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Mechanism of hydrogen transfer to imines from a hydroxycyclopentadienyl ruthenium hydride. Support for a stepwise mechanism†

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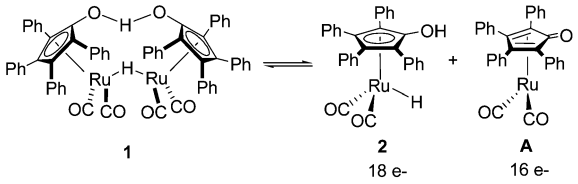
The negligible double kinetic deuterium isotope effect (k_{HH}/k_{DD} = 1.05) in the reaction where [2,3,4,5-Ph$_4$(η^5-C$_4$COH)Ru(CO)$_2$H (2) transfers a hydride and a proton to *N*-phenyl-[1-(4-methoxyphenyl)ethylidene]amine (4) indicates that no bond to hydrogen is broken or formed in the rate-determining step.

Transition metal-catalyzed hydrogen transfer has attracted considerable attention during the past 10–15 years.[1] A variety of new catalysts have been reported that are highly efficient for transferring hydrogen from a hydrogen donor (*e.g.* an alcohol) to a hydrogen acceptor (*e.g.* a ketone or an imine). Catalytic hydrogen transfer reactions have been successfully applied to enantioselective versions.[2]

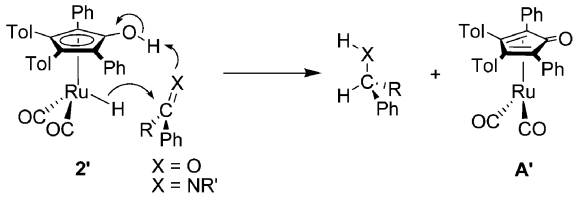
In 1985 Shvo reported on the dimeric catalyst **1** (Scheme 1),[3] which since then has been used in a number of hydrogen transfer reactions[4–10] These reactions include disproportion of aldehydes to esters,[4a] hydrogenation of carbonyl compounds,[4b] and Oppenauer-type oxidations of alcohols[1b,6] and amines.[7] It has also been shown that catalyst **1** is efficient for racemization of alcohols and this was used in combination with lipases for dynamic kinetic resolution of secondary alcohols.[8] Complex **1** has also been used for racemization of amines.[9]



Scheme 1

Catalyst **1** is in equilibrium with monomers **2** and **A** (Scheme 1). The monomer **2** is able to hydrogenate a hydrogen acceptor whereas the monomer **A** can dehydrogenate a hydrogen donor. These processes interconvert **2** and **A**.

In 2001 Casey and coworkers reported a mechanistic study on hydrogen transfer to carbonyls and imines from **2'** (Scheme 2).[11] From the large combined isotope effect observed for benzaldehyde (X = O, R = H) k_{RuHOH}/k_{RuDOD} = 3.6 together with individual isotope effects of 1.5 (RuD) and 2.2 (OD) a concerted mechanism



Scheme 2 Concerted mechanism proposed in ref. 11.

† Electronic supplementary information (ESI) available: experimental procedures and kinetic data. See http://www.rsc.org/suppdata/cc/b4/b410698a/

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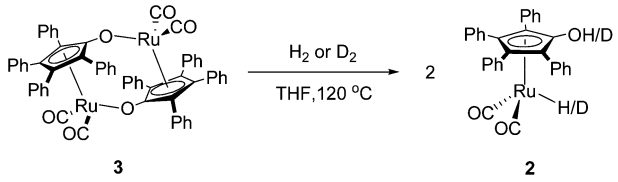
without coordination of the unsaturated substrate was proposed. A concerted mechanism was also observed by our group for the dehydrogenation of alcohols by **A**.[12]

We recently reported that transfer dehydrogenation of *N*-phenyl-1-phenylethylamine to the corresponding imine by **A**, generated from **1** *in situ*, gave deuterium isotope effects consistent with a stepwise mechanism.[7b] Thus, the combined isotope effect k_{CHNH}/k_{CDND} = 3.26 was equal to the individual isotope effect k_{CHNH}/k_{CDNH} = 3.24 and the other individual isotope effect (ND) was very small.

