Journal Name

ARTICLE

An air and moisture tolerant iminotrihydroquinoline-ruthenium(II) catalyst for the transfer hydrogenation of ketones

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Abstract: Reaction of 8-amino-5,6,7,8-tetrahydroquinoline with $RuCl_2(PPh_3)_3$ at room temperature affords the ruthenium(II) chelate $(8\text{-}NH_2\text{-}C_9H_{10}N)RuCl_2(PPh_3)_2$ (**E**), in which the two triphenylphosphine ligands are disposed mutually *cis*. By contrast, when the reaction is performed at reflux ligand oxidation/dehydrogenation occurs along with *cis-trans* reorganization of the triphenylphosphines to form the 8-imino-5,6,7-trihydroquinoline-ruthenium(II) complex, $(8\text{-}NH\text{-}C_9H_9N)RuCl_2(PPh_3)_2$ (**F**). Complex **F** can also be obtained in higher yield by heating a solution of **E** alone to reflux. Comparison of their molecular structures highlights the superior binding properties of the bidentate imine ligand in **F** over its amine-containing counterpart in **E**. Both complexes are highly effective in the transfer hydrogenation of a wide range of alkyl-, aryl- and cycloalkyl-containing ketones affording their corresponding secondary alcohols with loadings of as low as 0.1 mol%. Significantly, **F** can deliver excellent conversions even in bench quality 2-propanol in reaction vessels open to the air, whereas the catalytic efficiency of **E** is diminished by the presence of air but only operates efficiently under inert conditions.

Introduction

The hydrogenation of unsaturated carbonyl and imine substrates has attracted considerable attention with regard to developing more sustainable, efficient and environmentally friendly processes.[1,2] Besides the significant breakthrough made by Noyori,[3] some recent developments in metal-mediated transfer hydrogenation[4-7] have been achieved through ligand modification of Ru-[1b,4i-n,6] and Os-catalysts,[1b,4b,c,5e] and in particular those based on phosphine and amino-containing alkylpyridines by the groups of Baratta,[4] Yu[6] and Mezzetti[7] (see **A** – **D** in Chart 1). Driven by demand for such processes that can operate effectively in the presence of moisture and oxygen,[8] good stability, air/water tolerance and straightforward preparation represent desirable features of a potential catalyst.

However, to the best of our knowledge, there are only limited reports of efficient transfer hydrogenation catalysts that are capable of tolerating such conditions.[1a-b]

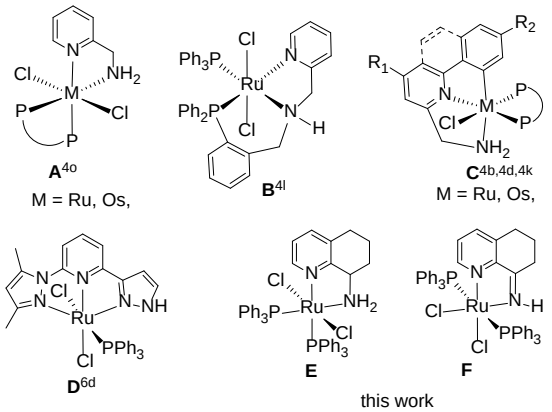

Chart 1. Ruthenium and osmium complexes that have been used effectively in transfer hydrogenation (**A** – **D**) along with the systems to be developed in this work (**E** and **F**)

In this article, we are concerned with the preparation of two structurally related ruthenium(II) complexes namely **E** and **F** (Chart 1), with the aim to explore their independent use in the transfer hydrogenation of ketones to secondary alcohols. In particular, we are interested in investigating how the distinct imine and primary amine donors impact on catalytic efficiency as well as on their tolerance to air and moisture conditions. Full details of the synthetic procedures for complexes and ligands are presented as is

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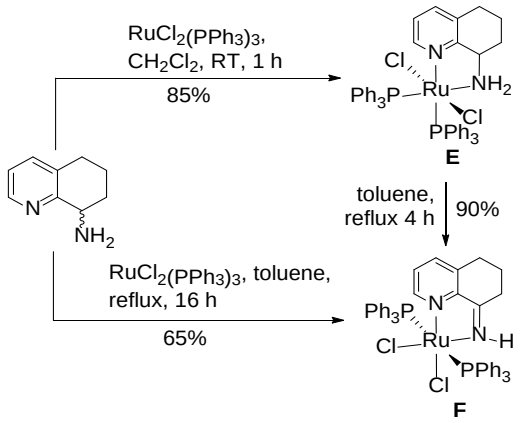
Electronic Supplementary Information (ESI) available: Figures, tables, and giving NMR spectra of the new complexes and a selected substrate; CCDC 1586459 for **E**, CCDC 1586458 for **F**. For ESI and crystallographic data in CIF or other electronic format see DOI:

an in-depth investigation of their catalytic performance in transfer hydrogenation of a diverse range of alkyl-, aryl- and cycloalkyl-containing ketones.

