ChemComm

This article is part of the

Hydrogen web- based thematic issue

showcasing the latest research on all aspects of hydrogen generation, storage and activation

Guest editors: Professors Ferdi Schüth, Douglas Stephan, Daniel DuBois and Mary DuBois

All articles in this issue are gathered together online at www.rsc.org/chemcomm/hydrogen

The hydrogenation of molecules with polar bonds catalyzed by a ruthenium(II) complex bearing a chelating *N*-heterocyclic carbene with a primary amine donor†‡

Wylie W. N. O, Alan J. Lough and Robert H. Morris*

Received 19th July 2010, Accepted 3rd September 2010
DOI: 10.1039/c0cc02664f

The complex [RuCp*(C–NH_2)(py)]PF_6 bearing a chelating *N*-heterocyclic carbene with an NH_2 group (C–NH_2) is an active catalyst for the H_2-hydrogenation of ketones, an epoxide, ester and ketimine in basic solution. A maximum turnover frequency of 17 600 h^{-1} is achieved under mild reaction conditions (25 °C) and economical use of hydrogen (8 bar) while the TOF of a related complex with a phosphine–amine ligand is much smaller.

A powerful concept in the design of homogeneous hydrogenation catalysts is the heterolytic splitting of dihydrogen[1] across a transition metal–amido bond.[2] This provides a bifunctional metal–hydride and protic amine grouping for the efficient, selective reduction of polar bonds to produce valuable alcohols and amines.[2] Ruthenium(II) complexes bearing a phosphine–amine (P–NH_2) ligand that catalyze efficiently the hydrogenation of ketones,[3] imines,[4] esters,[5] and other polar bonds[6] may utilize this mechanism.

The notion of replacing a phosphine with an *N*-heterocyclic carbene (NHC) donor is attractive with the promise of a reduction in the toxicity of catalyst precursors and contaminants in the hydrogenated products. We are interested in the design of catalysts with chelating primary amine and NHC (C–NH_2) ligands (donor-functionalized NHC)[7] that resemble those of the P–NH_2 analogues to achieve this goal of greener chemistry. This is synthetically challenging since free NHC are known to react with amines.[8] We have reported the synthesis of a C–NH_2 ligand by the reduction of a nitrile-functionalized imidazolium salt in the presence of $NiCl_2$ yielding complex **1a** (Fig. 1).[9] Of note, only a few transition metal complexes with a C–NH_2 ligand have been structurally characterized (Fig. 1).[9,10] Complex **1b** has good activity in the transfer hydrogenation of acetophenone in 2-propanol.[9] This encouraging result prompted us to design other ruthenium(II)-based catalyst systems with such a chelating C–NH_2 ligand. Herein we present the synthesis and catalytic activity of the ruthenium(II) complex **2** bearing a C–NH_2 and an electron rich pentamethylcyclopentadienyl ligand (Cp*). The P–NH_2 analogue **3a** was also prepared for comparison. The related complex RuCp*(κ^2-$PPh_2CH_2CH_2NH_2$)Cl (**3b**), was prepared *in situ* by Ikariya and co-workers.[6a,11]

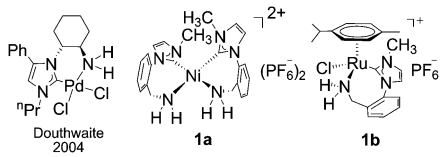
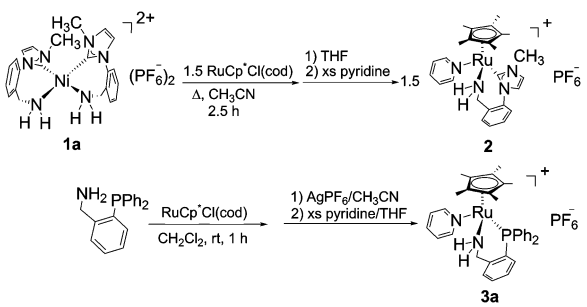


Fig. 1 Examples of metal complexes bearing a chelating *N*-heterocyclic carbene with a primary amine donor.

