

Heterolytic Cleavage of Hydrogen Molecule by Rhodium Thiolate Complexes That Catalyze Chemoselective Hydrogenation of Imines under Ambient Conditions

Yoshiyuki Misumi, Hidetake Seino,* and Yasushi Mizobe*

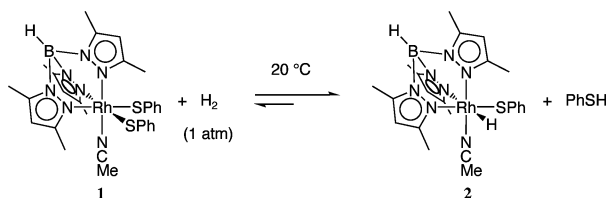
Institute of Industrial Science, The University of Tokyo, Komaba, Meguro-ku, Tokyo 153-8505, Japan

Received July 14, 2009; E-mail: ymizobe@iis.u-tokyo.ac.jp; seino@iis.u-tokyo.ac.jp

Heterolytic activation of dihydrogen is a key step in catalytic hydrogenation of polar bonds and hydrogen metabolism mediated by hydrogenases. Many transition-metal complexes, especially electron-poor ones, are known to be capable of cleaving H_2 generally in the manner that H^+ is split off from the highly acidic H_2 ligand to leave H^- on the metal center.¹ In this conversion, the proton is accepted by an external Lewis base or more efficiently by an internal ancillary ligand, as is typically observed in metal–ligand bifunctional catalysts represented by organoamide complexes.² Anionic S-donor ligands, RS^- and S^{2-} , are also expected to become internal proton acceptors, and some mechanisms proposed for the function of [NiFe]-hydrogenases postulate proton transfer from the coordinated H_2 to the Ni-bound terminal S(Cys) moiety.³ However, such reactions proceeding on thiolate complexes are uncommon.^{4–6} There are only a few cases that clearly confirm the formation of $M(H)–S(H)R$ from $M–SR$ with H_2 ⁵ and scarce applications to catalysis.⁶

We have been engaging in studies involving activation of small molecules by transition-metal thiolate complexes.⁷ We herein report that the bis(thiolate)Rh(III) complex having a tris(3,5-dimethylpyrazolyl)borate (Tp^{Me_2}) coligand, $[Tp^{Me_2}Rh(SPh)_2(MeCN)]$ (**1**),^{7b} reacts reversibly with H_2 to form the hydridothiolato complex $[Tp^{Me_2}RhH(SPh)(MeCN)]$ (**2**) and PhSH, as shown in Scheme 1. On the basis of this heterolysis of H_2 , a hydrogenation catalyst that operates under ambient temperature and pressure with high chemoselectivity toward imines has been developed.

Scheme 1



Treatment of a 10 mM solution of **1** in C_6D_6 with 1 atm H_2 at 20 °C for 2 h gave an equilibrium mixture containing **1**, **2**, and PhSH in a 1:10:10 ratio. When this mixture was set under a N_2 atmosphere, **1** was slowly regenerated. The 1H NMR spectrum of **2** showed a doublet at $\delta = 13.80$ ($J_{RhH} = 11.6$ Hz) due to the hydrido ligand and 10 singlets corresponding to the three inequivalent pyrazolyl groups (two methyls and one ring proton for each) and MeCN. Although we previously found **2** in the reaction of $[Tp^{Me_2}Rh(C_8H_{14})(MeCN)]$ with 1 equiv of PhSH, its isolation was hampered by simultaneous production of **1** ($1/2 \approx 1:2$).^{7e} Here, addition of hexane to an equilibrium mixture prepared from **1** under a H_2 atmosphere gave yellow crystals of pure **2**, with which the structure was fully determined by X-ray crystallography (see the Supporting Information).

