Tethered Ru(II) catalysts containing a Ru-I bond.

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Abstract.

Two new iodide-containing derivatives of the widely-adopted arene/Ru(II)/TsDPEN catalysts have been prepared and fully characterised, including through X-ray crystallography. They have been evaluated as catalysts for the asymmetric reduction of acetophenone under both transfer (ATH) and pressure hydrogenation (AH) conditions. The iodide-containing complexes are equally efficient in the ATH reaction, but less active in the AH reaction compared to the chloride derivatives.

Keywords.

Asymmetric transfer hydrogenation

Asymmetric hydrogenation

Reduction

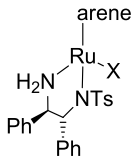
Ruthenium

Iodide

Asymmetric catalysis

1 Introduction.

Complexes of general structure [(η^6-arene)Ru(II)(TsDPEN)X] **1** (Figure 1), which are well-established catalysts for ketone and imine reduction[1] were first reported by Noyori et al in the mid 1990's.[2] Although initially employed in asymmetric transfer hydrogenation (ATH) using reagents such as isopropanol, formic acid or aqueous sodium formate,[2,3] they have also proven to be capable of catalysing reductions using hydrogen gas, i.e. asymmetric hydrogenation (AH).[4] This class of catalyst has been widely applied in numerous synthetic applications and total syntheses of complex natural product targets.[5] In the majority of applications, the chloride complex is employed.



1a (arene = η^6 p-cymene)
1b (arene = η^6 benzene)
1c (arene = η^6 hexamethylbenzene)
X = Cl, OTf

Figure 1. Structures of catalysts **1a-1c.**

In the ATH process (Figure 2a), the 16-electron species **2** is formed from **1a** (i.e. illustrated for arene = p-cymene) and this subsequently gains two hydrogen atoms from the reducing agent to form hydride **3**.[3] Transfer of the hydrogen atoms to a substrate subsequently generates an enantiomerically-enriched product whilst regenerating **2** and closing the catalytic cycle. Complex **2** can be also isolated and used directly in reductions.[3] In the case of AH (Figure 2b), the situation is slightly different as the reaction is carried out in methanol without added base.[4] In this case the complex first ionises to **4** before dihydrogen is split in a heterogeneous fashion to generate **3**. Hydride **3** reduces a substrate in the same manner as previously described to regenerate **2** which is subsequently protonated to close the catalytic cycle. In order

to improve the efficiency of the catalyst, the chloride in **1** is generally replaced by a better leaving group such as triflate[4] in order to facilitate the initial ionisation towards generation of the active catalyst 4 in methanol solvent. Alternatively, the active catalyst may be generated using a combination of **2** and triflic acid.[4a]

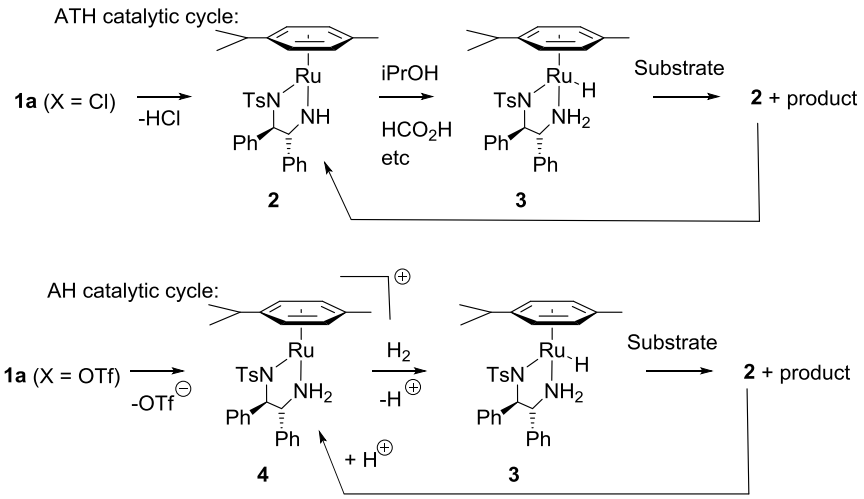


Figure 2. Catalytic cycles for ATH and AH reactions using catalysts **1.**

In the context of the importance of the counterion for active catalyst generation, iodide would seem an attractive alternative to chloride in **1**, however this variation has not been studied in detail. Williams, Blacker and co-workers have shown that catalysts such as $[Cp^*IrI_2]_2$ are highly active for hydrogen transfer processes for the alkylation of amines[6] and also dynamic kinetic resolution of chiral amines.[7] Xiao et al have reported that addition of iodide to an Ir-catalysed, non-asymmetric, reduction of nitrogen-containing heterocycles results in a significant rate increase.[8] This has been attributed to a change in the reaction mechanism. Klein Gebbick and Virboul[9] prepared water-soluble arene/Ru(II)/TsDPEN catalyst **5** containing a sulfonic acid group which contained an iodide counterion. This was prepared via a halide exchange with an $[(arene)RuCl_2]_2$ precursor prior to introduction of the TsDPEN. Through this sequence, the authors avoided the possibility of halide

