ChemComm

Cite this: *Chem. Commun.*, 2012, **48**, 12097–12099

www.rsc.org/chemcomm

COMMUNICATION

Introducing a mixed-valent dirhodium(II,III) catalyst with increased stability in C–H amination†

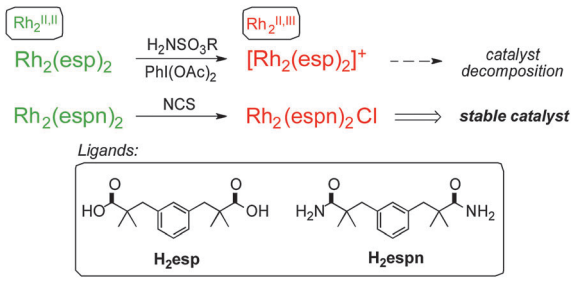
Katherine P. Kornecki and John F. Berry*

Received 12th September 2012, Accepted 30th October 2012
DOI: 10.1039/c2cc36614b

A new mixed-valent $Rh_2^{II,III}$ dimer, $[Rh_2(espn)_2Cl]$ ($espn^{2-}$ = α,α,α′,α′-tetramethyl-1,3-benzenedipropanamidate), is reported. This compound readily dissociates Cl^- at low concentrations in solution to form the active $[Rh_2(espn)_2]^+$ catalyst, which performs intramolecular C–H amination with TONs > 1400. This work expands the scope of $Rh_2^{II,III}$ dimers to nitrenoid chemistry.

Selective and efficient amination of C–H bonds is an increasingly important synthetic tool for introducing complex functionality into simple hydrocarbons.[1] Breakthroughs in C–H amination technology have come largely as a function of catalyst design: simple $Rh_2(OAc)_4$ derivatives have been shown to be decent catalysts for intramolecular C–H amination,[2] but one of the top catalysts for performing both intra- and intermolecular C–H amination is $[Rh_2(esp)_2]$ (**1**) (esp = α,α,α′,α′-tetramethyl-1,3-benzenedipropanoate), which was developed by Du Bois and co-workers in 2004.[3] Two important factors contribute to the success of **1** as a catalyst. First, the chelating dicarboxylate ligands provide added thermodynamic stability to **1** *via* the chelate effect. Similar catalyst design principles have been employed in Rh_2-carbenoid catalysts.[4] Accessibility of the $Rh_2^{II,III}$ state under catalytic conditions is another key feature of **1**; both Du Bois and we have recognized that the catalyst resting state in intermolecular amination reactions is an $Rh_2^{II,III}$ species. However, the oxidized $Rh_2^{II,III}$ complex of **1** degrades rapidly (~5 minutes in solution), which is believed to be the major cause of catalyst arrest.[5]

We have therefore been interested in purposefully designing complexes that are stable in the $Rh_2^{II,III}$ oxidation state to examine their performance as catalysts for C–H amination (Scheme 1). It is well known that N-donor ligands provide greater stabilization of metal–metal bonded compounds in high oxidation states than do O-donor ligands.[6] Doyle and co-workers have capitalized on this concept by using Rh_2 complexes with carboxamidate ligands as catalysts.[6c] One such catalyst, $[Rh_2(cap)_4]$ (cap = caprolactamate), has been shown to be active in its $Rh_2^{II,III}$ oxidation state for allylic oxidation of C–H bonds, as well as aziridination.[7] To apply this idea to C–H amination chemistry we chose to modify the H_2esp ligand to form the corresponding chelating diamide (H_2espn), and report the catalytic activity of its $Rh_2^{II,III}$ complex $[Rh_2(espn)_2Cl]$, **2a** (Fig. 1). It was recently reported that $Ru_2^{II,III}$ complexes preferentially catalyze allylic intramolecular amination under conditions nearly identical to Rh_2 amination chemistry,[8] as well as other reactions.[9] Since the $Ru_2^{II,III}$ manifold contains fewer electrons than $Rh_2^{II,III}$ species, it follows that modifying metal oxidation states may allow for fine tuning of the reactivity and selectivity profile of C–H amination.