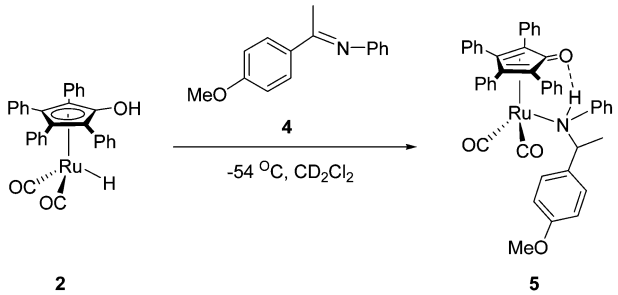
Here we report on the kinetic deuterium isotope effect for the reaction of **2** with a ketimine, which shows that the hydrogen transfer is not involved in the rate-determining step, thus ruling out the concerted mechanism of Scheme 2 for this imine.[11]

Hydride **2** was prepared from **3** in THF under hydrogen or deuterium atmosphere at 120 °C in a microwave oven for 20 min (Scheme 3).[13] The imine was prepared according to a literature procedure.[5]



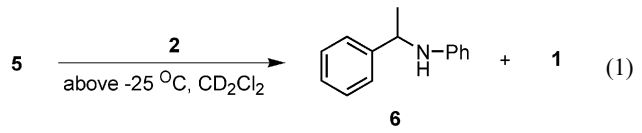
Scheme 3

The kinetic deuterium isotope effect in the reaction of **2** with ketimine **4** in CD_2Cl_2 was studied at −54 °C using **2** and dideuterated **2** (OD, Ru–D) (Scheme 4). The reaction showed second order kinetics with a first-order dependence on imine and **2**, respectively. (For the details of the kinetics see ESI.†) The product of this reaction at this temperature is the ruthenium amine complex **5**. The reaction is readily followed by ^{1}H NMR spectroscopy. The methoxy peak gives a characteristic signal in the ^{1}H NMR for imine **4** at δ 3.85 and two characteristic signals for the two diastereoisomers of complex **5** at δ 3.62 and 3.55 where the former is the kinetically favored diastereoisomer. The reactions were run under pseudo-first-order kinetics with an excess of **2** until over two half lives were over (24 min) integrating the methoxy peaks of imine **4** *versus* the two peaks of **5**.



Scheme 4

The observed rate constant for the formation of **5** (Scheme 4) for RuHOH was $k_{obs} = (1.24 \pm 0.08) \times 10^{-3}\ s^{-1}$ and for RuDOD it was $k_{obs} = (1.18 \pm 0.09) \times 10^{-3}\ s^{-1}$.[14] The kinetic isotope effect calculated from the results is therefore $k_{RuHOH}/k_{RuDOD} = 1.05 \pm 0.14$. This is in sharp contrast to the corresponding kinetic isotope effect observed for benzaldehyde which was 3.6.[11] The latter isotope effect shows that the transfer of hydrogen from ruthenium and oxygen to the aldehyde occurs within the rate-determining step. The low isotope effect of 1.05 for the transfer of hydrogen from **2** to imine **4** suggests another mechanism where the hydrogen transfer is not the rate-determining step. It should be noted that complex **5** is unstable at temperatures above −25 °C in the presence of hydride **2**. The products above −25 °C are the free amine **6** and dimer **1** (eqn. (1)). The free amine (**6**) is distinguishable by ^{1}H NMR at δ 3.75.



(1)

The ruthenium-mediated hydrogen transfer of imines appears to proceed through a mechanism different to that for carbonyl compounds. Even though there are many similarities between the two classes of compounds there are important differences. Amines and imines are more nucleophilic than alcohols and carbonyls. Therefore it is expected that amines and imines should coordinate better to ruthenium. This is evident when comparing the electronic properties of the substrates in transfer hydrogenation of imines,[5] transfer dehydrogenations of amines,[7a] and racemization of amines[9] where electron-rich substrates react faster than electron-deficient substrates suggesting a mechanism where the coordination of the substrate to ruthenium comes into the rate expression.‡ The negligible kinetic isotope effect in the reaction of **2** with imines implies that there is no hydrogen transfer in the rate-determining step.