scrambling during a deprotection step in which NaI was employed. In ATH tests, complex **5** (Figure 3) proved to be effective under aqueous conditions and gave an acetophenone reduction product of up to 94% ee. Some literature reports also describe the use of silver salts in AH reactions to assist with the removal of the chloride[4,10,11] however in studies carried out by ourselves in collaboration with Johnson Matthey we found that the addition of a variety of silver salts was detrimental to the AH of acetophenone with the closely related tethered catalyst **6** (Figure 3).[12,13]

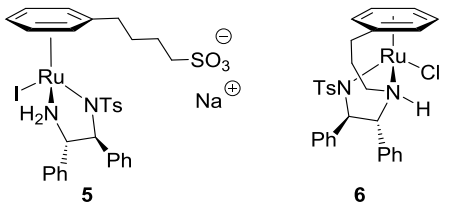
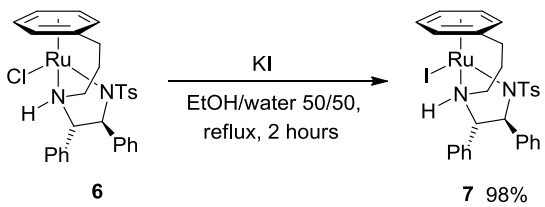


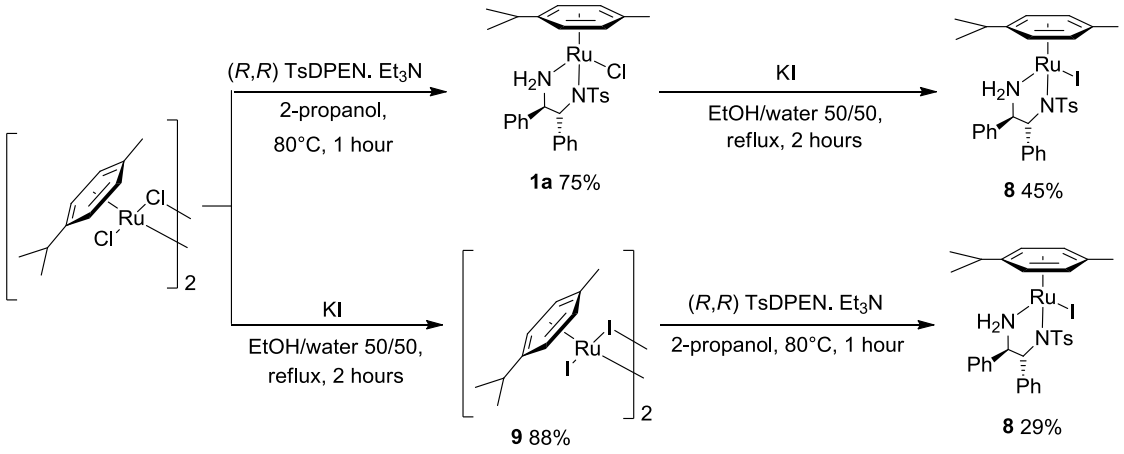
Figure 3. Structures of catalysts **5** and **6.**

2 Results and discussion.

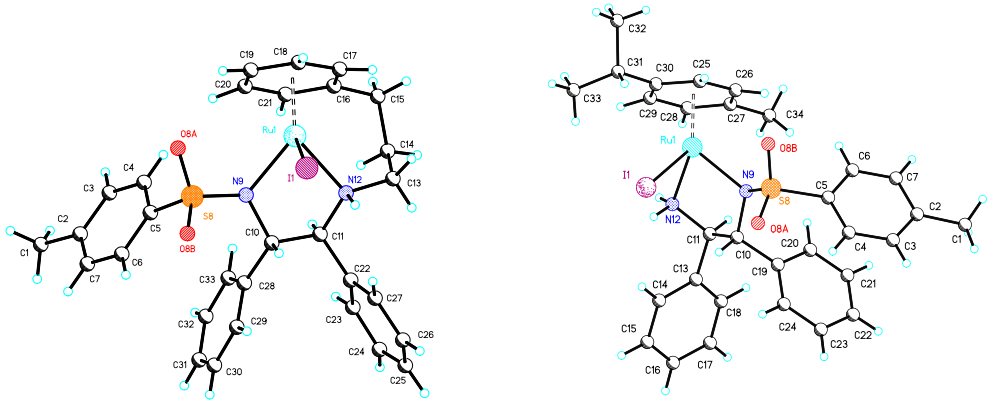
In order to investigate whether iodide may be a better leaving group than chloride in Ru(II)/TsDPEN catalysts, the tethered (**7**) and untethered (**8**) ruthenium iodide catalysts were prepared. Conversion of **6**[12] to **7** proceeded in excellent yield simply by refluxing with KI in EtOH/water (Scheme 1). Formation of catalyst **8** however proved to be less trivial with lower yields obtained due to the high solubility of both the monomer and its dimer precursor making isolation of the complexes more difficult (Scheme 2). Conversion of the pre-formed untethered ruthenium chloride catalyst **1a** into its iodo derivative **8** gave the product in a higher yield than formation of the iodo dimer **9**[9] followed by monomer formation. X-ray crystallographic structures were obtained for each complex (Figure 4).