Results and discussion

Synthesis and characterization



Scheme 1. Synthetic routes to **E** and **F**

In the first instance we focused on synthesizing (8-NH_2-$C_9H_{10}N$)$RuCl_2(PPh_3)_2$ (**E**) by reacting 8-amino-5,6,7,8-tetrahydroquinoline[9] with $RuCl_2(PPh_3)_3$.[10] Pleasingly, with dichloromethane as the solvent and under ambient conditions, **E** was isolated in 85% yield after one hour (Scheme 1). With a view to potentially forming the *trans* geometrical isomer of **E**, we also performed the reaction in toluene at reflux over 16 hours. Unexpectedly, on work-up the oxidized/dehydrogenated imine-containing product, (8-NH-C_9H_9N)$RuCl_2(PPh_3)_2$ (**F**), was isolated in 65% yield (Scheme 1). Moreover, heating **E** in toluene at reflux for 4 hours also resulted in this ligand oxidation/dehydrogenation to give **F** in 90% yield (Scheme 1). Indeed, monitoring of this reaction by ^{31}P NMR spectroscopy in $CDCl_3$ showed that full conversion to **F** could be achieved after just one hour at 100 °C (in a closed reactor) (see SI). Both ruthenium complexes have been characterized by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy, elemental analysis and have been the subject of single crystal X-ray diffraction studies.

The 8-amino-5,6,7,8-tetrahydroquinoline ligand itself, is not commercially available and can be prepared in two steps from 6,7-dihydro-5*H*-quinolin-8-one using a literature procedure.[9,11-13] As an additional purification step, the resulting oil was converted to its salt, 8-amino-5,6,7,8-tetrahydroquinoline hydrochloride, before being neutralized to afford 8-amino-5,6,7,8-tetrahydroquinoline in high purity in 42% yield.

Crystals of **E** and **F** suitable for the X-ray determinations were grown by the slow diffusion of *n*-pentane into their corresponding dichloromethane solutions. Views of each structure are shown in Figures 1 and 2; selected bond distances and angles are given in the figure captions.

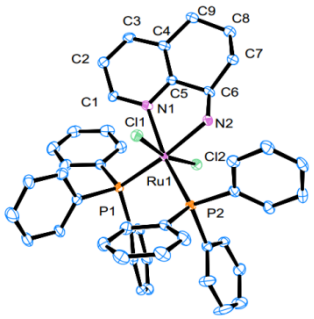


Figure 1. ORTEP representation of **E**. The thermal ellipsoids are shown at the 30% probability level; hydrogen atoms have been omitted for clarity. Bond lengths [Å] and angles [deg]: Ru1-Cl1 2.4239(17), Ru1-Cl2 2.4294(17), Ru1-P1 2.3258(16), Ru1-P2 2.3535(16), Ru1-N1 2.152(5), Ru1-N2 2.161(5), N2-C6 1.473(8); P2-Ru1-Cl2 96.80(6), P2-Ru1-Cl1 87.97(6), Cl1-Ru1-Cl2 167.74(6), P1-Ru1-P2 98.09(6), N1-Ru1-Cl1 82.45(15), N1-Ru1-Cl2 90.47(15), N2-Ru1-Cl2 84.47(16), N2-Ru1-Cl1 84.07(16), N2-C6-C5 108.2(5).

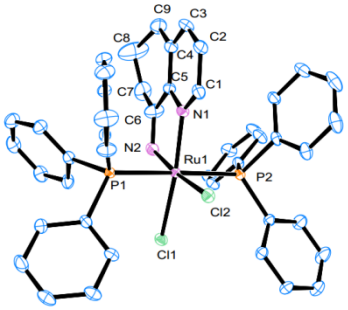


Figure 2. ORTEP representation of **F**. The thermal ellipsoids are shown at the 30% probability level; hydrogen atoms have been omitted for clarity. Bond lengths [Å] and angles [deg]: Ru1-Cl1 2.4451(9), Ru1-Cl2 2.4440(8), Ru1-P1 2.3606(8), Ru1-P2 2.3678(8), Ru1-N1 2.057(3), Ru1-N2 2.059(3), C6-N2 1.319(5); P1-Ru1-Cl1 89.37(3), P1-Ru1-Cl2 88.16(2), Cl1-Ru1-Cl2 96.77(3), P1-Ru1-P2 176.56(3), N1-Ru1-Cl1-168.53(8), N1-Ru1-Cl2 94.70(8), N2-Ru1-Cl1 89.46(9), N2-Ru1-Cl2,173.75(10), N2-C6-C7 114.8(3).