A mechanism for the hydrogen transfer from **2** to the ketimine is proposed in Scheme 5. If 18 e$^-$ complex **2** is in equilibrium with 16 e$^-$ complex **B** *via* an $\eta^5 \rightarrow \eta^3$ ring slippage, the imine can coordinate to give an 18 e$^-$ intermediate **C**. Subsequent fast hydride and proton transfer *via* π-bound imine would then yield the η^2 complex **D**, which would rearrange to η^4 ruthenium amine complex **7** (Scheme 5). It is likely that the ring slippage from $\eta^5 \rightarrow \eta^3$to give **B** is slow compared to the back reaction (**B** → **2**).

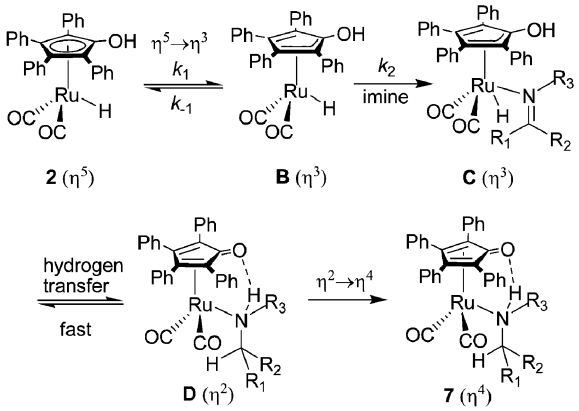
If $k_{-1} > k_2$ then **2** and **B** are in equilibrium. Then the rate expression for the formation of complex **7** can be formulated as in eqn. (2):

$$\frac{d[7]}{dt} = k_2[\text{imine}][B] = k_2K[\text{imine}][\mathbf{2}] = \text{const}[\text{imine}][\mathbf{2}] \qquad (2)$$

The rate expression is in agreement with the observed first-order dependence on both imine and **2** for the formation of the ruthenium amine complex **7**. An alternative mechanism, where a reversible transfer of a proton from **2** to imine gives protonated imine and an anionic hydride, followed by ring slippage and insertion, gives the same kinetics and would also explain the absence of isotope effect.[15] We cannot completely exclude direct hydride transfer from ruthenium to uncoordinated protonated imine in the latter mechanism (followed by association of ruthenium complex and amine) but it does not seem compatible with the very low isotope effect.

In the dehydrogenation of amines by **A** (the reverse reaction) a large isotope effect was previously observed.[7b] Considering the microscopic reversibility of Scheme 5 the amine would readily coordinate to **A** to give **7**. A $\eta^4 \rightarrow \eta^2$ ring slip of **7** in an equilibration process to give **D** followed by a rate limiting β-elimination would account for the large isotope effect observed.

In conclusion the low kinetic isotope effect of $k_{RuHOH}/k_{RuDOD} = 1.05 \pm 0.14$ observed in the hydrogen transfer from **2** to imine **4** shows that the rate-determining step for the reaction does not involve the hydrogen transfer step, and supports a stepwise mechanism.



Scheme 5

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Notes and references

‡ The presence of imine in the rate expression is also consistent with the outer sphere mechanism (*cf*. ref. 11)

1 (*a*) S. Gladiali and G. Mestroni, in *Transition Met. Org. Synth.*, (Eds.: M. Beller and C. Bolm), Wiley-VCH, Weinheim, 1998, **vol. 2**, p. 97; (*b*) J.-E. Bäckvall, R. L. Chowdhury, U. Karlsson and G.-Z. Wang, in *Perspectives in Coordination Chemistry*, (Eds.: A. F. Williams, C. Floriani and A. E. Merbach), Verlag Helvetica Chimica Acta, Basel, 1992, p. 463; (*c*) O. Pàmies and J.-E. Bäckvall, *Chem. Eur. J.*, 2001, **7**, 5052; (*d*) K. Abdur-Rashid, S. E. Clapham, A. Hadzovic, J. N. Harvey, A. J. Lough and R. H. Morris, *J. Am. Chem. Soc.*, 2002, **124**, 15104; (*e*) V. Rautenstrauch, X. Hoang-Cong, R. Churlaud, K. Abdur-Rashid and R. H. Morris, *Chem. Eur. J.*, 2003, **9**, 4954.