Scheme 1 Designing a stable mixed-valent $Rh_2^{II,III}$ catalyst.

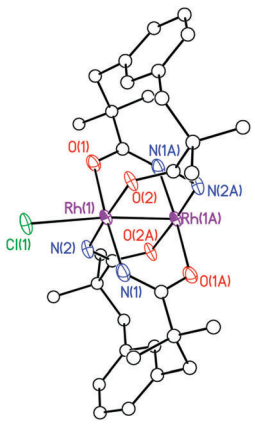


Fig. 1 Crystal structure of **2a**, the [2,2] isomer of $Rh_2(espn)_2Cl$. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. The Rh–Rh bond distance is 2.4155(9) Å.

The ligand H_2espn is conveniently prepared in 56% yield from H_2esp by converting to the diacid chloride followed by a reaction with aqueous ammonia. $Rh_2(espn)_2Cl$ is readily accessed

Department of Chemistry, University of Wisconsin - Madison, 1101 University Avenue, Madison, WI 53713, USA. E-mail: berry@chem.wisc.edu; Fax: +1 608-262-6143; Tel: +1 608-262-7534

† Electronic supplementary information (ESI) available. CCDC 900048 and 900049. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc36614b

in two steps from $[Rh_2(OAc)_4{\cdot}2MeOH]$ and H_2espn by first refluxing the two in chlorobenzene using a Soxhlet extraction apparatus having the thimble filled with K_2CO_3 and sand. This reaction yields an insoluble lime-green amorphous powder that is not isolated but is instead oxidized *in situ* by adding 1.1 equivalents of *N*-chlorosuccinimide to the reaction mixture. The desired catalyst **2a** is then isolated in moderate yield (50%). The initial ligand exchange reaction results in two structural isomers: *cis*-[2,2] $Rh_2(espn)_2Cl$ (**2a**) and [4,0] $Rh_2(espn)_2Cl$ (**2b**). These isomers are named following the convention for metal–metal bonded compounds with mixed donor equatorial ligands, *i.e.*, the [4,0] isomer has all of the amidate N atoms bound to one Rh atom and all the O atoms bound to the other. The *cis*-[2,2] isomer has a mix of two O and two N donor atoms on each Rh atom in a cis arrangement. The **2a** isomer is favored (4 : 1 ratio) and readily crystallizes from methylene chloride/acetone solutions, following chromatographic purification, to yield analytically pure material. We have tested both isomers in catalytic aminations (and both are equally active catalysts in terms of turnover number, see ESI,† Table S2), but the experiments reported herein have been done exclusively with the *cis*-[2,2] isomer (**2a**) since it is readily obtained in macroscopic quantities. The two isomers differ in their solid-state structures: **2b** is a distinct molecular species in the solid state (see ESI,† Fig. S2), whereas **2a** forms a coordination polymer with bridging chlorides (Fig. S1, ESI†).

Cyclic voltammetry (CV) experiments on **2a** show interesting electrochemical behavior (Fig. 2). The CV of **2a** shows three redox waves: $E_{1/2}(1)$ at −334 mV, $E_{1/2}(2)$ at 604 mV and $E_{1/2}(3)$ at 1005 mV (*versus* Fc/Fc^+ in CH_3CN) (Fig. 2a). $E_{1/2}(1)$ and $E_{1/2}(3)$ are reversible and become less intense as Cl^- concentration is increased. $E_{1/2}(2)$ is not perfectly reversible and is the dominant signal in the presence of excess Cl^- ions (see ESI,† Fig. S3). Furthermore, when the CV solution is doped with two equivalents of non-coordinating counterion, $K[B(Ar^f)_4]$ (Ar^f = (3,5-$CF_3(C_6H_3)$) and filtered through celite, $E_{1/2}(2)$ is no longer present (Fig. 2b). We therefore suggest that $E_{1/2}(1)$ and $E_{1/2}(3)$ correspond to chloride-free $[Rh_2(espn)_2]^{0/+}$ and $[Rh_2(espn)_2]^{+/2+}$ waves, respectively, and that $E_{1/2}(2)$ may be assigned to the $[Rh_2(espn)_2Cl]^{0/+}$ wave. Dissociation of the Cl^- ion may cause the irreversibility of $E_{1/2}(2)$. A dissociation constant of ~2.5 M was estimated based on CV data, which is quite large and