Scheme 1. Preparation of tethered ruthenium iodide catalyst (*S*,*S*)-**7**.



Scheme 2. Preparation of ruthenium iodide catalyst *(R,R)*-**8**.



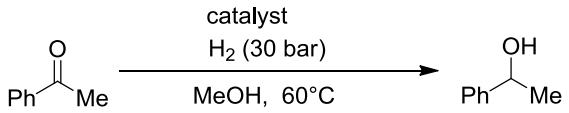
(a) (b)

Figure 4. Solid state X-ray crystallographic structures of (a) (*S*,*S*)-3C-tethered-RuI catalyst **7 (**CCDC 1016062) and (b) (*R*,*R*)-**8 (**CCDC 1016063) with atom labelling.

The X-ray structures are analogous to those reported for the RuCl complexes.[3a,12a] Each was formed as a single diastereomer, with the tosyl group oriented away from the iodide ligand and π/π-stacking between the tosyl group and neighbouring phenyl ring of TsDPEN. The Ru-I bond lengths were 2.77 and 2.78Å respectively for the tethered (**7**) and untethered (**8**) complexes.

With both iodo catalysts in hand a series of AH reactions were carried out with acetophenone as the substrate (Table 1). Comparisons were made with the more established chloride complexes **1a** and **6**.

Table 1. AH of acetophenone using tethered and untethered ruthenium chloride and iodide catalysts **1a, 6**-**8**.



1 mmol [0.5 M]

Entry	Catalyst	S[a]/C	Temp. (°C)	Time (hr.)	Conv.[b] (%)	Ee[b] (%)
1	(*R*,*R*)-untethered RuCl catalyst **1a**	100/1	40	16	94.6	94.3 (*R*)
2	(*R*,*R*)-untethered RuI catalyst **8**	100/1	40	16	67.0	92.7 (*R*)
3	(*R*,*R*)-untethered RuCl catalyst **1a**	500/1	60	16	9.1	87.3 (*R*)
4	(*R*,*R*)-untethered RuI catalyst **8**	500/1	60	16	4.4	61.0 (*R*)
5	(*S*,*S*)-tethered RuCl catalyst **6**	500/1	60	16	99.8	93.2 (*S*)
6	(*S*,*S*)-tethered RuCl catalyst **6**	1000/1	60	16	21.0	86.6 (*S*)
7	(*S*,*S*)-tethered RuI catalyst **7**	500/1	60	16	56.5	92.7 (*S*)
8	(*S*,*S*)-tethered RuI catalyst **7**	1000/1	60	16	4.6	75.3 (*S*)
9	(*S*,*S*)-tethered RuCl catalyst **6**	2000/1	60	64.5	39.8	86.3 (*S*)
10	(*S*,*S*)-tethered RuI catalyst **7**	2000/1	60	64.5	45.2	86.7 (*S*)

[a]Distilled acetophenone was used. [b]Determined by chiral GC.

The tethered iodo catalyst **7** was found to be more active than the untethered iodo catalyst **8**, however both iodo catalysts were less active than their chloro counterparts. Interestingly however, with a low catalyst loading and long reaction time (Table 1,

entries 9 and 10) the activity of the tethered chloro and iodo catalysts was comparable in terms of conversion and ee. This suggests that although less active than the chloro catalyst, the iodo derivative may exhibit increased stability, thus allowing greater conversion over long reaction times. The results suggest that the ionisation process is not improved with an Ru-I rather than Ru-Cl bond as was originally proposed. To study the reaction further the conversion was followed over a fixed time period using each tethered catalyst. When using the sealed Parr reactor for AH reactions however it was not possible to sample the same reaction at various time points for conversion analysis; conversion was found to stop after the first sample was taken due to exposure of the contents to air. Therefore in order to follow a reduction, several reactions were carried out for different lengths of time and the conversions of each were analysed. Each reaction was carried out in duplicate to confirm the results and identify anomalous results due to inaccurate weighing of catalyst or acetophenone. The same batch of catalyst, acetophenone and MeOH was used throughout. The results are shown in Figure 5. It was also observed (Table 1) that better ees were obtained at higher conversions and this remains the subject of ongoing investigations.

