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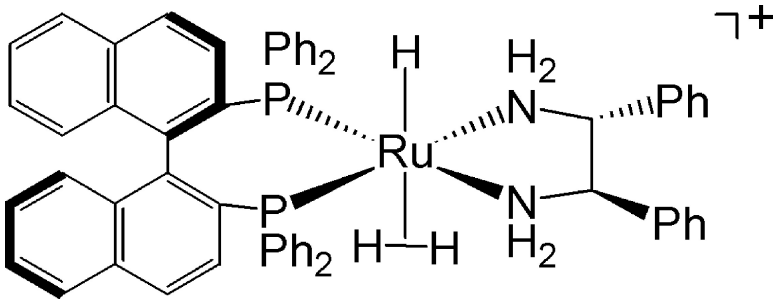

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A Ruthenium−Dihydrogen Putative Intermediate in Ketone Hydrogenation

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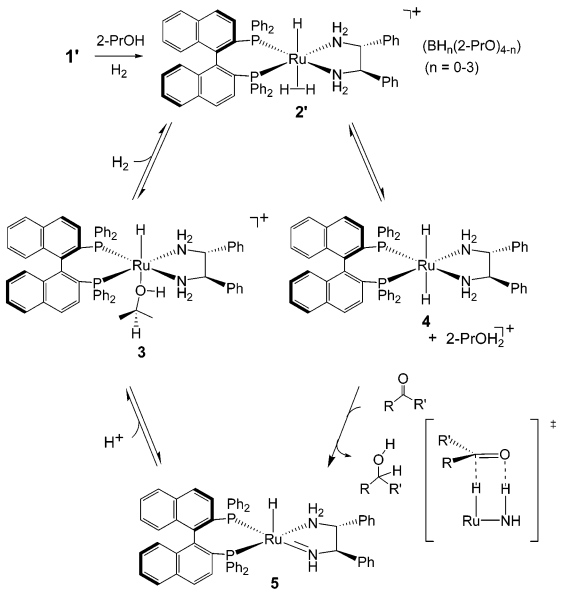
We report the first direct observation and reactivity study of a cationic, Ru−dihydrogen−hydride compound as a putative intermediate in an asymmetric ketone hydrogenation. The catalyst systems comprised of *trans*-(bisphosphine)$RuCl_2$(diamine) and a base, developed by Noyori et al., are the most active and selective catalysts for the asymmetric hydrogenation of aryl−alkyl and related ketones.[1a−e] Turnover numbers in the millions and enantiomeric excesses (ee's) greater than 99% have been achieved with these catalysts.[1b,e] The mechanisms of these and related hydrogenations have been studied by the groups of Noyori, Morris, Chen, and others.[1e,2−4] The predominant consensus of these studies is that the enantioselective step is a bifunctional addition of a nucleophilic hydride ligand on Ru and an acidic hydrogen on nitrogen to the carbon and oxygen atoms of the ketone group, respectively (Scheme 1). The catalyst species that are the most active toward this concerted, bifunctional addition are the dihydride complexes *trans*-(bisphosphine)$Ru(H)_2$(diamine) (e.g., Scheme 1, **4**).[2b] The mutually trans disposition of the hydride ligands in *trans*-(bisphosphine)-$Ru(H)_2$(diamine) activates them toward nucleophilic addition to the carbon center of the ketone.