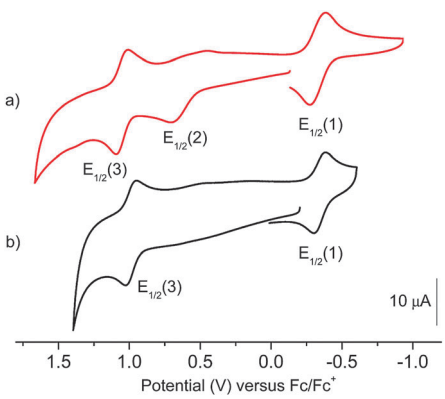


Fig. 2 (a) CV of **2a** (1 mM in 0.1 M tetrabutylammonium hexafluorophosphate in CH_3CN), (b) CV of **2a** plus two equivalents of non-coordinating counterion, BAr^f.

Table 1 Simple cyclization reactions at 0.05 mol% loading for catalysts **1** and **2a**

Substrate	Product	Catalyst **1** TON (Yield)	Catalyst **2a** TON (Yield)
S1		580 (29%)	1400 (70%)
S2		490 (25%)	1450 (72%)

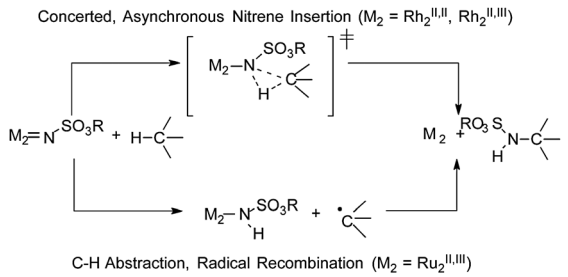
therefore indicative of weak chloride binding in solution. Importantly, lowering the concentration of **2a** in the CV solution also diminishes the $E_{1/2}(2)$ signal relative to the $E_{1/2}(1)$ and $E_{1/2}(3)$ signals, implying that the free $[Rh_2(espn)_2]^+$ cation is likely the only species present at the high dilutions relevant to catalysis.

The catalytic activity of compound **2a** has been tested with simple substrates in cyclization reactions with one equivalent of $PhI(OAc)_2$ as the oxidant in dichloromethane at room temperature (Table 1). To our surprise, **2a** catalyzed the cyclization of **S1** in dichloromethane at room temperature with remarkable efficiency. The cyclizations of **S1** and **S2** proceed to 100% conversion with loadings as low as 0.07 mol%. Under identical conditions, catalyst **1** achieves TONs nearing 600, which is quite remarkable within the scope of C–H amination chemistry. However, catalyst **2a** is able to perform many more turnovers prior to catalyst arrest. The enhanced longevity of **2a** in cyclizing simple substrates suggests that the enhanced stability of the $Rh_2^{II,III}$ oxidation state serves to prevent catalyst arrest. Unsurprisingly, using catalytic amounts of the reduced $Rh_2^{II,II}$ powder form of **2a** in the cyclization of **S1** and **S2** results in catalyst oxidation and identical TONs. However, it is worth noting that using the amorphous powder requires a significant induction period (~40 minutes) for the catalyst to solubilize. This induction period, in addition to a lack of structural information for the reduced species, render the use of the oxidized compound **2a** more favorable. The importance of **2a** lies in its structural similarity to **1**, and the fact that it is both stable and isolable in the $Rh_2^{II,III}$ state. These results refute the idea that Rh_2 dimers in only the (II,II) redox state can be active amination catalysts, and will allow for a discrete study of oxidation state influence on mechanism. Interestingly, the mixed-valent complex $Rh_2(cap)_4Cl$ was tested for competence in the cyclization of **S1** and no conversion was observed. This result implies that mixed-valency is not the only factor important in amination chemistry – the chelate effect may be critical as well.