Both structures consist of a ruthenium center surrounded by two nitrogen atoms belonging to a neutral N,N-chelating ligand, two chlorides and two triphenylphosphines to complete a distorted octahedral arrangement. The key difference between the structures relates to the nature of the N,N ligand (*viz.* 8-amino-5,6,7,8-tetrahydroquinoline in **E** and 8-imino-5,6,7-trihydroquinoline in **F**) and the disposition of each pair of phosphines or chlorides. Specifically in **E** the phosphines are *cis* [P1-Ru1-P2 98.09(6)°] and the chlorides *trans* [Cl1-Ru1-Cl2 167.74(6) °], while in **F** the phosphines are *trans* [P1-Ru1-P2 176.56(3)°] and the chlorides *cis* [Cl2-Ru1-Cll 96.77(3) °]. With regard to the N,N ligand, the N1-C5-C6-N2 torsion angles (-30.14° **E**, 3.85° **F**) highlight the deviation from co-planarity in **E** as a result of the sp^3-hybridized CH-NH_2 carbon (N2-C6-C5 108.2(5)°); in **F** this distortion is minimized with the incorporation of an imine C=NH unit into the chelate ring. Comparison of the C6-N2 distances in **E** (1.473(8) Å) and **F** (1.319(5) Å) further supports the presence of an imine unit in **F**. This variation in donor atoms of the N,N-ligand also affects the Ru-N distances

with those in **E** (2.152(5), 2.161(5) Å) longer than in **F** (2.057(3), 2.059(3) Å), underlining the more effective binding of the 8-imino-5,6,7-trihydroquinoline in **F**. There are also some differences in the Ru-P distances with those in **E** [2.3258(16), 2.3535(16) Å] shorter than those in **F** (2.3606(8), 2.3678(8) Å). Likewise, the Ru-Cl distances in **E** (2.4294(17), 2.4239(17) Å) are shorter than those in **F** (2.4451(9), 2.4440(8) Å). There are no intermolecular contacts of note.

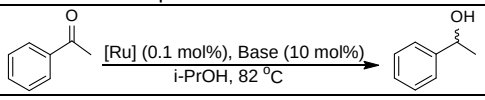
The $^{31}P\{^{1}H\}$ NMR spectrum (recorded in $CDCl_3$) of **E** shows two mutually coupled doublets at δ 42.98 and δ 39.09 with a two-bond coupling constant of *ca.* 31 Hz, consistent with a *cis* arrangement of the two phosphine ligands.[4o,10] In its ^{1}H NMR spectrum, signals for the aliphatic CH_2 and CH protons belonging to 8-amino-5,6,7,8-tetrahydroquinoline ligand are seen as multiplets in the range δ 1.5 - 3.5. In the $^{13}C\{^{1}H\}$ NMR spectrum, the *C*HN carbon is seen at δ 58.97 for **E** which is only shifted slightly downfield with respect to that seen in the free ligand (δ 47.09). For **F** the $^{31}P\{^{1}H\}$ NMR spectrum shows two relatively close doublets at δ 69.31 and 66.49 with a ^{2}J(PP) mutual coupling of *ca.* 113 Hz indicating that the two P atoms are in slightly different environments; this inequivalency is likely due to non-planarity of the saturated ring in the 8-imino-5,6,7-trihydroquinoline chelating ligand. As with **E**, the ^{1}H NMR spectrum of **F** shows signals for the CH_2 protons of the N,N ligand as multiplets between δ 1.57 and 2.61, while the C=N*H* proton is assigned as a 1H-singlet at δ 8.47. In the $^{13}C\{^{1}H\}$ NMR spectrum, the *C*=NH carbon is seen clearly at δ 160.60. Related ligand dehydrogenation involving the transformation of a $R_2CH\text{-}NH_2$ unit to a R_2C=NH group has been previously reported for complexes containing pyridylalkylamines and is likely that conversion of **E** to **F** follows in a similar manner.[14]

Catalytic evaluation in transfer hydrogenation

To explore the potential of the 8-amine-containing **E** and imine **F** to serve as catalysts for the transfer hydrogenation of ketones, **E** was used in the first instance to allow an optimization of the conditions (Table 1). The transfer hydrogenation of acetophenone to 1-phenylethanol was chosen as the transformation to be screened and a preliminary study initiated to determine the optimal catalyst loading, type of base as well as the most suitable loading of base.

The reactions were typically performed with freshly distilled and degassed 2-propanol at 82 °C over 30 minutes under an atmosphere of nitrogen. Initially, a selection of different bases, *t*-BuOK, *t*-BuONa, NaOMe, KOH and NaOH, was investigated with the loading of base set at 10 mol% and the loading of **E** fixed at 0.1 mol% (Table 1). Of the five bases, *t*-BuOK was found to achieve the best conversion of 94% (entry 2, Table 1); a similarly high conversion was notably achieved when **F** was used in place of **E** with *t*-BuOK again as the base (entry 9, Table 1). Meanwhile the blank tests performed in the absence of base (entry 1, Table 1) or without ruthenium catalyst showed no conversion to 1-phenylethanol (entry 8, Table 1). In addition, it was found that the combination of $RuCl_2(PPh_3)_2$ and 8-amino-5,6,7,8-tetrahydroquinoline as catalyst exhibited only a modest conversion (44%, entry 10, Table 1).

