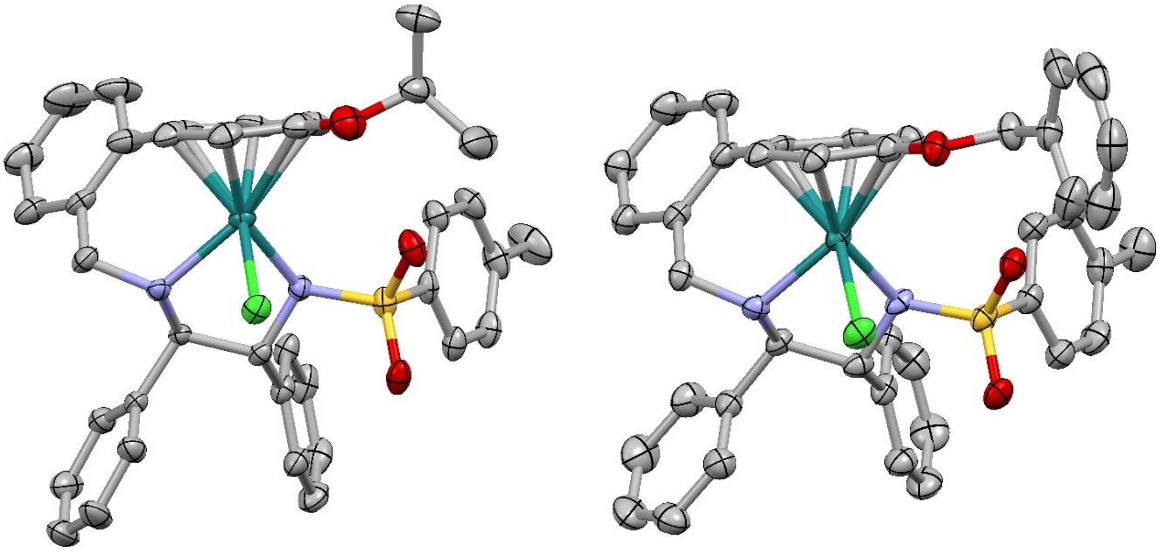


Fig. 3: Single crystal X-ray structure of complex **2** (left; CCDC 1016062) and **3** (right, CCDC 1016063) (ellipsoids are plotted at the 50% probability level; minor disordered components and hydrogen atoms omitted for clarity) (DOUBLE LINE FIGURE)

Compound Reference	**Complex 2**	**Complex 3**
Chemical Formula	$C_{37}H_{37}ClN_2O_3RuS$	$C_{41}H_{37}ClN_2O_3RuS \cdot CHCl_3$
Crystal system	Monoclinic	Orthorhombic
a/ Å	12.84674(10)	11.01638(12)
b/ Å	10.21786(8)	15.7699(2)
c/ Å	12.94691(10)	22.9663(3)
Space group	*P 2yb*	*P 2ac 2ab*
Goodness-of-fit on F^2	1.060	1.073
Final R_1 vaules ($I > 2\sigma(I)$)	0.0453	0.0357
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1196	0.0806
Final R_1 values (all data)	0.0458	0.0400
Final $wR(F^2)$ (all data)	0.1201	0.0853
Ru27 – Cnt_{Ar}/ Å	1.667700(10)	1.675036(18)
Ru27 – N11 / Å	2.108450(14)	2.122169(19)
Ru27 – N26 / Å	2.12215(2)	2.126897(18)

Table 1: Solid-state metrics for catalysts **2** and **3** (DOUBLE LINE FIGURE)

The performance of the novel catalysts **1** – **4** in ATH was evaluated using a series of benchmark ketones. Reductions were conducted using a 5:2 formic acid/ triethylamine azeotrope (FA/TEA) as the hydrogen source and 1 mol% catalyst loading at room temperature (*ca.* 25 °C) (Fig. 4). All of the reductions gave rise to

the expected enantioenriched product, resulting from the (*R,R*)- configuration complex; the results are tabulated in Table 2 and Table 3.

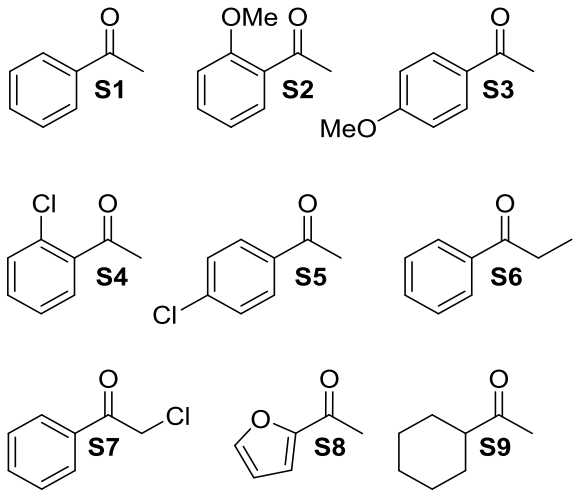
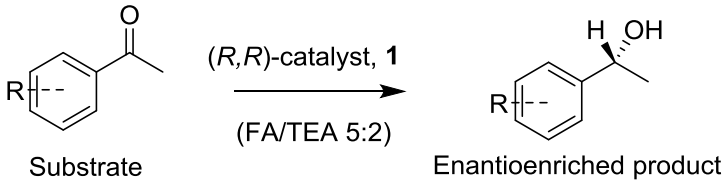


Fig. 4: Ketone substrates reduced by (*R,R*)-**1** – (*R,R*)-**3** (SINGLE LINE FIGURE)

The reduction of the acetophenone derivatives with catalyst **1** proceeded rapidly, with >99% conversion after 24 hours at S/C concentration of 100 for all but one substrate. The complex exhibited good enantioselectivities for the aryl ketones, ranging from 87 – 99%, presumably driven predominantly by the aforementioned mentioned directing effects.[6] This is in contrast to the cyclohexyl-methyl ketone which was reduced with a much lower, and reversed, enantioselectivity (48%). This is indicative of a lack of catalyst-substrate complementarity; the absence of an aryl ring prevents CH-π interactions. However, enantioselectivity in the case of saturated substrates is determined by weaker interactions and steric effects.[6]