To probe the selectivity of the nitrene oxidant in C–H amination reactions using **2a**, competition substrates **S3–S5** were examined (Table 2). Catalyst **1** is largely unselective in the cyclization of **S3** and **S4**, giving a 1 : 1 ratio of products in both cases.[8] Conversely, **2a** is more sensitive to the electronics of the substrate, perhaps implicating a greater degree of electrophilicity for **2a** *versus* **1**. However, this conclusion requires a more rigorous set of selectivity experiments than the few that are reported here. Competition between the 3° C–H bond and the benzylic C–H position in **S5** gives a profile that identically mirrors that of **1** with a 1 : 7 ratio preferring the 3° center: this selectivity is indicative of a concerted transition state.[3c] The recently reported $Ru_2(hp)_4Cl$

Table 2 Intramolecular competition reactions using 0.1 mol% of catalyst **2a**

Substrate	Product	%Conv.	**A** : **B** Ratio
S3	**A** + **B**	100%	1 : 4
S4	**A** + **B**	100%	1.4 : 1
S5	**A** + **B**	100%	1 : 7



Scheme 2 Possible pathways for C–H amination.

catalyst (**3**, with hp = 2-hydroxypyridinate) has opposite selectivity, and has been the subject of experimental and computational studies that indicate a two-step mechanism.[8]

The two limiting mechanisms for C–H amination *via* a dimetal nitrenoid that may be contemplated are shown in Scheme 2. A concerted, but asynchronous reaction mechanism has a great deal of experimental and computational support in $Rh_2^{II,II}$ catalyzed carbenoid reactions,[1a] and $Rh_2^{II,II}$ nitrenoid reactions are proposed to behave similarly.[3b] Alternatively, a two-step C–H abstraction/radical recombination mechanism may be considered that is similar to the classic mechanistic profile of Cytochrome P450.[10] We note that the selectivity of **2a** towards **S3** and **S5** is opposite that of **3**, and that we obtain identical selectivity for **S5** to that observed for **1**. These preliminary data suggest that **2a** likely utilizes a concerted asynchronous mechanism as in **1**, though the selectivity differences seen in **S4** suggest that the nitrene in **2a** is more electron deficient than the **1**-nitrene, consistent with the cationic nature of the former. We should note, however, that the concerted mechanism may be considered a special case of the C–H abstraction/radical rebound mechanism in which the rate of the radical rebound is infinitely faster than the rate of abstraction. Further experiments to determine where on the continuum between these two limiting cases catalyst **2a** lies are needed.

We have made some attempts to perform intermolecular C–H amination reactions using **2a**. Experiments were conducted using the highly activated H_2NTces (1,1,1-trichloroethylsulfamate ester) as the nitrogen atom source and diacetoxyiodobenzene as the oxidant in either dichloromethane or benzene. With several substrates, **2a** can achieve full conversion to the C–H amination products with catalyst loadings as low as 0.1 mol%, but the yield of the reaction depends critically on the concentration of the C–H substrate (see ESI,† Table S1). Unlike with catalyst **1**, which offers superior performance in intermolecular C–H amination, **2a** appears to catalyze a fast background reaction between H_2NTces and $PhI(OAc)_2$, yielding 2,2,2-trichloroethanol and sulfamic acid, among other unidentified and undesired products. Optimum yields with catalyst **2** are therefore only obtained when the reaction is carried out in neat hydrocarbon substrate.