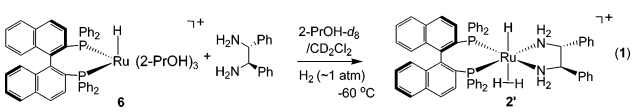
Scheme 1



Noyori et al. recently reported that the catalyst precursors *trans*-Ru((*R*)-tol-BINAP)(H)(η^1-BH_4)((*R*,*R*)-dpen) (**1**, tol-BINAP = 2,2′-bis(ditolylphosphino)-1,1′-binaphthyl, dpen = 1,2-diphenylethylenediamine) and analogues thereof hydrogenate ketones in 2-PrOH with high rates and ee in the absence of added base.[1b,e] The results from a mechanistic study suggested that these base-free hydrogenations in 2-PrOH proceed through the cationic dihydrogen intermediate *trans*-[Ru((*R*)-tol-BINAP)(H)(η^2-H_2)((*R*,*R*)-dpen)]$^+$ (**2**).[1e] Scheme 1 shows the proposed catalytic cycle with **2′** (the BINAP analogue of **2**, BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) as the catalytic intermediate. The BH_4^- ligand in the precursor **1′** reacts with 2-PrOH to form $(BH_n(2\text{-PrO})_{4-n})^-$ ($n = 0-3$), and the resulting solvento−Ru complex *trans*-[Ru((*R*)-BINAP)(H)(2-PrOH)((*R*,*R*)-dpen)]$^+$ (**3**) reacts with H_2 to form the cationic dihydrogen intermediate **2′**. It is proposed that in the absence of added base, the dihydrogen ligand in **2′** is sufficiently acidic to protonate 2-PrOH, generating the *trans*-dihydride compound **4** and presumably 2-$PrOH_2^+$. The *trans*-dihydride **4** is active toward the bifunctional addition to the ketone (vide supra) to generate the product alcohol and the neutral Ru−amide compound **5**. The amide **5** is then protonated at nitrogen to regenerate the solvento complex **3** that reacts with H_2 to regenerate the dihydrogen intermediate **2′**.

Although 2-PrOH is typically the optimum solvent for activity and enantioselectivity with these catalytic hydrogenations, it is not the optimum solvent for the observation of active catalytic intermediates. H−D exchange between 2-PrOH-d_8 and the hydride/dihydrogen ligands on the active Ru species prevents comprehensive NMR observations of putative catalytic intermediates and steps.[1e] The published ^{1}H NMR mechanistic studies of these hydrogenations, including the key concerted bifunctional addition step, are usually carried out either in nonprotic solvents[2c] or in solvent mixtures containing only small amounts of 2-PrOH. In fact, despite evidence for its existence and reactivity in the mechanism study by Noyori et al., the cationic dihydrogen putative intermediate **2** could not be directly observed and studied by ^{1}H NMR.[1e] We now report an independent synthesis and ^{1}H NMR study of the dihydrogen complex **2′** without H−D exchange in 2-PrOH-d_8 solvent.

We and co-workers reported that the catalyst precursor [Ru(BINAP)(1-5-η-C_8H_{11})](BF_4) reacts under 1 atm H_2 in weak oxygen donor solvents (e.g., acetone, THF) to produce cyclooctane and the labile, active olefin hydrogenation catalysts *fac*-[Ru(BINAP)(H)(solvent)$_3$]$^+$.[5a] In 2-PrOH, *fac*-[Ru((*R*)-BINAP)(H)(2-$PrOH)_3$]$^+$ (**6**) rapidly decomposes at room temperature, but it can be prepared without significant decomposition at about −60 °C.[5b] Further, there is no evidence of H−D exchange between the hydride ligand in *fac*-[Ru((*R*)-BINAP)(H)(2-PrOH-d_8)$_3$](BF_4) and 2-PrOH-d_8 at −60 °C. For the present study, we reacted **6** in mixtures of 2-PrOH-d_8/CD_2Cl_2 (between 4 and 2:1) with (*R*,*R*)-dpen under H_2 at −60 °C, to quickly form **2′**(BF_4) in ∼95% yield (eq 1).



Compound **2′** was identified using solution NMR by the hydride signal at −8.5 ppm (1H), the η^2-H_2 signal at −0.66 ppm (2H), and the signals from the BINAP and dpen ligands. The geometry of **2′** was established as follows. The hydride signal was an apparent broad triplet with $^2J_{P-H} \approx 22$ Hz, showing the hydride occupied a coordination site cis to both phosphine groups. The η^2-H_2 ligand

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can be completely exchanged with η^2-D_2 to form *trans*-[Ru((*R*)-BINAP)(H)(η^2-D_2)((*R*,*R*)-dpen)]$^+$ (**2′**-η^2-D_2) by flushing D_2 gas (1 atm) through the solution for several minutes at −60 °C. There is no H−D exchange between the hydride and η^2-D_2 groups of **2′**-η^2-D_2 detectable by ^{1}H or ^{2}H NMR at −60 °C. Hydrogen atom exchange between the H and η^2-H_2 ligands is extremely facile at low temperatures for the cationic Ru(II) complexes *cis*-[(phosphine)$_2$-Ru(H)(η^2-H_2)(diamine)]$^+$.[6] The absence of H−D exchange in **2′**-η^2-D_2 is conclusive evidence for a trans disposition of the H and η^2-D_2 ligands. Further evidence for this trans disposition is that the signal for the hydride of **2′** sharpens significantly and shifts to higher frequencies by ∼0.16 ppm upon exchange of η^2-H_2 for η^2-D_2. Similar sharpening, albeit with a smaller shift, was observed by Morris et al. with [Ru(dppe)$_2$(H)(H_2)]$^+$ (dppe = 1,2-diphenylphosphinoethane) and related compounds.[7] The sharpening of the hydride peak likely results from higher trans coupling with η^2-H_2 than with η^2-D_2.[7] The shift in peak position results from differences between the trans influence of η^2-H_2 and η^2-D_2.[7,8]