Table 2: Ketone Reductions using (*R,R*)-**1**



Entry	Ketone	Catalyst	Time (h)	% Conv[a]	% ee[a]
1	Acetophenone **S1**	(*R,R*)-**1**	24	99.5	96.6 (*R*)
2	2'-OMe **S2**	(*R,R*)-**1**	24	99.6	89.6 (*R*)
3	4'-OMe **S3**	(*R,R*)-**1**	24	92.1	91.3 (*R*)
4	2'-Cl **S4**	(*R,R*)-**1**	24	100	87.4 (*R*)
5	4'-Cl **S5**	(*R,R*)-**1**	24	99.5	89.9 (*R*)

6	α-Me **S6**	(*R,R*)-**1**	24	95.9	92.9 (*R)*
7	α-Cl **S7**	(*R,R*)-**1**	24	100	98.6 (*R)*
8	furyl-methyl **S8**	(*R,R*)-**1**	24	99.7	97.9 (*R)*
9	Cyclohexyl-methyl **S9**	*(R,R)*-**1**	24	99.2	48.0[b] (*S)*

1 mol% catalyst, 1 mmol ketone, 0.5ml FA/TEA, room temperature. a) conversion and ee determined by GC. b) ee determined by acetylation of alcohol followed by GC. (SINGLE LINE FIGURE)

The conversions achieved by the *O*-alkyl substituted ATH catalysts, **2** and **3**, were lower after 24 hours, requiring prolonged reaction times compared to **1**, and the addition of a CH_2Cl_2 cosolvent to improve solubility. However under these modified conditions they gave good conversion after 48 hours at room temperature. The selectivities of these catalyst systems were again high (93 – 99% for **2**; 82 – 99% for **3**) for the aryl substituted ketones.[11] Although most reactions were run at 1 mol% catalyst loading at rt, the loading could be reduced to 0.5 mol% at 40 °C (99.6% reduction in 24h) and to 0.1 mol% at 60 °C (99.5% conversion in 24h) although there was a slight reduction in enantioselectivity at the higher temperatures. At extended reaction times at rt and 40 °C, the ee did not deteriorate; further details are given in the Supporting Information. The general trend observed is that the OBn catalyst **3** displays a diminution of selectivity when compared to the OiPr catalyst **2**. This can be rationalised in the relative size of the 4-OR substituent and it can be concluded that while catalysts **2** and **3** have a similar local coordination environment, evidenced in the solid-state, the second coordination sphere is influenced by the presence of the 4'-OR substituent. As the size of the group increases (R = H < iPr < OBn) there is an inverse effect on the selectivity of the ATH reaction. This is exemplified in the case of the cyclohexyl derivative, which lacks CH-π interactions, and so is more sensitive to steric effects; reduction by **2** and **3** displays very low selectivity, 12.8% and 12.6% respectively, contrasting non-hindered catalyst **1** (48.0%) and the previously reported 4'-OMe (48%)[7b] variant which gave modest but significant enantioexcesses.

Table 3: Ketone Reductions using (*R,R*)-**2** and (*R,R*)-**3**

Entry	Ketone	Catalyst	Time (h)	% Conv[a]	% ee[a]
1	Acetophenone **S1**	(*R,R*)-**2**	48	100	99.0 (*R)*
2	2'-OMe **S2**	(*R,R*)-**2**	48	66.9	93.2 (*R)*
3	4'-OMe **S3**	(*R,R*)-**2**	48	100	>99 (*R)*
4	2'-Cl **S4**	(*R,R*)-**2**	48	100	90.2 (*R)*
5	4'-Cl **S5**	(*R,R*)-**2**	48	100	94.4 (*R)*
6	α-Me **S6**	(*R,R*)-**2**	48	100	97.2 (*R)*
7	α-Cl **S7**	(*R,R*)-**2**	48	100	99.2 (*R)*
8	furyl-methyl **S8**	(*R,R*)-**2**	48	100	99.6 (*R)*
9	Cyclohexyl-methyl **S9**	*(R,R)*-**2**	48	100	12.8[b](*S)*
10[C]	Acetophenone **13**	*(R,R)*-**2**	24	99.6	97.8 (*R)*

11[d]	Acetophenone **13**	*(R,R)*-**2**	24	99.6	95.4 (*R)*
12[e]	Acetophenone **13**	*(R,R)*-**2**	24	99.5	95.0 (*R)*
13	Acetophenone **S1**	(*R,R*)-**3**	48	100	95.6 (*R)*
14	2'-OMe **S2**	(*R,R*)-**3**	48	100	89.4 (*R)*
15	4'-OMe **S3**	(*R,R*)-**3**	48	100	86.4 (*R)*
16	2'-Cl **S4**	(*R,R*)-**3**	48	100	82.6 (*R)*
17	4'-Cl **S5**	(*R,R*)-**3**	48	100	91.8 (*R)*
18	α-Me **S6**	(*R,R*)-**3**	48	100	91.2 (*R)*
19	α-Cl **S7**	(*R,R*)-**3**	48	100	97.6 (*R)*
20	furyl-methyl **S8**	(*R,R*)-**3**	48	99.3	95.6 (*R)*
21	Cyclohexyl-methyl **S9**	*(R,R)*-**3**	48	100	12.6[b] (*S)*
22	Acetophenone **S1**	*(R,R)*-**4**	48	99.5	96 (*R)*

1 mol% catalyst, 1 mmol ketone, 0.5ml FA/TEA, 2.0 mL CH_2Cl_2, room temperature. a) conversion and ee determined by GC. b) ee determined by acetylation of alcohol followed by GC c) reaction conducted using 0.5 mol% catalyst at 40 °C. d) reaction conducted using 0.2 mol% catalyst at 60 °C. . e) reaction conducted using 0.1 mol% catalyst at 60 °C (SINGLE LINE FIGURE)

3 Conclusions

A series of 4'OR substituted 2-benzyl-tethered Ru(II)TsDPEN complexes, **1 - 4**, have been prepared by an established synthetic procedure and interrogated using solution-state NMR and X-ray crystallography. The asymmetric reductions of ketones using the new catalysts demonstrate their capability in ATH of a series of diverse acetophenone derivatives. The reductions results indicate that catalyst **1** forms the desired chiral alcohol products in the shortest reaction time (8 examples >99% conversions within 24 hours). For the *O*-alkyl compounds **2** and **3** reduction was less rapid, nevertheless high conversions and high enantioselectivities (**2**: 7 examples >99% conversion, >90.2% ee; **3**: 8 examples >99% conversion, >82.6% ee) were observed after 48 hours, leading to slightly higher overall enantioselectivities.