In conclusion, $Rh_2(espn)_2Cl$ (**2a**) is a new effective and highly efficient catalyst for intramolecular C–H amination reactions. This complex is unique because it is a mixed-valent $Rh_2^{II,III}$ species when it is introduced to catalytic reactions, unlike its predecessor $Rh_2(esp)_2$ (**1**), which becomes oxidized *in situ*. The effectiveness of **2a** suggests that cationic $Rh_2^{II,III}$ species may be key in designing even better catalysts for C–H amination. The parallels between $\mathbf{1}^+$ and **2a** are striking; given the indefinite stability of **2a** as a mixed-valent dimer, studies are ongoing in our lab to better understand the mechanistic groundwork that allows cationic complexes $\mathbf{1}^+$ and **2a** to perform so favorably in the C–H amination transformation.

We thank the Chemical Sciences, Geosciences, and Biosciences Division, Office of Basic Energy Sciences, Office of Science, U.S. Department of Energy for support (DE-FG02-10ER16204). We also wish to acknowledge helpful discussions with Justin Du Bois and other members of the CCI Center for Selective C–H Functionalization supported by NSF (CHE-1205646).

Notes and references

1 (*a*) H. M. L. Davies and J. R. Manning, *Nature*, 2008, **451**, 417–424; (*b*) J. Du Bois, *Org. Process Res. Dev.*, 2011, **15**, 758–762.
2 (*a*) R. Breslow and S. H. Gellman, *J. Am. Chem. Soc.*, 1983, **105**, 6728–6729; (*b*) C. G. Espino and J. A. DuBois, *Angew. Chem., Int. Ed.*, 2001, **40**, 598–600.
3 (*a*) C. G. Espino, K. W. Fiori, M. Kim and J. Du Bois, *J. Am. Chem. Soc.*, 2004, **126**, 15378–15379; (*b*) K. W. Fiori and J. Du Bois, *J. Am. Chem. Soc.*, 2007, **129**, 562–568; (*c*) K. W. Fiori, C. G. Espino, B. H. Brodsky and J. Du Bois, *Tetrahedron*, 2009, **65**, 3042–3051.
4 H. M. L. Davies and S. A. Panaro, *Tetrahedron Lett.*, 1999, **40**, 5287–5290.
5 (*a*) D. N. Zalatan and J. Du Bois, *J. Am. Chem. Soc.*, 2009, **131**, 7558–7559; (*b*) K. P. Kornecki and J. F. Berry, *Chem.–Eur. J.*, 2011, **17**, 5827–5832; (*c*) K. P. Kornecki and J. F. Berry, *Eur. J. Inorg. Chem.*, 2012, 562–568.
6 (*a*) J. L. Bear, B. Han, Z. Wu, E. Van Caemelbecke and K. M. Kadish, *Inorg. Chem.*, 2001, **40**, 2275–2281; (*b*) M. P. Doyle, R. Duffy, M. Ratnikov and L. Zhou, *Chem. Rev.*, 2009, **110**, 704–724; (*c*) M. P. Doyle, *J. Org. Chem.*, 2006, **71**, 9253–9260; (*d*) M. P. Doyle and T. Ren, *Prog. Inorg. Chem.*, John Wiley & Sons Inc., 2007, pp. 113–168.
7 (*a*) A. J. Catino, E. F. Raymon and M. P. Doyle, *J. Am. Chem. Soc.*, 2004, **126**, 13622–13623; (*b*) A. J. Catino, J. M. Nichols, R. E. Forslund and M. P. Doyle, *Org. Lett.*, 2005, **7**, 2787–2790.
8 M. E. Harvey, D. G. Musaev and J. Du Bois, *J. Am. Chem. Soc.*, 2011, **133**, 17207–17216.
9 L. Villalobos, Z. Cao, P. E. Fanwick and T. Ren, *Dalton Trans.*, 2012, **41**, 644–650.
10 B. Meunier, S. I. P. de Visser and S. Shaik, *Chem. Rev.*, 2004, **104**, 3947–3980.