

## Stoichiometric, Catalytic, and Enantioface-Selective Hydrogenation of C=N Bonds by an Ionic Mechanism

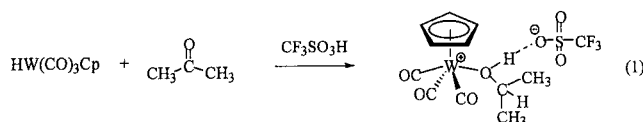
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Received October 10, 2000

The hydrogenation of carbon–carbon double bonds is a classic application of homogeneous catalysis, and numerous complexes are known to catalyze it. Furthermore, the use of chiral ligands to produce enantioface selectivity in such catalytic hydrogenations is now well developed.<sup>1</sup> The catalytic cycle for such reactions involves an olefin dihydride complex (with the addition of H<sub>2</sub>, step A, and the coordination of the olefin, step B, occurring in either order), giving the hydrogenated product by insertion and reductive elimination (Scheme 1).

However, there have been reports that transition metals can add the elements of hydrogen across double bonds *stoichiometrically* by a different mechanism. In separate papers in 1985 the Darensbourg<sup>2</sup> and Gibson<sup>3</sup> groups reported the reduction of aldehydes (ketones were much less reactive) by group 6 carbonyl hydrides and CH<sub>3</sub>CO<sub>2</sub>H. In 1987 Vos and co-workers reported the hydrogenation of acetone, by a hydride ligand and H<sup>+</sup> in aqueous solution.<sup>4</sup> In 1989 Bullock and Rappoli reported the hydrogenation of tetra-, tri-, and 1,1-disubstituted olefins by HMo(CO)<sub>3</sub>(C<sub>5</sub>H<sub>5</sub>) and CF<sub>3</sub>SO<sub>3</sub>H.<sup>5</sup> In 1992 we and the Bullock group reported the reduction of aldehydes and ketones under similar conditions, and isolated an isopropyl alcohol complex formed thereby (eq 1);<sup>6</sup> similar results have recently been reported with H<sub>2</sub>Re(NO)(CO)(PR<sub>3</sub>)<sub>2</sub>/CF<sub>3</sub>CO<sub>2</sub>H by Bakhmutov and co-workers.<sup>7</sup> Ionic hydrogenation has been extended to C=N double bonds by Ito and co-workers.<sup>8</sup> These reactions resemble the “ionic hydrogenations” long known with silanes as hydride donors.<sup>9</sup>



It has seemed likely that such reactions involve the rapid, reversible protonation of the substrate olefin or ketone, followed by hydride transfer from the metal (or the Si of the silane) (eq 2). As we would expect with such a mechanism, the rates of these

(1) For a recent mechanistic review, highlighting the work of the Brown and Halpern groups, see: Landis, C. R.; Brauch, T. W. *Inorg. Chim. Acta* **1998**, *270*, 285–297.

(2) Gaus, P. L.; Kao, S. C.; Youngdahl, K.; Darensbourg, M. Y. *J. Am. Chem. Soc.* **1985**, *107*, 2428–2434.

(3) Gibson, D. H.; El-Omrani, Y. S. *Organometallics* **1985**, *4*, 1473–1475.

(4) Geraty, S. M.; Harkin, P.; Vos, J. G. *Inorg. Chim. Acta* **1987**, *131*, 217–220. These results were mentioned briefly a year earlier, in: Kelly, J. M.; Vos, J. G. *J. Chem. Soc., Dalton Trans.* **1986**, 1045–1048.

(5) Bullock, R. M.; Rappoli, B. J. *J. Chem. Soc., Chem. Commun.* **1989**, 1447–1448. Full paper showing the metal hydrides that can be used: Bullock, R. M.; Song, J.-S. *J. Am. Chem. Soc.* **1994**, *116*, 8602–8612.

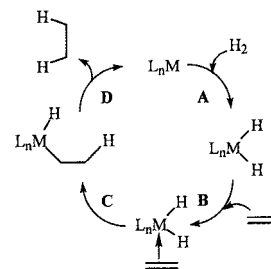
(6) Song, J.-S.; Szalda, D. J.; Bullock, R. M.; Lawrie, C. J. C.; Rodkin, M. A.; Norton, J. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1233–1235.

(7) Bakhmutov, V. I.; Vorontsov, E. V.; Antonov, D. Yu. *Inorg. Chim. Acta* **1998**, *278*, 122–126.

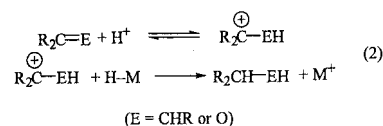
(8) Minato, M.; Fujiwara, Y.; Ito, T. *Chem. Lett.* **1995**, 647–648. Minato, M.; Fujiwara, Y.; Koga, M.; Matsumoto, N.; Kurishima, S.; Natori, M.; Sekizuka, N.; Yoshioka, K.-i.; Ito, T. *J. Organomet. Chem.* **1998**, *569*, 139–145.