Table 1. The effect of base and catalyst on the transfer hydrogenation of acetophenone[a]

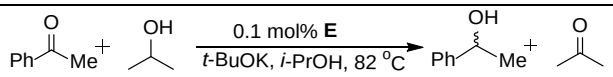


Entry	Catalyst	Base	Conversion (%)[b]
1	**E**	None	--
2	**E**	*t*-BuOK	94
3	**E**	*t*-BuONa	87
4	**E**	NaOMe	84
5	**E**	*i*-PrONa	63
6	**E**	KOH	65
7	**E**	NaOH	63
8	None	*t*-BuOK	--
9	**F**	*t*-BuOK	92
10	$RuCl_2(PPh_3)_3$/ 8-NH_2-$C_9H_{10}N$	*t*-BuOK	44

[a] Conditions: 8 mmol acetophenone, 8 μmol catalyst (0.1 mol%), 0.8 mmol base (10 mol%), 20 mL *i*-PrOH, 82 °C, 30 minutes.
[b] Determined by GC: based on acetophenone consumption with dodecane as the internal standard.

To ascertain the optimal quantity of *t*-BuOK required, the conversion of acetophenone was monitored with the amount of **E** fixed at 0.1 mol% and the loading of *t*-BuOK varied between 2 and 20 mol% (Table 2). A peak of 94% conversion was observed after 30 minutes using 10 mol% of *t*-BuOK.

Table 2. Transfer hydrogenation of acetophenone using **E** at different loadings of *t*-BuOK[a]



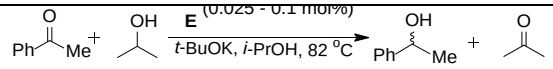
Entry	mol% of *t*-BuOK	Conversion (%)[b]
1	2	65
2	5	85
3	10	94
4	20	92

[a] Experimental conditions: 8 mmol acetophenone, 8 μmol **E**, 20 mL *i*-PrOH, monitored at 82 °C after 30 minutes.
[b] Determined by GC analysis: based on acetophenone consumption with dodecane as the internal standard.

With the amount of *t*-BuOK now fixed at 10 mol%, the amount of **E** was changed between 0.1 and 0.025 mol% resulting in conversions of 94% (0.1 mol%), 93% (0.05 mol%), 58% (0.03 mol%) and 16% (0.025 mol%) (Table 3). This lowering in conversions may be ascribed to the quicker decomposition of the lower concentration active species under strongly basic conditions.[8] Overall the optimal amounts of catalyst and base for the transfer hydrogenation were established as 0.1 mol% **E** and 10 mol% *t*-BuOK.

In order to investigate the tolerance of the ruthenium catalyst to air and moisture, the dry and degassed 2-propanol used initially was replaced with bench 2-propanol (analytical reagent) and the transfer hydrogenation of acetophenone carried out in the air. It was observed that the efficiency of **E** was greatly affected and the conversion dramatically decreased to 51% after 30 minutes with little improvement after 60 minutes (entry 1, Table 4). By contrast,

Table 3. Transfer hydrogenation of acetophenone at different catalyst loadings of **E** with *t*-BuOK as base[a]



Entry	mol% of **E**	Conversion (%)[b]
1	0.1	94
2	0.05	93
3	0.03	58
4	0.025	16

[a] Reaction conditions: 8 mmol acetophenone, 0.8 mmol *t*-BuOK, 20 mL *i*-PrOH, monitored at 82 °C after 30 minutes.
[b] The conversion to the product was measured by GC: based on acetophenone consumption with dodecane as the internal standard.

Table 4. Effects of air and water on the transfer hydrogenation of acetophenone using **E** or **F**

Entry	Cat.	atm.	H_2O	Conversion (%)		
				10 min	30 min	60 min
1[a]	**E**	air	none	44	51	54
2[a]	**F**	air	none	75	92	92
3[a]	**E**	N_2	none	92	94	94
4[b]	**E**	N_2	5 μL	91	93	93
5[b]	**E**	N_2	10 μL	83	88	91

[a] Conditions: 8 mmol acetophenone, 8 μmol catalyst (0.1 mol%), 0.8 mmol *t*-BuOK, 20 mL i-PrOH, 82 °C and open to the air or N_2; conversion was monitored by GC after 10, 30 and 60 minutes.
[b] Conditions as in 'a' but with distilled and degassed *i*-PrOH.