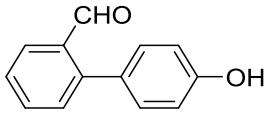
4 Experimental Section.

General Experimental Details.

All reagents and solvents were used as purchased and without further purification. All reactions were carried out under a nitrogen atmosphere unless otherwise specified. Anhydrous chlorobenzene was freeze-thaw degassed and stored under nitrogen over 3 Å molecular sieves. Reactions at elevated temperature were maintained by thermostatically controlled aluminium heating blocks or in oil baths. A temperature of 0 °C refers to an ice bath. NMR spectra were recorded on a Bruker AV (250 MHz), Bruker DPX (300 or 400MHz) or Bruker DRX (500 MHz) instrument. All chemical shifts are reported in ppm and are referenced to the solvent chemical shift, and coupling constants are given in Hz. Mass spectra were recorded on an Esquire 2000 and high resolution mass spectra were recorded on a Bruker Micro ToF or MaXis. IR spectra were recorded on a

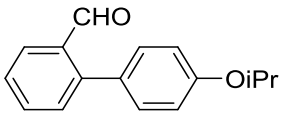
PerkinElmer spectrum100. Optical rotations were measured on an Optical Activity Ltd. AA1000. The chiral GC measurements were carried out on a PerkinElmer 8500 or Hewlett-Packard 1050 instrument linked to PC running DataApex Clarity software. HPLC was carried out on a Hewlett-Packard 1050 HPLC system. Melting points were determined on a Stuart scientific melting point apparatus and are uncorrected. Flash column chromatography was performed using silica gel of mesh size 230-400, Thin layer chromatography was carried out on aluminium backed silica gel 60 (F254) plates, visualized using 254nm UV light or permanganate stains as appropriate. Dichloro(ethyl benzoate)ruthenium(II) dimer ($[Ru(C_6H_5CO_2CH_2CH_3)Cl_2]_2$) was synthesised as previously described.[12]

Synthesis of 4'-hydroxy-[1,1'-biphenyl]-2-carbaldehyde 5



This compound is novel, however the procedure was adopted from a reported transformation.[7b] 2-Formylphenylboronic acid (1.00 g, 6.67 mmol) and bromophenol (0.769 g, 4.45 mmol), were dissolved in a 2M $Na_2CO_{3(aq)}$ solution (14 mL), ethanol (14 mL) and toluene (30 mL). $Pd(PPh_3)_4$ (0.257 g, 0.223 mmol) was added and the mixture was stirred under N_2 for 24 hours at 80 °C. The reaction mixture was cooled and H_2O (50 mL) and ethyl acetate (50 mL) were added. The organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 20:80) to obtain the product as a white solid. (0.467 g, 2.36 mmol, 53%). Mp 108-110 °C; (Found (ESI): $[M + Na]^+$, 221.0573, $C_{13}H_{10}NaO_2$ requires $[M + Na]^+$, 221.0578); ν_{max} 3220, 1656, 1595, 1397, 1225, 837 and 767 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 9.99 (1 H, s, ArCHO), 8.02 (1 H, d, *J* 7.8, ArH), 7.61-7.65 (1H, m, ArH), 7.43-7.49 (2 H, m, ArH), 7.25 (2 H, d, *J* 8.4, ArH), 6.96 (2 H, d, *J* 8.4, ArH), 6.03 (1 H, s, OH); δ_C (126 MHz, $CDCl_3$) 193.74, 156.18, 145.95, 134.08, 133.65, 131.53, 131.29, 129.90, 127.74, 127.45, 115.52; *m/z* (ESI) 221 (M^++ Na, 100 %), 419 ($[2M + Na]^+$, 11 %).

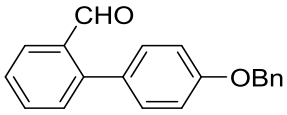
Synthesis of 4'-isopropoxy-[1,1'-biphenyl]-2-carbaldehyde 6



This compound is known and has been previously characterised.[13] 4-Isopropoxyphenyl boronic acid (2.95 g, 16.40 mmol), $Pd(PPh_3)_4$ (224 mg, 0.193 mmol) and Na_2CO_3 (2.17 g, 20.5 mmol) was dissolved in anhydrous DMF (70 mL). 2-bromobenzaldehyde (1.59 mL, 13.7 mmol) was added and the reaction heated to 130 °C under N_2 for 18 hours. The reaction was cooled to room temperature and diluted with sat. $NaHCO_{3(aq)}$ (150 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 10:90) to obtain the compound as a colourless oil (2.52 g, 10.5 mmol, 77 %). δ_H (400 MHz,

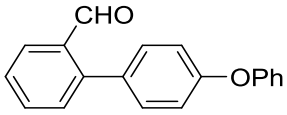
$CDCl_3$) 10.01 (1H, s, ArCHO), 8.00 (1 H, d, *J* 7.7, ArH), 7.62 (1 H, td, *J* 7.5, 1.4, ArH), 7.49 – 7.41 (2 H, m, ArH), 7.31 – 7.25 (2 H, m, ArH), 7.01 – 6.95 (2 H, m, ArH), 4.62 (1 H, sept., *J* 6.1, OC*H*$(CH_3)_2$), 1.39 (6 H, d, *J* 6.0, OCH(C*H*$_3)_2$); *m*/*z* (ESI) 263 (M^+ + 23, 70%) and 503 ($2M^+$ + 23, 100).