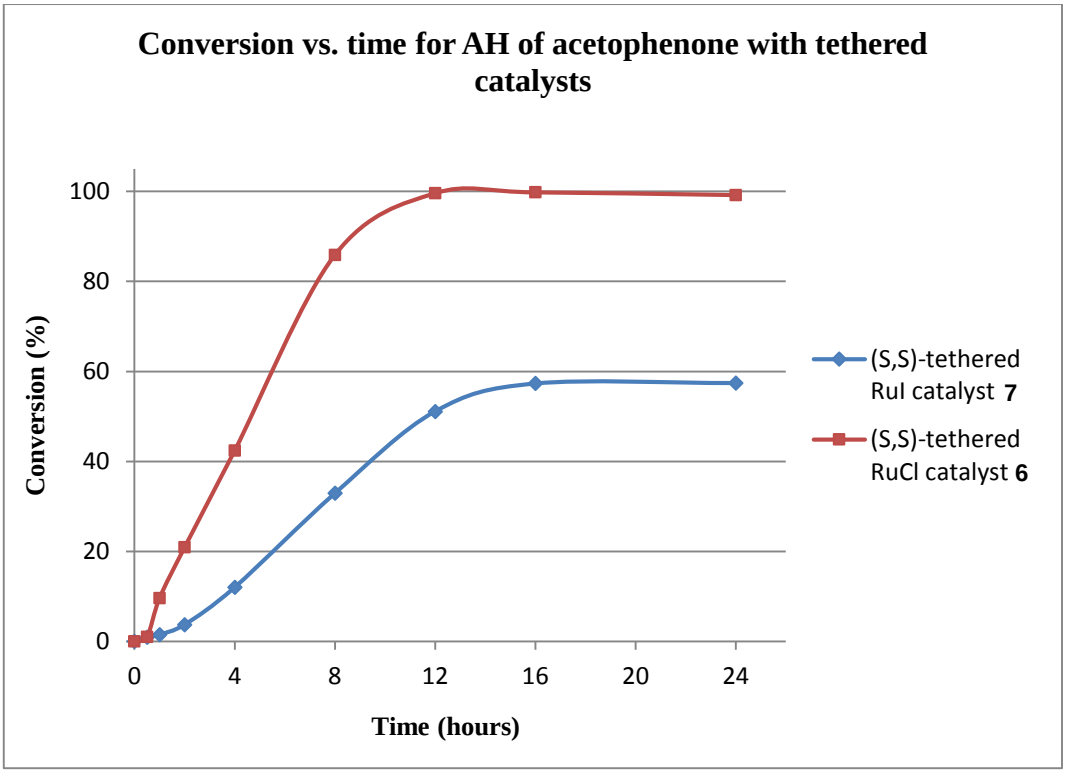
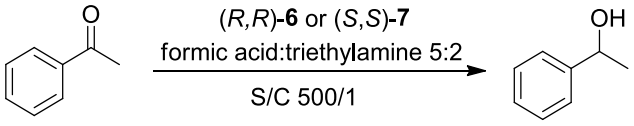


Figure 5. Analysis of conversion over time for AH of acetophenone using chloro **6** and iodo **7** tethered catalysts ([S] = 0.5 M, S/C 500, MeOH, 60 ^{o}C, 30 bar H_2.

The ruthenium iodide catalyst **7** is less active than the chloro derivative throughout the reaction process. The initial activation period is also longer for the iodo catalyst than the chloro catalyst. Catalyst **6** shows an activation period of ca. 30 min before a significant increase in reaction rate is seen, however the iodo catalyst **7** requires 1.5-2 hours before the reaction rate increases. However it is possible that the formation of HI during the reaction with the iodo catalyst **7** may be detrimental to the reaction.

The tethered iodo catalyst **7** was also applied to the ATH of acetophenone. Under these conditions, where ionisation of the catalyst is not necessary for formation of the active species due to the presence of base, iodo catalyst **7** exhibited an essential equal level of activity as the chloro catalyst **6** (Table 2).

Table 2. ATH of acetophenone using tethered catalysts **6** and **7**.



Entry	Catalyst	Temp. (°C)	Time (hr.)	Conv.[a] (%)	Ee.[a] (%)
1	(*R*,*R*)- tethered RuCl catalyst **6**	28	34	92.8	96.5 (*R*)
2	(*S*,*S*)-tethered RuI catalyst **7**	28	34	99.6	95.9 (*S*)
3	(*R*,*R*)- tethered RuCl catalyst **6**	60	2	99.8	95.0 (*R*)
4	(*S*,*S*)-tethered RuI catalyst **7**	60	2	99.4	95.3 (*S*)

[a]Determined by chiral GC analysis.