replacing **E** with **F** with the conditions of the transfer hydrogenation otherwise the same (bench 2-propanol and an air atmosphere), acetophenone was converted to 1-phenylethanol in 92% yield (entry 2, Table 4). It is apparent that **F** is less sensitive to oxygen and apparently more tolerant to the conditions than **E**. Indeed, when oxygen gas was separately passed through a solution of **E** and *t*-BuOK in 2-propanol for 1 hour at 82 °C, triphenylphosphine oxide (*ca.* 95%) was isolated (see SI) and what was presumed to be insoluble ruthenium oxide; similar deactivation of iridium catalysts has been reported.[8] In addition, monitoring of the $^{31}P\{^1H\}$ NMR spectrum of **E** during this catalyst deactivation at intervals of 1 min, 5 min, 10 min and 30 min (see SI), also showed the gradual formation of triphenylphosphine oxide. Alternatively, if the transfer hydrogenation using **E** was conducted under nitrogen with dry degassed 2-propanol, a 94% conversion of acetophenone was noted (entry 3, Table 4). To examine the influence of water, the reaction mediated by **E** was performed under nitrogen with controlled amounts of water introduced (5 μL: entry 4, Table 4) and (10 μL: entry 5, Table 4). Only slightly lower conversions (entries 4 and 5, Table 4) were observed suggesting that **E** displays some tolerance to moisture.

To examine the general applicability of **F** as an air and moisture tolerant catalyst, a broad range of ketone substrates were screened including aryl, alkyl and cycloalkyl examples differing in their electronic and steric properties (entries 1-20, Table 5). Typically, the catalytic runs were performed in the air using the optimal conditions established of 8 mmol ketone, 0.1 mol% **F**, 10 mol% *t*-BuOK at 82 °C over 30 minutes with bench 2-propanol. To complement this study, **E** was employed in a parallel investigation using the same ratio of substrate: catalyst: base, but under inert conditions and using dry and degassed solvent. Notably, the hydrogenation of all twenty ketones was achieved using **F** with conversions between 60 and 100% (entries 1-20, Table 5). Ketones incorporating aryl groups containing both electron withdrawing (entries 1-4, Table 5) and donating groups (entry 7, Table 5) were equally well hydrogenated. Similarly, ketones containing *n*-alkyl groups with and without halide substituents could be readily transformed (entries 8, 11, 12, 13, Table 5). In the same way, the cyclic ketones, cyclohexanone, cyclopentanone, adamantan-2-one, cyclododecanone along with cyclic systems appended with ester and acetal groups could be transformed to their corresponding alcohols with good conversions (entries, 14-17, 19, 20, Table 5). Indeed, the lowest conversion of 60% was obtained with the bis(arene)-fused cyclopentanone, 9-fluorenone. Inspection of the results obtained using **E** show good conversions albeit obtained under more rigorous conditions. Furthermore, high isolated yields of 90 and 88% of *tert*-butyl-4-hydroxypiperidine-1-carboxylate were obtained using both **E** and **F**, respectively (entry 17, Table 5). Clearly, both electronic and steric effects associated with the particular ketone influence the reactivity of **E** and **F**. For example, the electron-rich aromatic ketones (entries 8 - 10, Table 5) catalyzed by **E** gave somewhat higher yields of the corresponding alcohols when compared to that seen with **F**. Overall, this study highlights not only the versatility of imine-containing **F** as a transfer hydrogenation catalyst but also its ability to operate effectively in air and moisture-containing environments, conditions that lend themselves to industrial applications.

Conclusions

In summary, synthetic routes to 8-amino-5,6,7,8-tetrahydro-quinoline-containing **E** and imino-5,6,7-trihydroquinoline-containing **F** have been developed with the latter accessible by a dehydrogenative pathway involving **E**. Each complex has been independently assessed as a catalyst in the transfer hydrogenation of ketones to give secondary alcohols. Imine-containing **F** has proved an oxygen-stable catalyst for transfer hydrogenation allowing the transformations to be effectively carried out in the open air with bench solvent. By contrast, amine-containing **E** undergoes catalyst deactivation when exposed to air but is nevertheless an efficient catalyst in the absence of air and under dry conditions. Furthermore, the scope of **E** and **F** to mediate the transfer hydrogenation of more than twenty examples of ketones including aryl and alkyl ones as well as cycloalkyl ketones have been studied resulting in the formation of their corresponding alcohol products in good to high yields.

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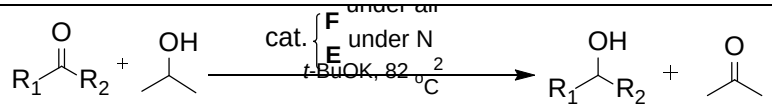
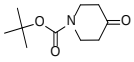
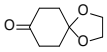
Table 5. Exploring the substrate scope of **F** as an air and moisture tolerant catalyst; the corresponding data for **E** under inert conditions are also tabulated[a]