Synthesis of 4'-(benzyloxy)-[1,1'-biphenyl]-2-carbaldehyde 7



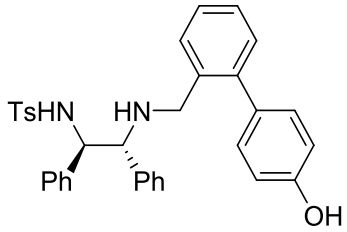
This compound is known and has been previously characterised.[13] 4-Benzyloxyphenyl boronic acid (3.65 g, 16.40 mmol), $Pd(PPh_3)_4$ (707 mg, 0.612 mmol) and Na_2CO_3 (2.17 g, 20.5 mmol) was dissolved in anhydrous DMF (70 mL). 2-bromobenzaldehyde (1.59 mL, 13.7 mmol) was added and the reaction heated to 130 °C under N_2 for 18 hours. The reaction was cooled to room temperature and diluted with sat. $NaHCO_{3(aq)}$ (150 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 10:90) to obtain the compound as a colourless oil (3.17 g, 10.99 mmol, 80 %). δ_H (400 MHz, $CDCl_3$) 10.01 (1H, s, ArCHO), 8.02 (1 H, dd, *J* 7.8, 1.3, ArH), 7.62 (1 H, dd, *J* 7.6, 1.4, ArH), 7.45 (6H, m, ArH), 7.39 – 7.35 (1H, m, ArH), 7.34 – 7.29 (2H, m, ArH), 7.12 – 7.06 (2H, m, ArH), 5.14 (2H, s, $ArCH_2O$); *m*/*z* (ESI) 283 (M^+ + 1, 3%) and 311 (M^+ + 23, 100).

Synthesis of 4'-(phenoxy)-[1,1'-biphenyl]-2-carbaldehyde 8



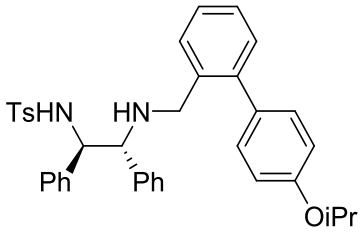
This compound is known and has been previously characterised.[14] 4-Phenoxyphenyl boronic acid (3.51 g, 16.40 mmol), $Pd(PPh_3)_2Cl_2$ (960 mg, 1.37 mmol) and Na_2CO_3 (2.17 g, 20.5 mmol) was dissolved in anhydrous DMF (70 mL). 2-bromobenzaldehyde (1.59 mL, 13.7 mmol) was added and the reaction heated to 130 °C under N_2 for 18 hours. The reaction was cooled to room temperature and diluted with sat. $NaHCO_{3(aq)}$ (150 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 10:90) to obtain the compound as a colourless oil (2.74 g, 9.99 mmol, 73 %). δ_H (400 MHz, $CDCl_3$) 10.02 (1 H, s, ArCHO), 8.02 (1 H, dd, *J* 7.8, 1.4, ArH), 7.63 (1 H, td, *J* 7.5, 1.5, ArH), 7.52 – 7.41 (2H, m, ArH), 7.42 – 7.35 (2 H, m, ArH), 7.33 (2 H, d, *J* 8.4, ArH), 7.15 (1 H, t, *J* 7.4, ArH), 7.09 (4 H, d, *J* 8.4, ArH); *m*/*z* (ESI) 297 (M^+ + Na, 100%).

Synthesis of N-((*R,R*)-2-(((4'-hydroxy-[1,1'-biphenyl]-2-yl)methyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide 9



This compound is novel, however the procedure was adopted from a reported transformation.[7b] 4'-Hydroxy-[1,1'-biphenyl]-2-carbaldehyde (200 mg, 1.010 mmol) and (*R,R*)-TsDPEN (370 mg, 1.010 mmol) were dissolved in anhydrous THF (6 mL) over 3 Å molecular sieves and stirred at room temperature for 18 hours. The solution was cooled to 0 °C and $LiAlH_4$ in THF (2.0 M, 1.01 mL, 2.722 mmol) was added dropwise and the reaction stirred at room temperature for 30 mins, followed by reflux for 30 mins. The reaction was quenched via the addition of sat. K/Na tartrate$_{(aq)}$ (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 20:80→40:60) to obtain the compound as a white solid (207 mg, 0.377 mmol, 35 %). Mp 118-120 °C; $[\alpha]_D^{19}$ -21.2 (*c* 0.125 in $CHCl_3$); (Found (ESI): $[M + H]^+$, 549.2202. $C_{34}H_{33}N_2O_3S$ requires $[M + H]^+$, 549.2212); ν_{max} 3275, 1612, 1517, 1453, 1156, 1091, 837, 764, 700 and 650 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.26 – 7.37 (6 H, m, ArH), 7.19 – 7.23 (1 H, m, ArH), 7.04 – 7.16 (6 H, m, ArH), 6.96 – 7.02 (3 H, m, ArH), 6.83 – 6.90 (4 H, m, ArH), 6.78 – 6.83 (2 H, m, ArH), 5.79 (1 H, s, TsNH), 4.21 (1 H, d, *J* 7.3, ArCH), 3.54 – 3.61 (2 H, m, ArCH + ArC*H*H), 3.34 (1 H, d, *J* 12.5, ArCH), 2.34 (3 H, s, $ArCH_3$); δ_C (126 MHz, $CDCl_3$) 154.90, 143.69, 141.91, 138.72, 138.37, 136.93, 136.76, 133.49, 133.42, 130.42, 130.01, 129.80, 129.11, 128.30, 127.97, 127.46, 127.42, 127.37, 127.31, 127.25, 127.22, 127.02, 115.37, 67.20, 63.08, 49.21; *m/z* (ESI) 549 (M^+ + H, 100%) and 571 (M^+ + Na, 12).