As reversible heterolysis of H_2 molecule at the Rh–S bond in **1** was disclosed, catalytic hydrogenation was examined to probe the reactivity of the resulting hydrogen atoms. As shown in Table 1, **1** was found to be effective for the hydrogenation of styrene and *N*-benzylideneaniline under 1 atm H_2 with low to moderate activity at 20–50 °C (entries 1–4). Although higher activity was expected toward the more polarized C=O bond, benzaldehyde and acetophenone were not hydrogenated under these conditions. Isolated **2** showed slightly higher activity than **1** toward styrene, implying that the active species in C=C reduction is close to **2** (entry 5). However, conversion of *N*-benzylideneaniline was much deteriorated when **2** alone was used, and therefore, not only the Rh–H but also the S–H hydrogen are essential for hydrogenating the C=N bond (entry 6). The activity of the diiodo complex $[Tp^{Me_2}RhI_2(MeCN)]$ (**3**) toward this substrate was also poor (entry 7), but the Se analogue of **1**, $[Tp^{Me_2}Rh(SePh)_2(MeCN)]$ (**4**),^{7c} was found to be much more active than **1**, even at 20 °C (entry 8). Whereas **3** remained almost intact under a H_2 atmosphere at 50 °C, **4** formed the hydrido complex analogously to **1**. These results indicate that catalytic activity for the hydrogenation of C=N bonds sharply depends on the ability to heterolyze H_2 molecules and that this is strongly affected by ligating elements.

Table 1. Hydrogenation of $PhCH=Z$ Catalyzed by $[Tp^{Me_2}RhX^1X^2(MeCN)]^a$

entry	catalyst (X^1 ; X^2)	Z	temp (°C)	time (h)	yield (%) ^b
1	1 (SPh; SPh)	CH_2	20	20	16
2	1 (SPh; SPh)	CH_2	50	10	72
3	1 (SPh; SPh)	NPh	20	20	21
4	1 (SPh; SPh)	NPh	50	10	63
5	2 (H; SPh)	CH_2	50	10	86
6	2 (H; SPh)	NPh	50	10	18
7	3 (I; I)	NPh	50	10	27
8	4 (SePh; SePh)	NPh	20	6	99
9	5 (<i>o</i> - $S_2C_6H_4$)	NPh	20	1	98
10 ^c	5 (<i>o</i> - $S_2C_6H_4$)	NPh	20	2	48

^a Conditions: substrate (1.00 mmol), catalyst (0.01 mmol), THF (5 mL), H_2 (1 atm). ^b Yields of ethylbenzene and *N*-benzylaniline were determined by GLC analyses. The sum of the yields of product and remaining substrate was no less than 98% in each reaction. ^c Conducted in benzene (5 mL).

To improve the catalytic efficiency, the benzenedithiolato complex $[Tp^{Me_2}Rh(o-S_2C_6H_4)(MeCN)]$ (**5**) was newly synthesized according to Scheme 2. The active intermediate generated from **5** may contain both RhH and SH moieties within the same molecule. As expected, **5** achieved much more rapid hydrogenation of *N*-benzylideneaniline at 20 °C than the other complexes mentioned above (Table 1, entry 9). Moreover, it was found that reduction of the C=C bond is suppressed and inertness toward the C=O bond is still preserved, as shown in Table 2. Thus, the C=N bonds in various aldimines are efficiently hydrogenated under ambient

temperature and pressure with coexisting C=C or C=O functions unaffected, with the exception that partial reduction occurred for the C=C bond conjugated with the C=N group (entry 3). On behalf of inertness to C=O bonds, reductive amination could be performed by mixing aldehyde and primary amine directly under hydrogenation conditions (entry 5). Conversion of a ternary iminium salt into a tertiary ammonium salt also took place quantitatively (entry 6).

Scheme 2

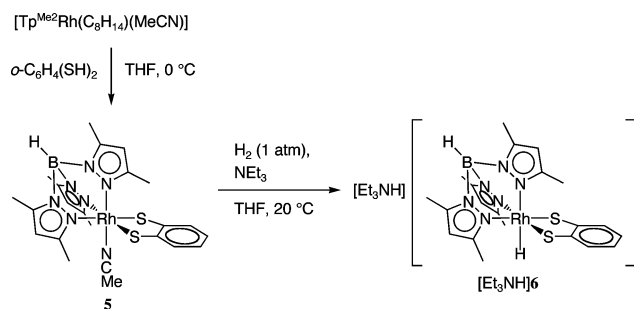


Table 2. Hydrogenation of Various Imines Catalyzed by **5**^a

entry	substrate	product (yield ^b)
1	PhCH=NCH ₂ Ph	PhCH ₂ NHCH ₂ Ph (97%)
2	PhCH=NCH ₂ CH=CH ₂	PhCH ₂ NHCH ₂ CH=CH ₂ (90%)
3	<i>E</i> -PhCH=CHCH=NPh	<i>E</i> -PhCH=CHCH ₂ NHPh (82%) PhCH ₂ CH ₂ CH ₂ NHPh (15%)
4	<i>m</i> -C ₆ H ₄ (CHO)(CH=NPh)	<i>m</i> -C ₆ H ₄ (CHO)(CH ₂ NHPh) (99%)
5 ^c	<i>n</i> -C ₇ H ₁₅ CHO + H ₂ NPh	<i>n</i> -C ₇ H ₁₅ CH ₂ NHPh (61%)
6	[PhCH=N(CH ₂) ₂ CH ₂ Ph][BF ₄]	[PhCH ₂ NH(CH ₂) ₂ CH ₂ Ph][BF ₄] (quant.)