For the ATH conditions investigated, both catalysts gave comparable results showing little difference in activity upon substitution of the chloride for an iodide in the catalyst. The mode of activation for catalysts in ATH processes is loss of the halide ligand brought about by the presence of a base such as Et_3N or KOH. The loss of both chloride and iodide in this way may proceed at equal rates, allowing equally rapid formation of the active Ru-hydride species and hence equal rates of reduction.

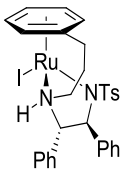
In conclusion, a systematic comparison of two iodine-containing derivatives of the well established Ru(II)/TsDPEN reduction catalysts demonstrates a similar activity to the established chloride complexes in ATH and a lower activity in AH. The reasons for this are unclear at present however the initiation may be slower for the iodide catalyst or the formation of HI in the reaction may be detrimental to the catalyst.

3 Materials and methods.

3.1 *General experimental details.*

All chemicals used in this project were obtained from Sigma Aldrich, Acros Organics, Alfa Aesar, TCI and Fischer Scientific. NMR analysis was carried out on a DPX-300 (300 MHz), DPX-400 (400 MHz), DRX-500 (500 MHz), AV III-600 (600 MHz) or AV II-700 (700 MHz) instrument using deuterated solvents including $CDCl_3$, d_6-DMSO, d_4-MeOD, d_8-THF, d_2-DCM or d_6-benzene. Low resolution mass spectrometry data was acquired using a Bruker Esquire 2000 (ESI) spectrometer or Bruker HCT + (Ultra) (ESI) spectrometer coupled to an Agilent 1100 HPLC system for sample injection, or an Agilent 6130B ESI (quad) mass spectrometer coupled to an Agilent Technologies 1260 Infinity HPLC system. GC/MS analysis was carried out on a Varian 4000 GC/MS with chemical ionisation. High resolution mass spectrometry data was obtained using a Bruker micro TOF spectrometer. Methanol was used as the solvent for LC/MS and high resolution mass spectrometry, and chloroform for GC/MS. Infrared spectroscopy data was acquired using a Perkin Elmer Spectrum One, Nicolet Avatar 320 or a Bruker ALPHA FT-IR spectrometer. Gas Chromatography analysis was carried out using a Hewlett Packard 5890 Gas Chromatograph or a Perkin-Elmer 8500 Gas Chromatograph. Integration was carried out with a Hewlett Packard HP3396A Integrator or a PC running DataApex Clarity software. Polarimetry was carried out using an Optical Activity Ltd. AA-1000 Polarimeter with a 2 dm cell using spectrophotemetric grade solvent. Melting point analysis was carried out on Stuart Melting Point SMP10 apparatus.

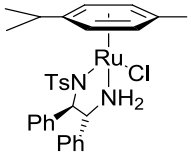
3.2 *N-[(1S, 2S)-1, 2-Diphenyl-2-(3-phenypropylamino)ethyl)-4-methylbenzenesulfonamide)ruthenium(II)iodide monomer* ***7.***



This compound is novel, however the procedure was adopted from a reported transformation.[9] To an argon purged flask was added (*S*,*S*)TsDPEN 3C tethered RuCl **6** catalyst (40 mg, 0.060 mmol) and KI (25 mg, 0.15 mmol). To this was then added 50% v/v EtOH/H_2O (4 mL). The resulting orange solution was stirred under reflux at 80°C for 2 hours. The reaction, which had become a red/purple colour, was cooled to room temperature and filtered. The collected precipitate was dried to give **7** as a red/purple solid (42 mg, 0.059 mmol, 98%). Purification was not necessary. Mp 170°C (decomposed); $[\alpha]_D^{28}$ +565 (*c* 0.1 in $CHCl_3$) (*S*, *S*); (found (ESI): M^+ - I +H, 585.1161 $C_{30}H_{32}N_2O_2RuS$ requires M, 585.1151); υ_{max} 3495, 3212, 2940, 1455, 1263, 1128, 1084, 936, 905, 806, 701, 659 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.17 (2H, d, *J* 7.6 Hz, C*H*Ar in tosyl), 7.12-7.07 (3H, m, C*H*Ar), 6.82-6.76 (5H, m, C*H*Ar), 6.66 (H, t, *J* 7.5 Hz, C*H*Ar), 6.59 (2H, d, *J* 7.6 Hz, C*H*Ar in tosyl), 6.48 (1H, t, *J* 5.6 Hz, C*H*Ar-Ru), 6.25 (1H, t *J*, 5.6 Hz, C*H*Ar-Ru), 6.10 (1H, t *J* 5.6 Hz, C*H*Ar-Ru), 5.60 (1H, d, *J* 5.6 Hz, C*H*Ar-Ru), 5.05 (1H, d, *J* 5.6 Hz, C*H*Ar-Ru), 4.81-4.78 (1H, m, N*H*), 4.09 (1H, d, *J* 11.0 Hz, C*H*NTs), 3.69 (1H, t, *J* 11.0 Hz, C*H*NH), 2.80-2.74 (1H, m, CH_2NH), 2.64-2.52 (2H, m, CH_2CH_2NH), 2.29-2.24 (4H, m and s overlapping, C*H* in CH_2NH and CH_3 overlapping), 2.19-2.10 (1H, m, CH_2ArRu), 1.99-1.93 (1H, m, CH_2ArRu); δ_C (100 MHz, $CDCl_3$) 142.40 (*C*Ar), 139.16 (*C*Ar), 138.50 (*C*Ar), 136.51 (*C*Ar), 129.20 (2 *C*HAr), 128.68 (*C*HAr), 128.26 (2 *C*HAr), 128.03 (4 *C*HAr), 127.19 (2 *C*HAr), 126.81 (2 *C*HAr), 126.27 (*C*HAr), 98.87 (*C*Ar-Ru), 93.44 (*C*HAr-Ru), 89.61 (*C*HAr-Ru), 81.98 (*C*HAr-Ru), 79.36 (*C*HAr-Ru), 77.44 (*C*HAr-Ru), 77.20