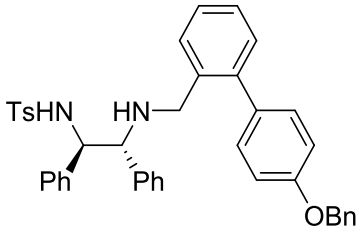
Synthesis of N-((*R,R*)-2-(((4'-isopropoxy-[1,1'-biphenyl]-2-yl)methyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide 10



This compound is novel, however the procedure was adopted from a reported transformation.[7b] 4'-Isopropoxy-[1,1'-biphenyl]-2-carbaldehyde (327 mg, 1.361 mmol) and (*R,R*)-TsDPEN (500 mg, 1.364 mmol) were dissolved in anhydrous THF (8 mL) over 3 Å molecular sieves and stirred at room temperature for 18 hours. The solution was cooled to 0 °C and $LiAlH_4$ in THF (2.0 M, 1.361 mL, 2.722 mmol) was added dropwise and the reaction stirred at room temperature for 30 mins, followed by reflux for 30 mins. The reaction was quenched via the addition of sat. K/Na tartrate$_{(aq)}$ (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 5:95→20:80) to obtain the

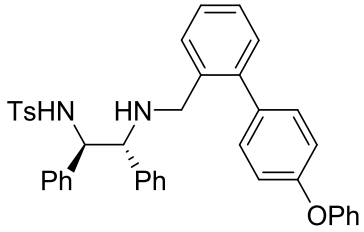
compound as a white solid (630 mg, 1.07 mmol, 79 %). Mp 57-61 °C; $[\alpha]_D^{23}$ -23.5 (*c* 0.10 in $CHCl_3$); (found (ESI): $[M + H]^+$, 591.2678. $C_{37}H_{39}N_2O_3S^+$ requires $[M + H]^+$, 591.2676); ν_{max} 3263, 2974, 1606, 1238, 1155, 1090, 762, 689, 665 and 560 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.32 – 7.26 (3 H, m, ArH), 7.20 – 7.14 (2 H, m, ArH), 7.13 – 6.95 (11H, m, ArH), 6.90 – 6.86 (2 H, m, ArH), 6.85 – 6.80 (2 H, m, ArH), 6.79 – 6.75 (2 H, m, ArH), 5.94 (1H, br. s, TsNH), 4.58 (1 H, sept., *J* 6.1, OC*H*$(CH_3)_2$), 4.18 (1 H, dd, *J* 7.4, 2.6, PhCH), 3.57 – 3.49 (2 H, m, PhCH + ArC*H*H), 3.30 (1 H, d, *J* 12.5, ArC*H*H), 2.31 (3 H, s, $ArCH_3$), 1.39 (3H, d, *J* 6.0, OCH(C*H*$_3$)(CH_3)), 1.38 (3H, d, *J* 6.0, OCH(CH_3)(C*H*$_3$)); δ_C (126 MHz, $CDCl_3$) 157.11, 142.68, 142.06, 138.95, 138.62, 137.16, 137.01, 133.22, 130.51, 130.01, 129.77, 129.17, 128.39, 128.07, 127.52, 127.48, 127.36, 127.33, 127.29, 127.15, 115.55, 69.96, 67.35, 63.14, 49.17, 22.35, 22.28, 21.56; *m/z* (ESI) 592 (M^+ + H, 100%) and 614 (M^+ + Na, 5).

Synthesis of N-((*R,R*)-2-(((4'-(benzyloxy)-[1,1'-biphenyl]-2-yl)methyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide 11



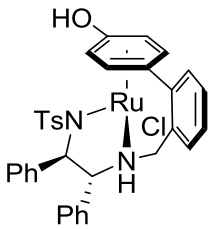
This compound is novel, however the procedure was adopted from a reported transformation.[7b] 4'-Benzyloxy-[1,1'-biphenyl]-2-carbaldehyde (392 mg, 1.361 mmol) and (*R,R*)-TsDPEN (500 mg, 1.364 mmol) were dissolved in anhydrous THF (8 mL) over 3 Å molecular sieves and stirred at room temperature for 18 hours. The solution was cooled to 0 °C and $LiAlH_4$ in THF (2.0 M, 1.361 mL, 2.722 mmol) was added dropwise and the reaction stirred at room temperature for 30 mins, followed by reflux for 30 mins. The reaction was quenched via the addition of sat. K/Na $tartrate_{(aq)}$ (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 5:95→20:80) to obtain the compound as a white solid (660 mg, 1.03 mmol, 76 %). Mp 60-65 °C; $[\alpha]_D^{23}$ -21.5 (*c* 0.10 in $CHCl_3$); (found (ESI): $[M + H]^+$, 639.2678. $C_{41}H_{39}N_2O_3S^+$ requires $[M + H]^+$, 639.2676); ν_{max} 3262, 3061, 3028, 1606, 1482, 1153, 697, 665, 560 and 547 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.50 (2 H, d, *J* 7.1, ArH), 7.43 (2 H, dd, *J* 8.3, 6.7, ArH), 7.37 (1 H, t, *J* 7.3, 1H), 7.33 – 7.27 (4 H, m, ArH), 7.21 – 7.15 (2 H, m, ArH), 7.13 – 7.01 (8 H, m, ArH), 6.97 – 6.92 (4 H, m, ArH), 6.91 – 6.87 (2 H, m, ArH), 6.81 – 6.76 (2 H, m, ArH), 5.92 (1 H, s, TsNH), 5.11 (2 H, s, OCH_2Ar), 4.19 (1 H, d, *J* 7.3, ArCH), 3.61 – 3.49 (2 H, m, ArCH + ArC*H*H), 3.31 (1 H, d, *J* 12.5, ArCH*H*), 2.31 (3 H, s, $ArCH_3$); δ_C (126 MHz, $CDCl_3$) 158.04, 142.69, 141.93, 138.94, 138.61, 137.19, 137.17, 136.97, 133.80, 130.51, 130.02, 129.82, 129.18, 128.81, 128.78, 128.40, 128.18, 128.08, 127.69, 127.53, 127.51, 127.37, 127.13, 114.70, 70.20, 67.35, 63.13, 49.22, 21.55; *m/z* (ESI) 639 (M^+ + H, 100%), 662 (M^+ + Na, 5) and 677 (M^+ + K, 2).