2 (*a*) R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97; (*b*) J. Mao and D. C. Baker, *Org. Lett.*, 1999, **6**, 841; (*c*) S. J. M. Nordin, P. Roth, T. Tarnai, D. A. Alonso, P. Brandt and P. G. Andersson, *Chem. Eur. J.*, 2001, **7**, 1431; (*d*) D. G. I. Petra, P. C. J. Kamer, A. L. Spek, H. E. Schoemaker and P. W. N. M. van Leeuwen, *J. Org. Chem.*, 2000, **65**, 3010; (*e*) A. Bøgevig, I. M. Pastor and H. Adolfsson, *Chem. Eur. J.*, 2004, **10**, 294.

3 Y. Blum, D. Czarkie, Y. Rahamim and Y. Shvo, *Organometallics*, 1985, **4**, 1459.

4 (*a*) N. Menashe and Y. Shvo, *Organometallics*, 1991, **10**, 3885; (*b*) Y. Shvo, D. Czarkie and Y. Rahamim, *J. Am. Chem. Soc.*, 1986, **108**, 7400.

5 J. S. M. Samec and J.-E. Bäckvall, *Chem. Eur. J.*, 2002, **8**, 2955.

6 (*a*) G.-Z. Wang, U. Andreasson and J.-E. Bäckvall, *J. Chem. Soc., Chem. Commun.*, 1994, 1037; (*b*) M. L. S. Almeida, M. Beller, G-Z. Wang and J.-E. Bäckvall, *Chem. Eur. J.*, 1996, **2**, 1533; (*c*) G. Csjernyik, A. H. Éll, L. Fadini, B. Pugin and J.-E. Bäckvall, *J. Org. Chem.*, 2002, **67**, 1657.

7 (*a*) A. H. Éll, J. S. M. Samec, C. Brasse and J.-E. Bäckvall, *Chem. Commun.*, 2002, 1144; (*b*) A. H. Éll, J. B. Johnson and J.-E. Bäckvall, *Chem. Commun.*, 2003, 1652.

8 (*a*) A. L. E. Larsson, B. A. Persson and J.-E. Bäckvall, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1211; (*b*) B. A. Persson, A. L. E. Larsson, M. L. Ray and J.-E. Bäckvall, *J. Am. Chem. Soc.*, 1999, **121**, 1645; (*c*) F. F. Huerta, A. Minidis and J.-E. Bäckvall, *Chem. Soc. Rev.*, 2001, **30**, 321; (*d*) O. Pàmies and J.-E. Bäckvall, *Chem. Rev.*, 2003, **103**, 3247; (*e*) M. J. Kim, Y. Ahn and J. Park, *Curr. Opin. Biotechnol.*, 2002, **13**, 578.

9 O. Pàmies, A. H. Éll, J. S. M. Samec, N. Hermanns and J.-E. Bäckvall, *Tetrahedron Lett.*, 2002, **43**, 4699.

10 J. H. Choi, N. Kim, Y. J. Shin, J. H. Park and J. Park, *Tetrahedron Lett.*, 2004, **45**, 4607.

11 C. P. Casey, S. W. Singer, D. R. Powell, R. K. Hayashi and M. Kavana, *J. Am. Chem. Soc.*, 2001, **123**, 1090.

12 J. B. Johnson and J.-E. Bäckvall, *J. Org. Chem.*, 2003, **68**, 7681.

13 Casey and coworkers have reported the same reaction without microwave assistance (see ref. 11).

14 Six/seven different experiments were run for both RuHOH and RuDOD individually.

15 Proton transfer to ketones in a pre-equilibrium has been discussed as a possible mechanism in catalytic ionic hydrogenations: R. M. Bullock, *Chem. Eur. J.*, 2004, **10**, 2366.