The ^{1}H NMR signal for the η^2-H_2 ligand is at higher frequencies (−0.66 ppm) than most, and the H−D coupling (∼37 Hz) is large, showing the η^2-H_2 ligand in **2′** retains an unusually high degree of free H_2 character.[9−11] Further, as shown by the facile exchange with D_2 gas at −60 °C, the η^2-H_2 ligand in **2′** is labile. Reaction of **2** with $NaBH_4$ displaces the η^2-H_2 ligand upon warming to room temperature to generate the η^1-BH_4 adduct **1**. Flushing the hydrogen atmosphere with argon at −60 °C also resulted in loss of η^2-H_2 from the complex. Rather than form the expected solvento complex **3** (Scheme 1), flushing the hydrogen atmosphere with argon also resulted in loss of the hydride ligand, presumably as H_2, and formation of an unidentified Ru species. The loss of the η^2-H_2 and H ligands from **2′** is not reversed by replenishing the atmosphere with hydrogen. Morris et al. reported that β-hydride elimination occurs down the dpen ligand in benzene solutions of the dihydride **4**.[2b,12] Perhaps a similar process occurs in 2-PrOH solutions of **3**. Another possibility is loss of a protic hydrogen on nitrogen with the hydride ligand to generate H_2. *Thus, these and related hydrogenations should be kept saturated with H_2 to avoid decomposition of the catalyst.* Compound **2′** is stable under H_2 at room temperature for periods of minutes.

The putative catalytic sequence **2′** → **4** → **5** was investigated as follows. The neutral dihydride **4** compound was not detected by NMR in solutions of **2′**. The kinetic or thermodynamic acidity of the dihydrogen ligand in **2′** is, therefore, not sufficient to protonate 2-PrOH-d_8 to a detectable extent at −60 °C. H−D exchange between 2-PrOH-d_8 and the Ru−H and η^2-H_2 groups occurs at an appreciable rate upon warming to about −20 °C, suggesting that deprotonation of **2′** to form [$(CD_3)_2$CD-OHD]$^+$ occurs reversibly and to a small extent at higher temperatures. To investigate whether this deprotonation is significant to ketone hydrogenation, a stoichiometric reaction was carried out between **2′** and the common ketone substrate acetophenone. There was no reaction between acetophenone and **2′** when mixed at −60 °C and then warmed to room temperature. Thus, if the dihydride compound **4** did form, it was not present in sufficient amounts to reduce acetophenone under these conditions. To investigate the behavior of this system under catalytic conditions, the hydrogenation of acetophenone using **2′** as catalyst was attempted in 2-PrOH solvent (4 atm H_2, 30 °C, 2000 equiv of ketone, no base). The reaction produced miniscule amounts (∼0.1%) of 1-phenylethanol product after 3 h and little further product after 24 h. The catalytic hydrogenation was dramatically faster in the presence of $NaBH_4$ (Ru:B ∼ 1:1). A 32% conversion (640 turnovers) was achieved after 3 h. The ee of the catalytic hydrogenation (81% (*S*)) with BH_4^- present is in line with the ee reported by Noyori et al. using the BH_4^- adduct **1** as the catalyst precursor.[1b,e] We found the catalytic hydrogenation was also rapid (500 turnovers, 78% (*S*)) using **2′** and *t*-BuOK (1 equiv). The cationic dihydrogen compound **2′** thus requires added base or BH_4^- to be active toward this catalytic hydrogenation.

This report shows that catalyst species containing active hydrogen ligands, such as **2′**, can be prepared at low temperatures in 2-PrOH-d_8-rich solutions without H−D exchange, thereby allowing their conclusive ^{1}H NMR characterization and study. Rapid H−D exchange with the solvent at room temperature suggests that **2′** is weakly acidic. Compound **2′** does not, however, generate sufficient active catalyst for rapid ketone hydrogenations under the base-free conditions used for this study. Traces of base (stoichiometric in Ru) are required that likely are consumed to convert **2′** into the active catalyst. There are three types of active hydrogen atoms in **2′**, the dihydrogen ligand, the hydride, and the hydrogen atoms bonded to nitrogen. Low temperature studies are underway in these laboratories to investigate the mechanisms of exchange between these active hydrogens and the solvent and to investigate how **2′** is converted into the active catalyst by base.