(*C*H), 70.00 (*C*H), 48.57 (*C*H_2), 29.59 (*C*H_2), 26.08 (*C*H_2), 21.25 (*C*H_3); *m/z* (ESI) 585.0 (M^+ + 1).

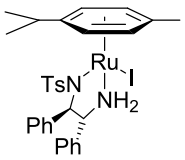
3.3 *N-[(1R,2R)-2-(Amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide(p-cymene)ruthenium(II)chloride monomer* ***1a****.*



This compound is known and has previously been fully characterised.[3a] To a nitrogen purged, dried round bottom flask, was added [(*p*-cymene)$RuCl_2$]$_2$ (50 mg, 0.080 mmol) was added (*R,R*)-TsDPEN (59 mg, 0.16 mmol). To this was then added Et_3N (32 mg, 0.32 mmol) and degassed anhydrous IPA (5 mL). The resulting orange solution was stirred at reflux (80°C) for 1 hour. The reaction was cooled to room temperature, and the solvent removed under reduced pressure to leave an orange solid. The solid was washed with water and filtered. The solid was dried and then recrystallised from hot MeOH to give the product as an orange solid (75 mg, 0.12 mmol, 75%). Mp 182-184°C; $[\alpha]_D^{27}$ -45 (*c* 0.01 in $CHCl_3$) (*R,R*) (lit.[186] $[\alpha]_D^{29}$ -80.5 (*c* 1.05 in $CHCl_3$) (*R,R*)); (found (ESI): M^+ + H, 601.1468. $C_{31}H_{35}N_2O_2RuS$ requires M, 601.1465); υ_{max} 3216, 1452, 1265, 1126, 1083, 913, 806, 696, 572 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 6.98-6.96 (5H, m, C*H*Ar), 6.72-6.68 (5H, m, C*H*Ar), 6.56 (2H, t *J* 7.7 Hz, C*H*Ar), 6.38-6.37 (2H, m, C*H*Ar), 5.90 (1H, br s, C*H*Ar-Ru), 5.80 (1H, br s, C*H*Ar-Ru), 5.73-5.70 (2H, m, C*H*Ar-Ru), 3.73 (1H, d *J* 10.5 Hz, C*H*NTs), 3.61-3.56 (1H, m, C*H*NH_2), 3.24-3.11 (1H, m, N*H*$_2$), 3.11-3.09 (1H, m, C*H*$(CH_3)_2$), 2.31 (3H, s, *p*-C*H*$_3(C_6H_4)SO_2$), 2.21 (3H, s, ^{i}Pr(C_6H_4)C*H*$_3$), 1.63 (1H, br s, N*H*$_2$), 1.20 (6H, d *J* 6.0 Hz, $(CH_3)_2$CH); δ_C (100 MHz, $CDCl_3$) 143.34 (*C*Ar), 139.74 (*C*Ar), 138.89 (*C*Ar), 138.67 (*C*Ar), 129.03 (*C*HAr), 127.83 (2 *C*HAr), 127.78 (2 *C*HAr), 127.30 (4 *C*HAr),

126.70 (2 *C*HAr), 126.56 (2 *C*HAr), 125.87 (*C*HAr), 93.89 (*C*Ar-Ru), 85.63 (*C*HAr-Ru), 82.00 (*C*HAr-Ru), 80.11 (*C*HAr-Ru), 71.60 (*C*HAr-Ru), 69.39 (*C*HAr-Ru), 46.18 (*C*H), 30.54 (2 *C*H_3), 22.15 (*C*H_3), 18.84 (*C*H_3); *m/z* (ESI) 601 (M^+ -35 + 1,). Data matches that previously reported for this compound.[3a]