(9) For a review, see: Kursanov, D. N.; Parnes, Z. N.; Loim, N. M. *Synthesis* **1974**, 633–651.

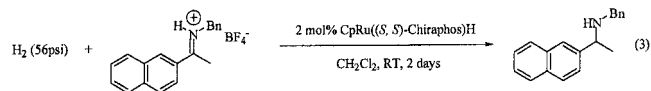
## Scheme 1



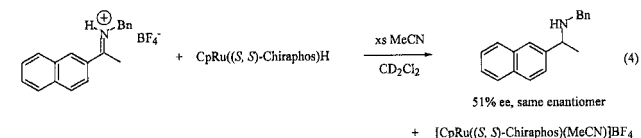
reactions increase with acidity<sup>4–6</sup> and are first-order in substrate.<sup>6</sup>



These ionic hydrogenation reactions *lend themselves to selective polar C=X double bonds over C=C double bonds*.<sup>10–12</sup> We now report that such a transformation works *catalytically* and *with enantioface selectivity* when a piano-stool ruthenium hydride complex is used. With an iminium cation (generated in situ from the corresponding imine and HBF<sub>4</sub>·OME<sub>2</sub>) (eq 3) as substrate, we obtained ~90% conversion to the ammonium salt, with (after basic workup) an ee of 60%.<sup>13</sup>



When the same substrate is treated with a stoichiometric amount of hydride (no H<sub>2</sub>), in the presence of a donor ligand, a similar ee is obtained (eq 4). Acetonitrile stabilizes the ruthenium cation, providing a clean organometallic product.



A series of catalytic reactions using methyl aryl pyrrolidinium cations as substrates produce varying ee's (Table 1).

The analogous stoichiometric hydride transfer reactions are shown in Table 2. Hydride transfer does not occur from CpRu((S)-BINAP)H (presumably because a triarylphosphine is not sufficiently electron-rich) or from CpRu((S,S)-DIOP)H ((S,S)-DIOP = (4*S*,5*S*)-(+)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane) (perhaps because of the size of its chelate ring).<sup>14</sup> The enantiomeric excesses in Table 2 are similar to those in the catalytic reactions in Table 1, demonstrating that *hydride transfer* from the transition metal to the cation is the *enantioselectivity-determining* step in the catalytic cycle, and that the mechanism is ionic.

(10) (a) Noyori, R. *Acta Chem. Scand.* **1996**, *50*, 380–390. (b) Noyori, R.; Ohkuma, T. *Pure Appl. Chem.* **1999**, *71*, 1493–1501.

(11) Ohkuma, T.; Ooka, H.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 10417–10418.

(12) The Bullock group has submitted a report of the catalysis of the ionic hydrogenation of ketones by Mo and W hydrides: Bullock, R. M.; Voges, M. H. *J. Am. Chem. Soc.* **2000**, *122*, 12594–12595.

(13) The ee was determined by addition of (*S*)-*O*-acetylmandelic acid to a solution of the amine in CDCl<sub>3</sub> or CD<sub>2</sub>Cl<sub>2</sub> (Lee, N. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 5985).

(14) Berning, D. E.; Noll, B. C.; DuBois, D. L. *J. Am. Chem. Soc.* **1999**, *121*, 11432–11447.

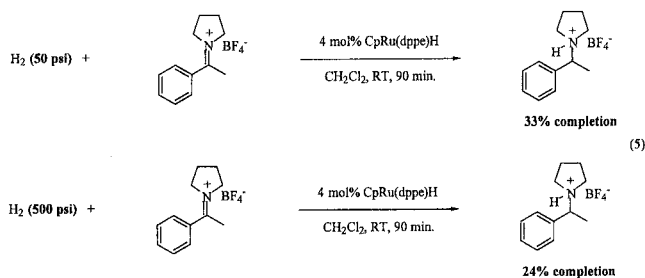
Table 1

Hydride	X	amine yield	ee, configuration of amine
CpRu((S, S)-Chiraphos)H	H	80%	35%, (R) (S, S)-Chiraphos =
CpRu((S, S)-Chiraphos)H	Cl	57%	56%, (R)
CpRu((R, R)-Norphos)H	H	74%	48%, (S) (R, R)-Norphos =
CpRu((R, R)-Norphos)H	Cl	82%	60%, (S)

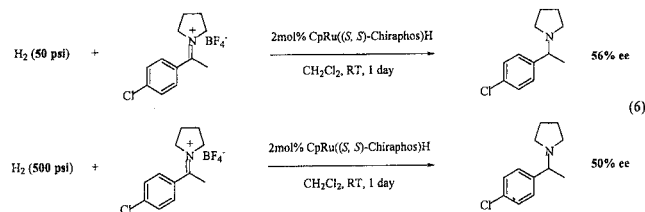
Table 2

Hydride	X	ee, configuration of amine
CpRu((S, S)-Chiraphos)H	H	38%, (R)
CpRu((S, S)-Chiraphos)H	Cl	55%, (R)
CpRu((R, R)-Norphos)H	H	54%, (S)
CpRu((R, R)-Norphos)H	Cl	54%, (S)