Synthesis of N-((*R,R*)-2-(((4'-isopropoxy-[1,1'-biphenyl]-2-yl)methyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide 12



This compound is novel, however the procedure was adopted from a reported transformation.[7,b] 4'-Phenoxy-[1,1'-biphenyl]-2-carbaldehyde (373 mg, 1.361 mmol) and (*R,R*)-TsDPEN (500 mg, 1.364 mmol) were dissolved in anhydrous THF (8 mL) over 3 Å molecular sieves and stirred at room temperature for 18 hours. The solution was cooled to 0 °C and $LiAlH_4$ in THF (2.0M, 1.361 mL, 2.722 mmol) was added dropwise and the reaction stirred at room temperature for 30 mins, followed by reflux for 30 mins. The reaction was quenched via the addition of sat. K/Na tartrate$_{(aq)}$ (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (SiO_2; EtOAc/Hexane; 5:95→20:80) to obtain the compound as a white solid (736 mg, 1.18 mmol, 87 %). Mp 59-66 °C; $[\alpha]_D^{23}$ –10.0 (*c* 0.10 in $CHCl_3$); (found (ESI): $[M + H]^+$, 625.2521. $C_{40}H_{37}N_2O_3S^+$ requires $[M + H]^+$, 625.2519); ν_{max} 3469, 3263, 3063, 3029, 2972, 1607, 1453, 1235, 1154, 1041, 737 and 546 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.41 – 7.35 (2H, m, ArH), 7.32 – 7.27 (4 H, m, ArH), 7.23 – 7.00 (13 H, m, ArH), 6.98 – 6.86 (6 H, m, ArH), 6.84 – 6.78 (2 H, m, ArH), 5.93 (1 H, d, *J* 4.0, TsNH), 4.22 (1 H, dd, *J* 7.4, 3.3, ArCH), 3.63 – 3.48 (2 H, m, ArCH + ArC*H*H), 3.32 (1 H, d, *J* 12.6, ArCH*H*), 2.30 (3 H, s, $ArCH_3$); δ_C (126 MHz, $CDCl_3$) 157.13, 156.50, 142.71, 141.66, 138.89, 138.54, 137.15, 136.92, 135.98, 130.40, 130.27, 129.94, 129.80, 129.18, 128.45, 128.11, 127.61, 127.58, 127.52, 127.49, 127.42, 127.40, 127.13, 123.58, 119.25, 118.50, 67.36, 63.11, 49.06, 21.55; *m/z* (ESI) 625 (M^+ + H, 100%), 648 (M^+ + Na, 6) and 677 (M^+ + K, 2).

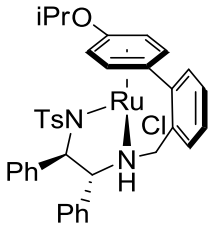
Synthesis of 4-hydroxy (*R,R*)-TsDPENRuCl complex 1



This compound is novel, however the procedure was adopted from a reported transformation.[7a,b] $[Ru(C_6H_5CO_2CH_2CH_3)Cl_2]_2$ (137.5 mg, 0.239 mmol) and (*R,R*)-TsDPENbiphenylOH (263.0 mg, 0.479 mmol) were dissolved in anhydrous CH_2Cl_2 (10.0 mL) and stirred at room temperature for 30 minutes. The solvent was removed in vacuo and redissolved in anhydrous degassed chlorobenzene (20.0 mL) and heated at 120 °C for four hours. The solvent was removed in vacuo and the crude material was purified by column chromatography (SiO_2; CH_2Cl_2/EtOAc; 85:15) to obtain the compound as a dark brown solid (121 mg, 0.177 mmol, 37 %). Mp 118-122 °C (dec); $[\alpha]_D^{23}$ -15.9 (*c* 0.095 in $CHCl_3$); (found (ESI): $[M - Cl]^+$, 649.1052.

$C_{34}H_{31}N_2O_3RuS^+$ requires [M - Cl]$^+$, 649.1102); ν_{max} 3350, 2974, 2892, 1130, 1086, 1046, 665 and 575 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.58 – 7.54 (1 H, m, ArH), 7.53 – 7.49 (1 H, m, ArH), 7.39 – 7.33 (2 H, m, ArH), 7.24 – 7.19 (1 H, m, ArH), 7.16 – 7.05 (3 H, m, ArH), 6.94 – 6.89 (2 H, m, ArH), 6.81 – 6.77 (2 H, m, ArH), 6.76 – 6.70 (2 H, m, ArH), 6.63 – 6.55 (2 H, m, ArH), 6.51 – 6.41 (2 H, m, ArH), 6.29 – 6.20 (2 H, m, ArH), 5.20 – 5.11 (2 H, m, ArH), 4.90 – 4.79 (1 H, m, PhCH), 4.55 (1 H, d *J* 11.4, ArC*H*H), 4.17 (1 H, d, *J* 10.3, NH), 3.88 (1 H, d, *J* 12.1, ArCH*H*), 3.64 (1 H, s, OH), 3.37 – 3.28 (1 H, m, PhCH), 2.32 (3 H, s, CH_3); δ_C (126 MHz, $CDCl_3$) 141.73, 139.77, 138.24, 135.74, 134.50, 132.79, 131.81, 129.99, 129.74, 129.65, 128.97, 128.88, 128.72, 128.23, 127.31, 126.98, 126.57, 69.25, 21.37; *m/z* (ESI) 649 (M$^+$ - Cl, 100%).