3.4 *N-[(1R,2R)-2-(Amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide(p-cymene)ruthenium(II)iodide monomer **8**.*



This compound is novel, however the procedures were adopted from a reported transformation.[9] Method A: To an argon-purged flask was added [Ru(*p*-cymene)Cl_2]$_2$ (50 mg, 0.080 mmol) and KI (133 mg, 0.80 mmol) followed by 50% v/v EtOH/H_2O (4 mL). The resulting red solution was then stirred under reflux at 80°C for 2 hours. The reaction solution, now purple, was cooled to room temperature and filtered. The collected precipitate was dried to give [Ru(*p*-cymene)I_2]$_2$ **9** (68 mg, 0.070 mmol, 88%) as a purple solid. To the crude product (60 mg, 0.060 mmol) in an argon purged, dried flask was then added (*R,R*)-TsDPEN (44 mg, 0.12 mmol), followed by Et_3N (24 mg, 0.24 mmol) and anhydrous IPA (5 mL). The resulting purple solution was stirred under reflux at 80°C for 1 hour. The reaction was then cooled to room temperature and the solvent removed under reduced pressure. The residue was then washed with 1 mL of water before again being dried to leave the crude as a purple solid. The solid was recrystallised from hot MeOH to leave the purified product **8** as a purple/red solid (26 mg, 0.035 mmol, 29%).

Method B: To complex **1a** (130 mg, 0.205 mmol) was added KI (83 mg, 0.50 mmol) and anhydrous IPA (10 mL). The reaction was stirred at reflux (80°C) for 2 hours and then cooled to room temperature. The solid was collected by filtration to give the product as a red solid (67 mg, 0.092 mmol, 45%). Mp 198°C (decomposed); $[\alpha]_D^{28}$ +13 (*c* 0.05 in $CHCl_3$) (*R,R*); (found (ESI): M^+ - I + H, 601.1466. $C_{31}H_{36}N_2O_2RuS$ requires M, 601.1465); υ_{max} 3494, 3213,2935, 1455, 1263, 1128, 1084, 1059, 937, 906, 806, 701, 659 cm^{-1}; δ_H (400 MHz, MeOD) 7.14-7.11 (5H, m, C*H*Ar), 6.93-6.90 (2H, m, C*H*Ar), 6.86-6.79 (3H, m, C*H*Ar), 6.69-6.61 (4H, m, C*H*Ar), 5.74-5.72 (1H, m, C*H*Ar-Ru), 5.68-5.65 (2H, m, C*H*Ar-Ru), 5.57 (1H, br s, C*H*Ar-Ru), 4.61 (1H, br s, NH_2), 4.01-3.98 (1H, m, C*H*NTs), 3.78-3.75 (1H, m, C*H*NH_2), 3.34 (2H, br s, MeOH, C*H*$(CH_3)_2$ and *NH*$_2$ overlapping), 2.56 (3H, s, *p*-C*H*$_3$$(C_6H_4)SO_2$), 2.27 (3H, s, ^{i}Pr-$(C_6H_4)$-C*H*$_3$), 1.42 (6H, d *J*, 6.8 Hz, CH(C*H*$_3$)$_2$); δ_C (150 MHz, *d*$_6$-DMSO) δ_C (150 MHz, DMSO) 140.35 (*C*Ar), 139.79 (*C*Ar), 138.99 (*C*Ar), 135.03 (*C*Ar), 129.45 (2 *C*HAr), 129.28 (*C*HAr), 128.63 (4 *C*HAr), 128.12 (2 *C*HAr), 127.32 (2 *C*HAr), 126.83 (2 *C*HAr), 126.56 (*C*HAr), 88.25 (*C*HAr-Ru), 86.45 (*C*HAr-Ru), 73.77 (*C*HAr-Ru), 72.04 (*C*HAr-Ru), 55.39 (*C*Ar-Ru), 40.53 (*C*Ar-Ru), 40.42 (*C*H), 40.39 (*C*H), 33.46 (2 *C*H_3), 24.46 (*C*H), 23.63 (*C*H_3), 21.21 (*C*H_3); *m/z* (ESI) 601.0 (M^+ + 1).

3.5 *X-ray crystallographic data for (S,S)-**7** (CCDC 1016062) and (b) (R,R)-**8** (CCDC 1016063).*

The full data is given in the .cif files for each complex. CCDC1016062 tethered RuI complex **7** with one molecule of MeOH. Formula: $C_{30}H_{31}IN_2O_2RuS.0.5(CH_3OH)$, unit Cell Parameters: a 11.7063(2) b 9.65672(16) c 13.5915(3), P21. CCDC1016063 –

non-tethered RuI complex **8**. Formula: $C_{31}H_{35}IN_2O_2RuS$, Unit Cell Parameters: a 8.8762(6) b 13.4321(7) c 26.712(3) P212121.