When the pressure is varied, there is no change in the rate or enantiomeric excess of the catalytic reaction. Thus, hydrogen does not participate in the turnover-limiting or enantioselectivity-determining steps. When the hydrogenation catalysis was stopped before completion after the same amount of time with different H<sub>2</sub> pressures, there was little change in the conversion (eq 5, dppe = 1,2-bis(diphenylphosphino)ethane).



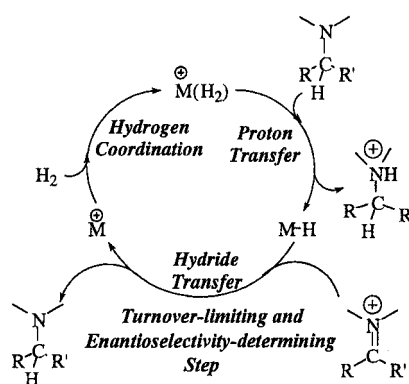
The ee also does not change when the pressure is varied (eq 6).



Monitoring catalysis by <sup>1</sup>H NMR also points to *hydride transfer* as the turnover-limiting step.<sup>15</sup> When a pressure NMR tube is charged with the same iminium cation and hydride under 75 psi of H<sub>2</sub>, only the hydride is observed while substrate is still present. No dihydrogen or dihydride species are observed during

(15) A similar equivalence between the rates of the catalytic and the stoichiometric reactions was observed when the hydrogenation of cyclohexanone was catalyzed by H<sub>4</sub>Ru(PPh<sub>3</sub>)<sub>3</sub>: Linn, D. E., Jr.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 2969–2974.

Scheme 2



the catalysis. *Transfer of hydride* is therefore necessarily the slow step in the reaction. Only after complete depletion of substrate is the known<sup>16</sup> ratio of dihydride and dihydrogen complexes observed. Upon substrate depletion, the hydride comprised ~25% of the Ru hydride region of the spectrum. Readdition of more iminium cation restarted the reaction, and it went to near completion.

A catalytic cycle consistent with the above experimental observations is proposed. The selectivity and rate all appear to depend exclusively on H<sup>-</sup> transfer as the key step (Scheme 2).

The use of P–P\* ruthenium hydride complexes in asymmetric hydrogenation is well established: Bergens<sup>17</sup> and Gridnev<sup>18</sup> have isolated Ru and Rh hydrides that observably insert the C=C of enamides, and Noyori has offered compelling evidence that a Ru hydride is involved in the asymmetric transfer hydrogenation of ketones.<sup>19</sup> However, we are unaware of any previous cases in which the mechanism has been shown to be ionic. Our system permits the asymmetric hydrogenation of imines (from which iminium cations can be generated in situ), but such C=N bonds can be hydrogenated with better enantioselectivities by established catalysts.<sup>20,21</sup> We are unaware of any previous reports of the asymmetric hydrogenation of tetra-alkyl-substituted C=N cations. Catalytic ionic hydrogenation can be done in an ionizing solvent and new catalysts screened easily by determining the enantioselectivity of stoichiometric hydride transfer.

**Acknowledgment.** We thank the NSF for financial support under Grant CHE-997446, and J. Penney, M. Rodkin, and A. K. Rappé for valuable input.

**Supporting Information Available:** Experimental procedures and characterization of all new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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 (17) Wiles, J. A.; Bergens, S. H. *Organometallics* **1998**, *17*, 2228–2240.  
 (18) Gridnev, I. D.; Higashi, N.; Asakura, K.; Imamoto, T. *J. Am. Chem. Soc.* **2000**, *122*, 7183–7194.  
 (19) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 285–288.  
 (20) Asymmetric hydrogenation without mechanistic detail has been reported for iminium cations generated in situ: Broger, E. A.; Burkart, W.; Hennig, M.; Scalone, M.; Schmid, R. *Tetrahedron: Asymmetry* **1998**, *9*, 4043–4054.

(21) With a phenyl methyl imine related to our substrates the Buchwald group (Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952–8965) has reported ee's of 77–85% with a chiral titanocene catalyst. Such hydrogenations are presumed (e.g., in Scheme 3 in the previous reference) to involve substrate *coordination* as part of a traditional insertion mechanism, whereas an ionic hydrogenation involves hydride transfer to an *uncoordinated* substrate. Imine hydrogenations have been reviewed: Blaser, H.-U.; Spindler, F. Hydrogenation of Imino Groups. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., and Yamamoto, H., Eds.; Springer-Verlag: New York, 1999; Vol. 1, pp 247–265.