Synthesis of 4-isopropoxy (*R,R*)-TsDPENRuCl complex 2

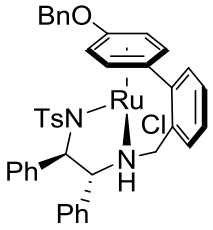


This compound is novel, however the procedure was adopted from a reported transformation.[7a,b] $[Ru(C_6H_5CO_2CH_2CH_3)Cl_2]_2$ (80.0 mg, 0.139 mmol) and (*R,R*)-TsDPENbiphenylOiPr (164.5 mg, 0.279 mmol) were dissolved in anhydrous CH_2Cl_2 (3.0 mL) and stirred at room temperature for 30 minutes. The solvent was removed in vacuo and redissolved in anhydrous degassed chlorobenzene (3.0 mL) and heated at 120 °C for four hours. The solvent was removed in vacuo and the crude material was purified by column chromatography (SiO_2; CH_2Cl_2/EtOAc; 85:15; followed by CH_2Cl_2/MeOH; 97:3→90:10) to obtain the compound as a dark yellow solid (100 mg, 0.137 mmol, 49 %). Mp 123-130 °C (dec); $[\alpha]_D^{23}$ +100.5 (*c* 0.10 in $CHCl_3$); (found (ESI): [M - Cl]$^+$, 691.1590. $C_{37}H_{37}N_2O_3RuS^+$ requires [M - Cl]$^+$, 691.1572); ν_{max} 3468, 3262, 3063, 3030, 2972, 1608, 1453, 1175, 1119, 697, 567 and 518 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.68 – 7.63 (1 H, m, ArH), 7.57 (1 H, t, *J* 7.5, ArH), 7.42 (1 H, td, *J* 7.6, 1.3, ArH), 7.25 (1 H, s, ArH), 7.14 – 7.05 (5H, m, ArH), 7.02 (1 H, d, *J* 7.4, ArH), 6.85 (2 H, d, *J* 8.0, ArH), 6.73 (2 H, t, *J* 7.3, ArH), 6.60 (2 H, t, *J* 7.5, ArH), 6.41 (2H, d, *J* 7.6, ArH), 6.34 (1 H, dd, *J* 5.8, 1.7, ArH), 5.73 (1 H, dd, *J* 6.6, 1.7, ArH), 5.46 (1 H, d, *J* 5.8, ArH), 5.31 (1 H, sept, *J* 6.0, OC*H*$(CH_3)_2$), 5.16 (1H, d, *J* 6.5, ArH), 4.89 (1 H, d, *J* 12.2, NH), 4.58 (1 H, dd, *J* 14.4, 3.1, ArCH*H*), 4.06 (1 H, d, *J* 11.2, PhCH), 3.81 (1 H, dd, *J* 14.1, 2.4, PhCH), 3.09 (1 H, app. t, *J* 11.7, ArCH*H*), 2.24 (3 H, s, $ArCH_3$), 1.52 (3 H, d, *J* 6.0, OCH(C*H*$_3$)(CH_3)), 1.40 (3 H, d, *J* 6.0, OCH(CH_3)(C*H*$_3$)),); δ_C (126 MHz, $CDCl_3$) 142.22, 139.39, 138.82, 136.27, 134.52, 132.92, 132.04, 130.10, 129.73, 129.51, 129.27, 128.72, 128.46, 128.00, 127.68, 126.67, 126.60, 126.35, 115.53, 87.66, 81.73, 80.64, 77.30, 77.22, 75.46, 72.68, 69.17, 53.96, 31.06, 22.82, 21.43, 21.38; *m/z* (ESI) 691 (M$^+$ - Cl, 100%).

The compound was also prepared in the presence of 4Å molecular sieves following the above procedure using $[Ru(C_6H_5CO_2CH_2CH_3)Cl_2]_2$ (40 mg, 0.0.062 mmol) and (*R,R*)-TsDPENbiphenylOiPr (82 mg, 0.138 mmol)

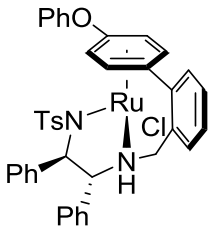
CH_2Cl_2 (1.5 mL), chlorobenzene (1.5 mL) and 4Å molecular seives. The product was purified following the method described above and was isolated as a brown solid (45.3 mg, 58.2 mmol, 42%).

Synthesis of 4-benzyloxy (*R,R*)-TsDPENRuCl complex 3



This compound is novel, however the procedure was adopted from a reported transformation.[7a,b] $[Ru(C_6H_5CO_2CH_2CH_3)Cl_2]_2$ (120.0 mg, 0.209 mmol) and (*R,R*)-TsDPENbiphenylOBn (267.4 mg, 0.419 mmol) were dissolved in anhydrous CH_2Cl_2 (15.0 mL) and stirred at room temperature for 30 minutes. The solvent was removed in vacuo and redissolved in anhydrous degassed chlorobenzene (15.0 mL) and heated at 120 °C for four hours. The solvent was removed in vacuo and the crude material was purified by column chromatography (SiO_2; CH_2Cl_2/EtOAc; 85:15) to obtain the compound as a dark yellow solid (135 mg, 0.174 mmol, 42 %). Mp 126-129 °C (dec); $[\alpha]_D^{23}$ -68.6 (*c* 0.102 in $CHCl_3$); (found (ESI): $[M - Cl]^+$, 737.1420. $C_{41}H_{35}N_2O_3RuS^+$ requires $[M - Cl]^+$, 737.1417); ν_{max} 3467, 3260, 3051, 3227, 1559, 1493, 1276, 760, 561 and 549 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.62 (1 H, dd, *J* 7.7, 1.4, ArH), 7.56 (3 H, d, *J* 7.4, ArH), 7.40 (4 H, ddd, *J* 16.4, 7.7, 6.2, ArH), 7.25 (2H, d, *J* 8.2, ArH), 7.16 – 7.05 (4 H, m, ArH), 6.99 (1 H, d, *J* 7.5, ArH), 6.82 (2H, d, *J* 8.0, ArH), 6.73 (1 H, t, *J* 7.4, ArH), 6.60 (2 H, t, *J* 7.6, ArH), 6.47 (1 H, dd, *J* 5.9, 1.7, ArH), 6.41 (2 H, d, *J* 7.5, ArH), 5.91 (1 H, dd, *J* 6.6, 1.7, ArH), 5.70 (1 H, d, *J* 11.9, OC*H*HPh), 5.57 (1 H, d, *J* 11.8, OCH*H*Ph), 5.40 (1 H, d, *J* 5.8, ArH), 5.15 (1 H, d, *J* 6.5, ArH), 4.91 (1 H, d, *J* 12.3, NH), 4.60 (1 H, dd, *J* 14.3, 3.1, ArC*H*H), 4.12 (1 H, d, *J* 11.2, PhCH), 3.82 (1 H, dd, *J* 14.3, 2.4, ArCH*H*), 3.11 (1 H, app.t, *J* 11.7, PhCH), 2.23 (3 H, s, $ArCH_3$); δ_C (126 MHz, $CDCl_3$) 142.32, 139.38, 138.80, 136.30, 136.12, 134.41, 132.74, 132.05, 130.13, 129.80, 129.53, 129.17, 128.77, 128.74, 128.70, 128.56, 128.53, 128.49, 128.30, 128.05, 127.58, 126.75, 126.38, 126.27, 114.69, 88.69, 81.46, 81.03, 78.47, 76.86, 75.69, 71.99, 69.26, 53.99, 21.37; *m/z* (ESI) 639 (M^+ - RuCl, 12%) and 739 (M^+ - Cl, 100).