We previously showed that the transfer of the C–NH_2 ligand from **1a** to $[Ru(p\text{-cymene})Cl_2]_2$ in acetonitrile yielded **1b** in moderate yield.[9] Thus, a transmetalation reaction of **1a** and 1.5 equiv. of RuCp*(cod)Cl (cod = 1,5-cyclooctadiene) in acetonitrile, and subsequent workup in tetrahydrofuran (THF) and excess pyridine afforded complex **2** in 64% yield as oxygen-sensitive orange-red needles (Scheme 1). Of note, the use 2 equiv. of RuCp*(cod)Cl and subsequent workup in THF and toluene mixtures afforded crystallization of small amounts of [RuCp*(η^6-toluene)]PF_6[12] as a side product. Complex **3a** was synthesized from the reaction of 2-(diphenylphosphino)benzylamine[13] and RuCp*(cod)Cl in dichloromethane. Subsequent halide abstraction with $AgPF_6$ and addition of excess pyridine at ambient temperature afforded a moderately oxygen-sensitive yellow solid in 67% yield (Scheme 1).

Diagnostic NMR features include the $Ru–C_{carbene}$ resonance at 198.0 ppm in the ^{13}C NMR spectrum of complex **2** in acetone-d_6 and the PPh_2 peak at 44.7 ppm as a singlet in the $^{31}P\{^1H\}$ NMR spectrum of **3a** in CD_2Cl_2. These complexes demonstrate fluxional behaviour at ambient temperature (25 °C) due to restricted rotation of the $Ru–N_{pyridine}$ bond. Cooling these samples to −40 °C allows the observation of the aromatic protons, as well as the diastereotopic protons for the CH_2 linker between the primary amine group and the phenylene spacer (see ESI‡).



Scheme 1 Synthesis of ruthenium(II) complexes **2** and **3a**.

Davenport Laboratory, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario M5S 3H6, Canada. E-mail: rmorris@chem.utoronto.ca

† This article is part of a ChemComm 'Hydrogen' web-based themed issue.

‡ Electronic supplementary information (ESI) available: Experimental procedures in the synthesis of complexes **2** and **3a** and details for catalysis. CCDC 784228 (**3a**) and 784229 (**2**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0cc02664f

Complex **2** and **3a** were unambiguously characterized by X-ray diffraction studies (Fig. 2 and 3). Both complexes adopt a piano stool geometry about the ruthenium centre, with the corresponding chelating and pyridine ligands. The $Ru–C_{carbene}$ bond (2.03(1) Å) in **2** is shorter than that of complex **1b** (2.092(5) Å),[9] but in the expected range of analogous $RuCp^*(NHC)L_2$ complexes.[14] The $Ru–PPh_2$ bond length is similar to those reported by Ikariya and co-workers.[15]

Complex **2**, when reacted with potassium *tert*-butoxide in THF, is an efficient catalyst for the H_2-hydrogenation of acetophenone (Table 1). Full conversion to 1-phenylethanol is achieved within 30 min under 8 bar of H_2 in THF at 25 °C with a catalyst to base to substrate (C/B/S) ratio of 1/8/2515. On the other hand, full conversion is achieved in 10 min under similar catalytic conditions when 2-propanol was used with a TOF of 17 600 h^{-1}. Complex **2** also catalyzed the transfer hydrogenation of acetophenone in 2-propanol at 25 °C, but

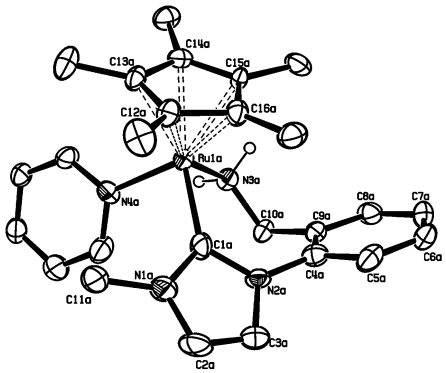


Fig. 2 ORTEP diagram of $[RuCp^*(C–NH_2)(py)]PF_6$, (**2**) depicted with thermal ellipsoids at 30% probability. The counter anions and most of the hydrogens have been omitted for clarity. Only one asymmetric unit is shown. Selected bond distances (Å) and bond angles (deg): Ru(1a)–C(1a), 2.03(1); Ru(1a)–N(3a), 2.195(7); Ru(1a)–N(4a), 2.156(8); Ru(1a)–C(12a), 2.176(9); C(1a)–Ru(1a)–N(3a), 91.9(3); N(3a)–Ru(1a)–N(4a), 90.9(4); C(1a)–Ru(1a)–N(3a), 81.3(3).