Entry	R_1	R_2	Conversion (%) using **F**[b]	TOF (h^{-1})	Conversion (%) using **E**[c]	TOF (h^{-1})
1	Me	3-BrC_6H_4	93	1860	97	1940
2	Me	4-BrC_6H_4	96	1920	96	1920
3	Me	4-FC_6H_4	91	1820	92	1840
4	Me	2,4-$Cl_2C_6H_3$	95	1900	99	1980
5	Et	Ph	94	1880	90	1800
6	Et	3-ClC_6H_4	100	2000	86	1440
7	Et	4-MeC_6H_4	90	1800	89	1780
8	Me	$PhCH_2CH_2$	91	1820	96	1920
9	Ph	Ph	91	1820	93	1860
10	Me	1-naphthyl	88	1760	94	1880
11	Me	$CH_3(CH_2)_5$	96	1920	93	1860
12	Me	$Cl(CH_2)_4$	93	1860	93	1860
13	Et	Et	100	2000	94	1880
14	-$CH_2(CH_2)_3CH_2$-		100	2000	100	2000
15	-$CH_2(CH_2)_2CH_2$-		92	1840	94	1880
16	-$CH_2(CH_2)_9CH_2$-		76	1520	70	1400
17			96	1920	99	1980
18			60	1200	63	1260
19			95	1900	96	1920
20			99	1980	99	1980

[a] Reaction conditions: 8 mmol ketone, 8 μmol **E** or **F**, 0.8 mmol *t*-BuOK, 20 mL *i*-PrOH, monitored at 82 °C over 30 minutes.
[b] Using bench *i*-PrOH in the air; the conversion was determined by GC: based on ketone consumption with dodecane as the internal standard.
[c] Using distilled and degassed *i*-PrOH under nitrogen; the conversions was determined by GC: based on ketone consumption with dodecane as the internal standard.

Experimental section

General information

All manipulations involving ruthenium complexes were carried out under a nitrogen atmosphere using standard Schlenk techniques. 2-Propanol (analytical reagent) was either used directly from the bottle or was dried over sodium wire, distilled and stored under nitrogen before being degassed prior to use. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and ^{31}P (202 MHz) spectra were recorded on a Bruker AVIII–500 NMR spectrometer. GC analysis was carried out on an Agilent 6820 instrument using a polar capillary column (part number 19091N-113 HP-INNOWAX): injector temp. 300 °C; detector temp. 300 °C; column temp. 40 °C; withdraw time 2 min, then 20 °C/min to 270 °C over 20 min. The percentage conversions were determined based on the consumption of the ketone, with dodecane as an internal standard.[15-17] Complex $RuCl_2(PPh_3)_3$ was synthesized according to the literature procedure.[10]

Synthesis of 8-amino-5,6,7,8-tetrahydroquinoline

The two-step procedure was based on that described in the literature.[9,11-13] In the first step, 1-phenylethanamine (10.4 mL, 82.2 mmol) was added to a stirred solution containing 6,7-dihydro-5H-quinolin-8-one (12.0 g, 82.2 mmol) and $NaBH(OAc)_3$ (25.6 g, 120.8

mmol) in 1,2-dichloroethane (100 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 16 h (monitored by TLC) before being quenched with a saturated aqueous solution of $NaHCO_3$ until basic. The mixture was diluted with water and extracted with ethyl acetate (3 x 50 mL). The organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to afford amine intermediate 1-phenylethyl (5,6,7,8-tetrahydroquinolin-8-yl)amine as a yellow liquid (20.0 g, 95%). In the second step, the amine was taken up in acetic acid (4 mL) and dry MeOH (200 mL) and the solution flushed with nitrogen and transferred to a stainless steel 250 mL autoclave, equipped with a magnetic stirring bar. 10% Palladium on carbon (5.5 g) was then added to the mixture. The autoclave was purged by three cycles of pressurization/venting with hydrogen gas (10 bar), then pressurized with hydrogen (35 bar), sealed and disconnected from the hydrogen source. The vessel was stirred and heated to 50 °C (bath temperature) for 18 h. After cooling to room temperature and venting the hydrogen pressure, the reaction mixture was filtered and concentrated under reduced pressure to afford a green oil. Concentrated HCl (35% wt%) (8 - 10 mL) was then added dropwise followed by cold MeOH to give 8-amino-5,6,7,8-tetrahydroquinoline hydrochloride as a white solid. The free base could be formed by treating the HCl salt with an ammonium hydroxide solution and dichloromethane to give 8-amino-5,6,7,8-tetrahydroquinoline as a yellow oil (5.5 g, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.7 Hz, 1H, H_{Py}), 7.36 (dd, *J* = 7.7, 1.5 Hz, 1H, H_{Py}), 7.06 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Py}), 4.00 (dd, *J* = 7.8, 5.4 Hz, 1H, C*H*), 2.86 – 2.70 (m, 2H, CH_2), 2.23-2.16 (m, 1H, CH_2), 2.03 (s, 2H, NH_2), 2.00 – 1.91 (m, 1H, CH_2), 1.83 – 1.65 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.61, 147.08, 136.80, 131.63,121.73, 51.43 (CH_2*C*H), 32.06, 29.07, 19.99.