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Note Added after ASAP Publication. There was an error in Scheme 1 in the version published ASAP on March 1, 2005. The correct version was posted on March 3, 2005.

Supporting Information Available: Experimental procedures and spectral characterization of **2′**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Ohkuma, T.; Ishii, D.; Takeno, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 6510−6511. (b) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40−73. (c) Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931−7944. (d) Ohkuma, T.; Koizumi, M.; Muniz, K.; Hilt, G.; Kabuto, C.; Noyori, R. *J. Am. Chem. Soc.* **2002**, *124*, 6508−6509. (e) Sandoval, C. A.; Ohkuma, T.; Muniz, K.; Noyori, R. *J. Am. Chem. Soc.* **2003**, *125*, 13490−13503.

(2) (a) Abdur-Rashid, K.; Lough, A. J.; Morris, R. H. *Organometallics* **2000**, *19*, 2655−2657. (b) Abdur-Rashid, K.; Faatz, M.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7473−7474. (c) Abdur-Rashid, K.; Clapham, S. E.; Hadzovic, A.; Harvey, J. N.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 15104−15118. (d) Rautenstrauch, V.; Hoang-Cong, X.; Churlaud, R.; Abdur-Rashid, K.; Morris, R. H. *Chem.−Eur. J.* **2003**, *9*, 4954−4967. (e) Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* **2004**, available online.

(3) Alonso, D. A.; Brandt, P.; Nordin, S. J. M.; Andersson, P. G. *J. Am. Chem. Soc.* **1999**, *121*, 9580−9588.

(4) Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, R. K.; Kavana, M. *J. Am. Chem. Soc.* **2001**, *123*, 1090−1100.

(5) (a) Wiles, J. A.; Bergens, S. H.; Vanhessche, K. P. M.; Dobbs, D. A.; Rautenstrauch, V. *Angew. Chem., Int. Ed.* **2001**, *40*, 914−919. (b) Wiles, J. A.; Daley, C. J. A.; Hamilton, R. J.; Leong, C. G.; Bergens, S. H. *Organometallics* **2004**, *23*, 4564−4568.

(6) Heinekey, D. M.; Mellows, H.; Pratum, T. *J. Am. Chem. Soc.* **2000**, *122*, 6498−6499.

(7) (a) Earl, K. A.; Jia, G.; Maltby, P. A.; Morris, R. H. *J. Am. Chem. Soc.* **1991**, *113*, 3027−3039. (b) Bautista, M. T.; Cappellani, E. P.; Drouin, S. D.; Morris, R. H.; Schweitzer, C. T.; Sella, A.; Zubkowski, J. *J. Am. Chem. Soc.* **1991**, *113*, 4876−4887.

(8) Crabtree, R. H.; Habib, A. *Inorg. Chem.* **1986**, *25*, 3698−3699.

(9) Jessop, P. G.; Morris, R. H. *Coord. Chem. Rev.* **1992**, *121*, 155−284.

(10) (a) Heinekey, D. M.; Oldham, W. J., Jr. *Chem. Rev.* **1993**, *93*, 913−26. (b) Heinekey, D. M.; Lledós, A.; Lluch, J. M. *Chem. Soc. Rev.* **2004**, *33*, 175−182.

(11) (a) Kubas, G. J.; Ryan, R. R.; Swanson, B. I.; Vergamini, P. J.; Wassermann, H. *J. Am. Chem. Soc.* **1984**, *106*, 451−452. (b) Kubas, G. J.; Nelson, J. E.; Bryan, J. C.; Eckert, J.; Wisniewski, L.; Zilm, K. *Inorg. Chem.* **1994**, *33*, 2954−2960. (c) Kubas, G. J. *J. Organomet. Chem.* **2001**, *635*, 37−68. (d) Kubas, G. J. *Metal Dihydrogen and Sigma-Bond Complexes: Structure, Theory and Reactivity*; Kluwer Academic/Plenum Publishers: New York, 2001.

(12) Morris, R. H.; Song, D. *Organometallics* **2004**, *23*, 4406−4413.

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