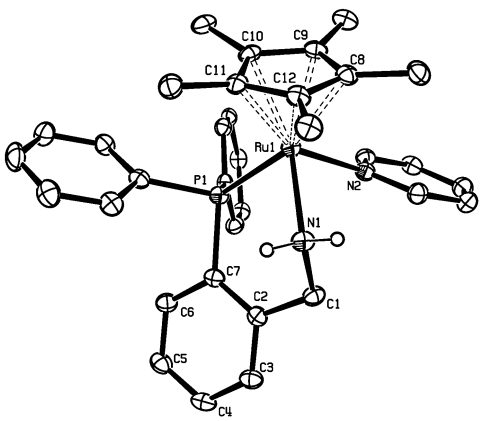
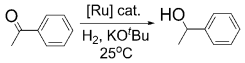


Fig. 3 ORTEP diagram of $[RuCp^*(P–NH_2)(py)]PF_6$, (**3a**) depicted with thermal ellipsoids at 30% probability. The counter anions and most of the hydrogens have been omitted for clarity. Selected bond distances (Å) and bond angles (deg): Ru(1)–P(1), 2.3140(8); Ru(1)–N(1), 2.188(2); Ru(1)–N(2), 2.171(2); Ru(1)–C(9), 2.186(3); P(1)–Ru(1)–N(1), 84.89(7); N(1)–Ru(1)–N(2), 87.35(9); P(1)–Ru(1)N(2), 95.72(7).

Table 1 The hydrogenation of acetophenone catalyzed by complex **2** in the presence of KO^tBu[a]



Entry	$P(H_2)$/bar	C/B/S ratio[b]	Conversion[c] (%/min)		TOF[d]/h^{-1}
1	2	1/8/2515	16/60	99/120	3110
2	8	1/8/2515	30/20	98/30	10 300
3[e]	8	1/8/11500	29/30	97/90	7240
4[f]	8	1/8/2515	46/4	98/10	17 600
5[g]	–/Ar	1/8/1200	53/30	82/120	1270

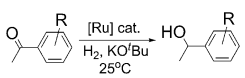
[a] Reactions were carried out in a 50 mL Parr hydrogenation reactor in THF (6 mL) at 25 °C unless otherwise stated; potassium *tert*-butoxide was used as base. [b] C/B/S: Catalyst/base/substrate. [c] Conversions were determined by GC and were reported as an average of two runs. [d] Determined from the slope of the linear portion of [alcohol] *vs.* time plot. [e] No solvent was used. [f] 2-Propanol was used as solvent. [g] Conducted under an argon environment and 2-propanol was used as solvent.

with a smaller TOF value (Table 1, entry 5). By comparison, complex **3a** is a poor precatalyst which when activated (C/B/S = 1/8/200) produces a maximum conversion of 8% in 4 h under 25 bar of H_2 in THF at 50 °C. The related complex **3b** catalyzed the hydrogenation of acetophenone under 1 atm of H_2 in 2-propanol at 50 °C (Ru/KOH/substrate = 1/1/100) with 16% conversion in 1 h.[11] In terms of selectivity and broad substrate scope (*vide infra*), complex **2** is superior to these and a few other ruthenium(II) complexes with NHC ligands that have been reported to catalyze the hydrogenation of ketones and aldehydes[14b,16] and it is comparable to or better than many $P–NH_2$ systems of ruthenium(II).[4,17]

Some results of the H_2-hydrogenation of substituted acetophenones are listed in Table 2. In general, TOF values decrease with increasing donor ability at the 4′ position of the aryl group on the ketone. On the other hand, an increase in substituent bulk on the acyl group gave variable TOF values. Pinacolone is effectively hydrogenated but not 1*R*-(−)-Fenchone (Table 3, entries 1–5).

In the case of ketone hydrogenation, a sigmoidal type conversion curve was observed with a variable induction period (10–30 min) depending on the ketone of interest. The mercury test[18] was employed in the hydrogenation of 4′-chloroacetophenone to test for the possibility of catalysis

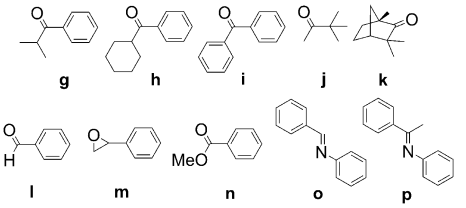
Table 2 The hydrogenation of substituted acetophenones catalyzed by complex **2** in the presence of KO^tBu[a]



Entry	R	Conversion (%/min)		TOF/h^{-1}
1	2′-Chloro-	46/40	99/60	2400
2	3′-Chloro-	41/15	99/20	8050
3	4′-Chloro-	45/15	99/25	7800
4	4′-Bromo-	18/15	99/30	6970
5	4′-Methoxy-	42/15	99/25	5180

[a] Reactions were carried out in a 50 mL Parr hydrogenation reactor in THF (6 mL) at 8 bar of H_2 pressure at 25 °C. Potassium *tert*-butoxide was used as base. The C/B/S ratio was 1/8/1500.