Synthesis of E[40]

$RuCl_2(PPh_3)_3$[10] (400 mg, 0.42 mmol) and 8-amino-5,6,7,8-tetrahydroquinoline (64.5 mg, 0.44 mmol) were treated with dichloromethane (5 mL) and the suspension stirred at room temperature for 1 h. The mixture was then concentrated and *n*-pentane (4 mL) added to afford a yellow precipitate. The precipitate was filtered, washed with *n*-heptane (3 × 1 mL) and dried to give **E** as a yellow solid (0.302 g, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.9 Hz, 1H, H_{Py}), 7.55 (t, *J* = 7.9 Hz, 5H, H_{Ph}), 7.43 (t, *J* = 8.2 Hz, 5H, H_{Ph}), 7.37 – 7.31 (m, 2H, H_{Ph}), 7.20 (dd, *J* = 15.7, 7.7 Hz, 7H, H_{Ph}), 7.08 – 7.01 (m, 7.6 Hz, 11H, H_{Ph}), 6.97 (t, *J* = 7.7 Hz, 1H, H_{Py}), 6.58 – 6.50 (m, 1H, H_{Py}), 3.35 (dd, *J* = 5.0, 2.7 Hz, 1H, C*H*), 3.06 (dd, *J* = 7.5, 6.1 Hz, 1H, CH_2), 2.78-2.65 (m, 2H, CH_2), 2.05 – 1.74 (m, 3H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.49, 135.23, 135.15, 134.68, 134.61, 133.82, 133.33, 133.26, 128.80, 127.46, 127.39, 127.30, 127.23, 127.10, 127.03, 58.97 (CH_2*C*H), 32.57, 27.08, 21.65. ^{31}P NMR (202 MHz, $CDCl_3$) δ 42.98 (d, *J* = 31.5 Hz), 39.09 (d, *J* = 30.9 Hz). Anal. Calcd for $C_{45}H_{41}Cl_2N_2P_2Ru$: C, 64.06; H, 4.90; N, 3.32%. Found: C, 64.26; H, 4.95; N, 3.37%.

Synthesis of F

$RuCl_2(PPh_3)_3$ (400 mg, 0.42 mmol) and 8-amino-5,6,7,8-tetrahydroquinoline (64.5 mg, 0.44 mmol) were treated with toluene (10 mL) and stirred for 16 h at 110 °C. On cooling to room temperature the suspension was filtered and dried to give **F** as a red solid (0.220 g, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H, N*H*), 7.96 – 7.86 (m, 1H, H_{Py}), 7.69 – 7.48 (m, 8H, H_{Ph}), 7.24 – 7.14 (m, 12H, H_{Py}), 7.09 – 6.86 (m, 1H, H_{Py}), 6.63 – 6.39 (m, 1H, H_{Py}), 2.61 (d, *J* = 35.0 Hz, 2H, CH_2), 1.93 (q, *J* = 24.5 Hz, 2H, CH_2), 1.57 (d, *J* = 15.0 Hz, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.60 ($C_{C=NH}$), 156.23 (C_{py}), 136.64, 136.38, 135.39, 135.32, 134.84, 134.77, 134.37, 133.99, 133.83, 133.49, 133.42, 132.61, 132.24, 132.11, 128.96, 128.69, 128.63, 127.63, 127.47, 127.40, 127.27, 127.20, 122.18, 56.62 (CH_2*C*H), 33.22, 27.80, 21.28. ^{31}P NMR (202 MHz, $CDCl_3$) δ 69.31 (d, *J* = 111.2 Hz), 66.49 (d, *J* = 114.9 Hz). Anal. Calcd for $C_{45}H_{41}Cl_2N_2P_2Ru$: C, 64.06; H, 4.90; N, 3.32%. Found: C, 64.18; H, 4.98; N, 3.37%.

Catalyst Deactivation

Oxygen gas was bubbled through a mixture of **E** (200 mg, 0.23 mmol), *t*-BuOK (46 mg, 0.40 mmol) and 2-propanol (15 mL) using ultrasound stirring at 82 °C for 1 h. The reaction mixture was filtered and the resulting black polymeric solid washed with dichloromethane. The filtrate was then immediately cooled to 0 °C forming white crystals, which was shown by ^{1}H/^{13}C/^{31}P NMR spectroscopy as triphenylphosphine oxide (125 mg, 95%).[18] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 11.9, 7.7 Hz, 6H), 7.51 (t, *J* = 7.4 Hz, 3H), 7.43 (td, *J* = 7.6, 2.4 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 132.16, 132.08, 131.94, 131.92, 128.56, 128.46. ^{31}P NMR (202 MHz, $CDCl_3$) δ 29.14 (s).

General procedure for the transfer hydrogenation of ketones under nitrogen or air

(a) Under nitrogen. The selected ketonic substrate (8.0 mmol) was dissolved in dry and degassed 2-propanol (15 mL) under a nitrogen atmosphere and the solution stirred and heated to 82 °C. On reaching this temperature, a solution of base (0.16 – 1.6 mmol) in 2-propanol (4 mL) was introduced followed by a solution of either **E**, **F** (2.0 – 8.0 μmol) or $RuCl_2(PPh_3)_3$/8-amino-5,6,7,8-tetrahydroquinoline in 2-propanol (1 mL), taking the total volume of solvent to 20 mL. At the specified reaction time (10 – 60 min), 0.1 mL of the reaction mixture was sampled and immediately diluted with 0.5 mL of 2-propanol precooled to 0 °C, dodecane introduced, before being analyzed by GC. The composition of the reaction mixture was confirmed by running GC of a mixture of pure ketone, alcohol and dodecane.