Synthesis of 4-phenoxy (*R,R*)-TsDPENRuCl complex 4



This compound is novel, however the procedure was adopted from a reported transformation.[7a,b] $[Ru(C_6H_5CO_2CH_2CH_3)Cl_2]_2$ (77.0 mg, 0.134 mmol) and (*R,R*)-TsDPENbiphenylOPh (168.0 mg, 0.268 mmol) were dissolved in anhydrous CH_2Cl_2 (5.0 mL) and stirred at room temperature for 30 minutes. The solvent was removed in vacuo and redissolved in anhydrous degassed chlorobenzene (10.0 mL) and heated at 120 °C for

four hours. The solvent was removed in vacuo and the crude material was purified by column chromatography (SiO_2; CH_2Cl_2/EtOAc; 85:15) to obtain the compound as a dark yellow solid (62 mg, 0.079 mmol, 31 %). Mp 125-136 °C (dec); $[\alpha]_D^{23}$ +63.4 (*c* 0.082 in $CHCl_3$); (found (ESI): $[M - Cl]^+$, 725.1416. $C_{40}H_{35}N_2O_3RuS^+$ requires $[M - Cl]^+$, 725.1417); ν_{max} 3467, 3261, 3189, 2923, 1531, 1454, 1445, 1191, 759, 697 and 574 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.62 (1 H, d, *J* 7.5, ArH), 7.55 (3 H, d, *J* 7.6, ArH), 7.45 – 7.39 (3 H, m, ArH), 7.28 – 7.26 (2 H, m, ArH), 7.22 (1 H, t, *J* 7.3, ArH), 7.16 – 7.06 (4 H, m, ArH), 6.96 (1 H, d, *J* 7.6, ArH), 6.84 (2 H, d, *J* 7.9, ArH), 6.74 (1 H, t, *J* 7.3, ArH), 6.67 – 6.55 (4 H, m, ArH), 6.46 (2 H, d, *J* 7.5, ArH), 5.85 (1 H, d, *J* 6.3, ArH), 5.36 (1 H, d, *J* 5.6, ArH), 5.10 (1 H, d, *J* 6.3, ArH), 5.00 (1 H, d, *J* 13.3, NH), 4.61 (1 H, d, J 13.9, ArC*H*H), 4.17 (1 H, d, *J* 11.1, PhCH), 3.79 (1 H, dd, *J* 14.3, 2.0, ArCH*H*), 3.13 (1 H, t, *J* 11.7, PhCH), 2.24 (3 H, s, $ArCH_3$); δ_C (126 MHz, $CDCl_3$) 154.51, 142.18, 139.31, 139.04, 135.85, 134.15, 132.41, 131.95, 130.13, 129.96, 129.88, 129.59, 128.90, 128.77, 128.59, 128.00, 127.53, 126.83, 126.34, 125.68, 124.43, 122.11, 90.79, 83.47, 81.87, 79.72, 76.61, 75.65, 69.03, 53.64, 30.41, 21.35; *m*/*z* (ESI) 625 (M^+ - RuCl, 62%) and 725 (M^+ - Cl, 100).

Asymmetric Reductions.

General Procedure for racemic reductions.

Ketone (1.0 eq) was added to $NaBH_4$ (2.0 eq) in MeOH (0.1 mL per mmol of ketone) under N_2 and stirred at room temperature for 3 hours. The solution was diluted with H_2O (10 mL) and EtOAc. The aqueous layer was extracted with EtOAC (3 × 10 mL) and the combined organic layers washed with H_2O and dried over anhydrous $MgSO_4$. The sample was purified by column chromatography (SiO2; EtOAc/Hexane; 20:80) to remove the catalyst.

General Procedure for asymmetric transfer hydrogenation in FA/TEA.

To a mixture of the catalyst 5mg (0.0073 mmol) in FA/TEA (5/2) (1.0 mL) was added ketone (0.73 mmol), and the mixture was stirred at room temperature under an inert atmosphere. The reaction was monitored by TLC. The reaction mixture was diluted sat. $NaHCO_{3(aq)}$ (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic layers washed with H_2O and dried over anhydrous $MgSO_4$. The sample was then purified by column chromatography (SiO_2; EtOAc/Hexane; 50:50) to remove the catalyst. For catalysts **2** and **3** the ATH reactions were conducted using a CH_2Cl_2 co-solvent (2 mL)

Declarations of interest: none.

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through support from Advantage West Midlands (AWM) and the European Regional Development Fund (ERDF).

Appendix A

Supplementary material CCDC 1016062 and 1016063 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www. ccdc.cam.ac.uk/data_request/cif.

Appendix B

Supplementary data including ^{1}H and ^{13}C NMR spectra and ATH reduction GC chromatograms can be found at XXXXXX

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[10] The electron-poor arene solvent does not form a strong interaction with Ru(II) centres and so does not compete with the substrate in the reaction.

[11] Repeated attempts were made to collect a usable dataset for catalyst **4**; despite the crystallinity of the sample this was not possible. This catalyst gave an acetophenone reduction product of 99.5% conversion and 96% ee under the conditions used in Table 3, but, since it was formed in lower yield, was not tested extensively against the full set of ketones.

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