Table 3 The hydrogenation of organic molecules with polar bonds catalyzed by complex **2** in the presence of KO^{t}Bu[a]



Entry	Substrate	Conversion (%/min)		TOF/h^{-1}
1	**g**	75/5	99/15	13 400
2	**h**	49/60	99/120	1110
3	**i**	42/5	99/15	8100
4	**j**	58/5	99/15	10 400
5	**k**	0/60	1/120	0
6	**l**	1/60	1/120	0
7[b]	**m**	9/120	13/180[e]	67
8[c]	**n**	10/120	23/180	209
9[c,d]	**n**	48/60	78/120	838
10[e]	**o**	0/60	0/120	0
11[e]	**p**	28/60	43/120	247

[a] Unless otherwise stated, all reactions were carried out in a 50 mL Parr hydrogenation reactor in THF (6 mL) at 8 bar of H_2 pressure and 25 °C. Potassium *tert*-butoxide was used as base. The C/B/S ratio was 1/8/1500. [b] 2-Propanol was used as solvent. Branched to linear alcohol ratio: 89 : 11. [c] Tridecane was used as an internal standard for GC analysis. [d] Reaction was carried out at 25 bar of H_2 pressure and 50 °C. [e] Conversion determined by ^{1}H-NMR spectroscopy.

by ruthenium nanoparticles. The catalytic activity was not perturbed during the course of the reaction (see ESI‡). Catalysis conducted in 2-propanol did not have an induction period. We postulate that the product alcohol might auto-catalyze the heterolytic splitting of dihydrogen by acting as a proton shuttle.[1c,11,19]

The H_2-hydrogenation of other polar bonds catalyzed by complex **2** with base was also investigated. Thus, benzaldehyde and *N*-(benzylidene)aniline were not hydrogenated, and *N*-(1-phenylethylidene)aniline was hydrogenated to its tertiary amine in 43% conversion within 2 h (Table 3, entries 6, 10 and 11). On the other hand, complex **2** catalyzed the hydrogenolysis of styrene oxide in 2-propanol at 25 °C with a TOF of 67 h^{-1} to produce phenylethanol with branched to linear ratio of 89 : 11 (Table 3, entry 7). A similar branched to linear alcohol ratio was observed when **3b** was used as a catalyst, yet with a smaller TOF value (32 h^{-1}).[6a]

The homogenous hydrogenation of esters is usually challenging. Most ruthenium(II) catalysts require a high temperature and H_2 pressure with low substrate loadings to achieve conversion to the alcohol.[5a,17b,20] Complex **2** catalyzed the hydrogenation of methyl benzoate to benzyl alcohol and methanol at 25 °C and 8 bar H_2 with a TOF of 209 h^{-1}, or at 50 °C and 25 bar H_2 with a TOF of 838 h^{-1} and appreciable substrate loading (C/B = 1/1500) (Table 3, entries 8 and 9). No other side products were observed. The precatalyst *trans*-$RuCl_2(\kappa^2\text{-}PPh_2CH_2CH_2NH_2)_2$, provides comparable activity but at higher temperature (100 °C) and H_2 pressure (50 bar).[5a]

In summary, we have presented the synthesis and catalytic activity of complexes **2** and **3a**. Complex **2** provides an active catalyst for the hydrogenation of a variety of polar bonds under mild conditions in basic medium.

NSERC Canada is thanked for a Discovery Grant to R.H.M. NSERC Canada and the Ministry of Education of Ontario are thanked for graduate scholarships to W.W.N.O.