3.6 *Pressure hydrogenation of ketones catalysed by tethered ruthenium catalysts (S/C 500/1).*

To an oven dried test tube was added the catalyst (0.002 mmol) and ketone (1 mmol). To the test tube was then added anhydrous MeOH (2 mL) and the tube was transferred to the Parr reactor which was then sealed and purged with H_2 before being charged with H_2 to 30 bar. The reactor was then heated to 60°C and the reactions stirred at this temperature and pressure for the required time. The reactions were cooled, the pressure released and the reaction mixture filtered through silica with 1:1 EtOAc:petroleum ether 40-60. The filtrate was then analysed by GC. The remainder of the filtrate was concentrated under vacuum to leave the alcohol product which was then analysed by ^1H and ^{13}C NMR and its optical rotation obtained. Where necessary the product was purified by column chromatography (silica gel, 0-50% EtOAc in petroleum ether 40-60).

3.7 *Reduction of ketones using the tethered catalysts by asymmetric transfer hydrogenation.*

Formic acid/triethylamine FA/TEA (5:2 azeotropic mixture) (1mL) and ketone (1.5 mmol) were added to a flask containing catalyst (0.003 mol, 500:1) and this was heated to 40ºC. Aqueous $NaHCO_3$ (5 mL) was added and the product was extracted with EtOAc (3 x 5 mL). The EtOAc was dried with Na_2SO_4, filtered and the solvent removed to give the alcohol product.

3.8 *Analysis of reduction products.*

GC Sample preparation: A small amount of the reaction solution was removed by syringe and filtered through a narrow column of silica with 1:1 EtOAc:petroleum ether 40-60. The filtrate was dried under reduced pressure. 2 mg of the residue was then dissolved in EtOAc (1 mL) and 1 μL of this solution was injected on the GC.

3.9 *(R)-1-Phenylethanol.*

Enantiomeric excess and conversion determined by GC analysis: Chrompac cyclodextrin-β-236M-19 50m x 0.25 mm x 0.25 μm, T = 115°C, P = 15psi H_2, det = FID 220°C, inj = 220°C, ketone 9.2 min., *R* isomer 14.2 min., *S* isomer 15.6 min. $[\alpha]_D^{24}$ +64.5 (*c* 1.0 in $CHCl_3$) 96.7% ee. (*R*) (lit.[96] $[\alpha]_D^{27}$ +54.9 (*c* 1.0 in $CHCl_3$) 96% ee. (*R*)); δ_H (400 MHz, $CDCl_3$) 7.37-7.31 (4H, m, C*H*Ar), 7.28-7.24 (1H, m, C*H*Ar), 4.87 (1H, q, *J* 6.5 Hz, C*H*), 2.00 (1H, br s, O*H*), 1.48 (3H, d, *J* 6.5 Hz, CH_3).

4 Conclusions

In conclusion, we have reported the synthesis and characterisation of the iodide-containing derivatives of the well-established class of arene/Ru(II)/TsDPEN catalysts which are widely used for asymmetric reduction of ketones and imines. It was found that whilst the new catalysts are highly efficient for the asymmetric transfer hydrogenation of a representative ketone, they are less active in the asymmetric hydrogenation reaction.

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Supplementary data. This contains the NMR spectra for compounds **7** and **8**, X-ray crystallographic data and the method for the determination of the ee of 1-phenylethanol.

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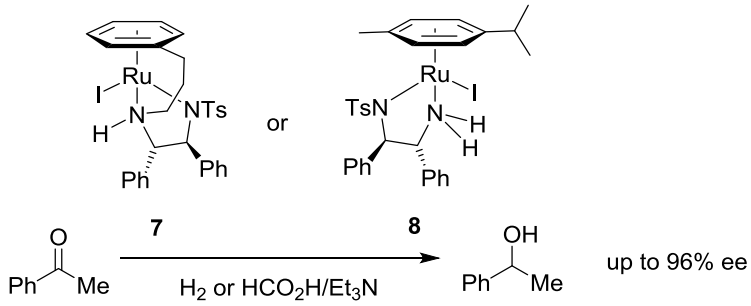
Graphical abstract

Two new Ru(II) complexes have been prepared and evaluated as catalysts for the asymmetric reduction of acetophenone under both transfer and pressure hydrogenation conditions. The complexes are iodide-containing derivatives of the widely-adopted arene/Ru(II)/TsDPEN catalysts commonly used in these transformations.



Highlights

- Iodide-containing arene/Ru(II)/TsDPEN complexes have been prepared and characterise.

- The new catalysts work efficiently as catalysts in asymmetric transfer hydrogenation an asymmetric hydrogenation of acetophenone.

- The iodide complexes are equally efficient in the ATH reaction, but less active in the AH reaction compared to the chloride or triflate derivatives.