(b) Under air. The selected ketonic substrate (8.0 mmol) was dissolved in bench 2-propanol (15 mL) in a vessel open to the air and the solution stirred and heated to 82 °C. On reaching this temperature, a solution of *t*-BuOK (0.8 mmol) in 2-propanol (4 mL) was introduced followed by a solution of either **E** or **F** (6.75 mg, 8.0 μmol) in 2-propanol (1 mL), taking the total volume of solvent to 20 mL. At the specified reaction time (10 – 60 min), 0.1 mL of the reaction mixture was sampled and immediately diluted with 0.5 mL of 2-propanol precooled to 0 °C, dodecane introduced, before being analyzed by GC. The composition of the reaction mixture was confirmed by running GC of a mixture of pure ketone, alcohol and dodecane.

Synthesis of *tert*-butyl 4-hydroxypiperidine-1-carboxylate (entry

17, Table 5)

(a) Using **F** as catalyst. *tert*-Butyl-4-oxopiperidine-1-carboxylate (1.59 g, 8.0 mmol) was dissolved in bench 2-propanol (15 mL) in a vessel open to the air and the solution stirred and heated to 82 °C. *t*-BuOK (89.6 mg, 0.8 mmol) in 2-propanol (4 mL) was introduced followed by a solution of **F** (6.75 mg, 8.0 µmol) in 2-propanol (1 mL). After 30 min of stirring at 82 °C, the solution was cooled to room temperature and concentrated to afford the crude product. The residue was purified by silica gel chromatography with petroleum ether/EtOAc (v:v = 3:1) as eluent to afford *tert*-butyl-4-hydroxypiperidine-1-carboxylate[19] as a light yellow oil (1.45 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.87 – 3.81 (m, 3H), 3.02 (ddd, *J* = 13.2, 9.7, 3.3 Hz, 2H), 2.17 (s, 1H), 1.92 – 1.76 (m, 2H), 1.48 (d, *J* = 12.6 Hz, 2H), 1.45 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.83, 79.55, 67.79, 41.24, 34.20, 28.44.

(b) Using **E** as catalyst. Using the same procedure and molar ratios as described in (a) above, but under an atmosphere of nitrogen and with dry and degassed 2-propanol as solvent and **E** as catalyst, *tert*-butyl-4-hydroxypiperidine-1-carboxylate[19] was isolated as a light yellow oil (1.41 g, 88%). The ^{1}H and ^{13}C NMR data obtained of the product were as given above.

X-ray crystallographic studies

The single crystal X-ray diffraction studies for **E** and **F** were carried out on a Rigaku Saturn 724+ CCD with graphite-monochromatic Mo-Kα radiation (λ = 0.71073 Å) at 173(2) K. Cell parameters were obtained by global refinement of the positions of all collected reflections (See SI, Table S1). Intensities were corrected for Lorentz and polarization effects and empirical absorption. The structures were solved by direct methods and refined by full-matrix least squares on F^2. All hydrogen atoms were placed in calculated positions. The structural solution and refinement were performed using the SHELXL-97 package.[20]

Associated Content

The authors declare no competing financial interest.

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Graphical for Table of Contents

An air and moisture tolerant iminotrihydroquinoline-ruthenium(II) catalyst for the transfer hydrogenation of ketones

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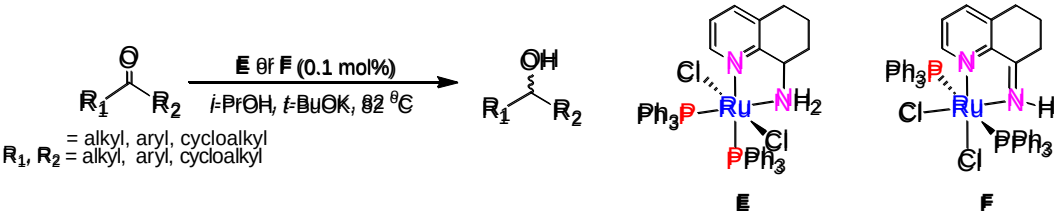

Both amine- and imine-containing **E** and **F** have been prepared by reactions of 8-amino-5,6,7,8-tetrahydroquinoline with $RuCl_2(PPh_3)_3$, the latter *via* a thermally induced route involving ligand oxidation/dehydrogenation. Both **E** and **F** are highly effective in the transfer hydrogenation of a wide range of ketones with **F** notably operating in bench quality 2-propanol and in vessels open to the air.