Notes and references

1 (*a*) G. J. Kubas, *Chem. Rev.*, 2007, **107**, 4152–4205; (*b*) R. H. Morris, *Can. J. Chem.*, 1996, **74**, 1907–1915; (*c*) M. Ito and T. Ikariya, *Chem. Commun.*, 2007, 5134–5142.
2 (*a*) T. Ikariya, K. Murata and R. Noyori, *Org. Biomol. Chem.*, 2006, **4**, 393–406; (*b*) S. E. Clapham, A. Hadzovic and R. H. Morris, *Coord. Chem. Rev.*, 2004, **248**, 2201–2237.
3 R. Guo, A. J. Lough, R. H. Morris and D. Song, *Organometallics*, 2004, **23**, 5524–5529.
4 K. Abdur-Rashid, R. W. Guo, A. J. Lough, R. H. Morris and D. T. Song, *Adv. Synth. Catal.*, 2005, **347**, 571–579.
5 (*a*) L. A. Saudan, C. M. Saudan, C. Debieux and P. Wyss, *Angew. Chem., Int. Ed.*, 2007, **46**, 7473–7476; (*b*) W. Kuriyama, Y. Ino, O. Ogata, N. Sayo and T. Saito, *Adv. Synth. Catal.*, 2010, **352**, 92–96.
6 (*a*) M. Ito, M. Hirakawa, A. Osaku and T. Ikariya, *Organometallics*, 2003, **22**, 4190–4192; (*b*) M. Ito, A. Sakaguchi, C. Kobayashi and T. Ikariya, *J. Am. Chem. Soc.*, 2007, **129**, 290–291.
7 (*a*) X. Cui and K. Burgess, *Chem. Rev.*, 2005, **105**, 3272–3296; (*b*) A. T. Normand and K. J. Cavell, *Eur. J. Inorg. Chem.*, 2008, 2781–2800; (*c*) R. Corberan, E. Mas-Marza and E. Peris, *Eur. J. Inorg. Chem.*, 2009, 1700–1716.
8 D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J. P. Melder, K. Ebel and S. Brode, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1021–1023.
9 W. W. N. O, A. J. Lough and R. H. Morris, *Organometallics*, 2009, **28**, 6755–6761.
10 L. G. Bonnet, R. E. Douthwaite, R. Hodgson, J. Houghton, B. M. Kariuki and S. Simonovic, *Dalton Trans.*, 2004, 3528–3535.
11 M. Ito, M. Hirakawa, K. Murata and T. Ikariya, *Organometallics*, 2001, **20**, 379–381.
12 W. W. N. O, A. J. Lough and R. H. Morris, *Acta Crystallogr., Sect. E: Struct. Rep. Online*, 2010, **66**(10), m1264.
13 J. P. Cahill, F. M. Bohnen, R. Goddard, C. Kruger and P. J. Guiry, *Tetrahedron: Asymmetry*, 1998, **9**, 3831–3839.
14 (*a*) W. Baratta, E. Herdtweck, W. A. Herrmann, P. Rigo and J. D. Schwarz, *Organometallics*, 2002, **21**, 2101–2106; (*b*) C. Gandolfi, M. Heckenroth, A. Neels, G. Laurenczy and M. Albrecht, *Organometallics*, 2009, **28**, 5112–5121; (*c*) A. P. da Costa, J. A. Mata, B. Royo and E. Peris, *Organometallics*, 2010, **29**, 1832–1838.
15 M. Ito, A. Osaku, C. Kobayashi, A. Shiibashi and T. Ikariya, *Organometallics*, 2009, **28**, 390–393.
16 (*a*) V. L. Chantler, S. L. Chatwin, R. F. R. Jazzar, M. F. Mahon, O. Saker and M. K. Whittlesey, *Dalton Trans.*, 2008, 2603–2614; (*b*) J. P. Lee, Z. F. Ke, M. A. Ramirez, T. B. Gunnoe, T. R. Cundari, P. D. Boyle and J. L. Petersen, *Organometallics*, 2009, **28**, 1758–1775.
17 (*a*) W. L. Jia, X. H. Chen, R. W. Guo, C. Sui-Seng, D. Amoroso, A. J. Lough and K. Abdur-Rashid, *Dalton Trans.*, 2009, 8301–8307; (*b*) M. L. Clarke, M. B. Diaz-Valenzuela and A. M. Z. Slawin, *Organometallics*, 2007, **26**, 16–19; (*c*) M. B. Diaz-Valenzuela, S. D. Phillips, M. B. France, M. E. Gunn and M. L. Clarke, *Chem.–Eur. J.*, 2009, **15**, 1227–1232.
18 C. A. Jaska and I. Manners, *J. Am. Chem. Soc.*, 2004, **126**, 9776–9785.
19 A. Hadzovic, D. Song, C. M. MacLaughlin and R. H. Morris, *Organometallics*, 2007, **26**, 5987–5999.
20 (*a*) M. C. van Engelen, H. T. Teunissen, J. G. de Vries and C. J. Elsevier, *J. Mol. Catal. A: Chem.*, 2003, **206**, 185–192; (*b*) J. Zhang, G. Leitus, Y. Ben-David and D. Milstein, *Angew. Chem., Int. Ed.*, 2006, **45**, 1113–1115; (*c*) S. Takebayashi and S. H. Bergens, *Organometallics*, 2009, **28**, 2349–2351.