^a Conditions: substrate (1.00 mmol), **5** (0.01 mmol), THF (5 mL), H₂ (1 atm), 20 °C, 1 h. ^b NMR determination (entries 1–3, 6) or isolated yields (entries 4 and 5). ^c Octanal (1.01 mmol) was added to a solution of aniline (1.02 mmol) and **5** (0.020 mmol) under a H₂ atmosphere.

In contrast to **1**, no observable change in **5** occurred under 1 atm H₂. However, addition of NEt₃ to its THF solution caused rapid formation of an off-white solid, which was characterized as [Et₃NH][Tp^{Me2}Rh(*o*-S₂C₆H₄)] ([Et₃NH]**6**). The hydrido ligand in **6**[−] exhibited an ¹H signal at −18.90 (d, *J*_{RhH} = 14.8 Hz) and an IR absorption for ν(Rh–H) at 2104 cm^{−1}. Because of the appearance of the ν(N–H) band at 2670 cm^{−1} characteristic of tertiary ammonium cation, **6**[−] was identified as a monoanion. From this result, it is plausible that {Tp^{Me2}Rh(*o*-S₂C₆H₄)} and H₂ form an adduct that may shift H⁺ to the imine and also that the resulting **6**[−] transfers H[−] to this iminium cation. This mechanism, namely, ionic hydrogenation,⁸ is supported by the decrease in the catalytic rate in the less-polar benzene medium (Table 1, entry 10).⁹ The major catalytic cycle of imine reduction by **1** is also considered to be similar, because the anionic hydrido complex analogous to **6**[−] can be prepared from **1** under the same conditions. Such a reaction pathway mediated by formation of an active iminium ion has been proposed in some other catalytic systems.¹⁰ The preferential addition of H₂ to the C=N bond over the C=O bond as observed here is uncommon.¹¹ Presumably, the H₂ adduct of the Rh species is not acidic enough to protonate O atom, and the nucleophilicity of **6**[−] is not strong enough to reduce the nonactivated C=O bond. On the other hand, hydrogenation of acetophenone by a Ru thiolate complex has been proposed to proceed via the concerted transfer

of hydride and proton to the C=O bond,⁶ as is widely accepted for bifunctional molecular catalysts.²

It is still unclear whether deprotonation from the H₂ adducts of Rh thiolate complexes occurs directly at the stage of η²-H₂ or after formation of Rh(H)–S(H) species. However, their catalytic functions may have some relevance to [Fe]-hydrogenases, which generate a proton and transfer a hydride to an organic molecule at a monoiron site bound to a cysteine residue.^{12,13}

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Supporting Information Available: Experimental details and X-ray analysis data for **2** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) (a) Brothers, P. J. *Prog. Inorg. Chem.* **1981**, 28, 1. (b) Morris, R. H. *Can. J. Chem.* **1996**, 74, 1907. (c) Kubas, G. J. *Adv. Inorg. Chem.* **2004**, 56, 127.
- (2) Recent reviews: (a) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, 40, 40. (b) Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* **2004**, 248, 2201. (c) Ito, M.; Ikariya, T. *Chem. Commun.* **2007**, 5134.
- (3) Recent reviews: (a) Volbeda, A.; Fontecilla-Camps, J. C. *Dalton Trans.* **2003**, 4030. (b) De Lacey, A. L.; Fernández, V. M.; Rousset, M.; Cammack, R. *Chem. Rev.* **2007**, 107, 4304. (c) Siegbahn, P. E. M.; Tye, J. W.; Hall, M. B. *Chem. Rev.* **2007**, 107, 4414. (d) Tard, C.; Pickett, C. J. *Chem. Rev.* **2009**, 109, 2245. (e) Gloaguen, F.; Rauchfuss, T. B. *Chem. Soc. Rev.* **2009**, 38, 100.
- (4) (a) Sellmann, D.; K  ppler, J.; Moll, M. *J. Am. Chem. Soc.* **1993**, 115, 1830. (b) Jessop, P. G.; Morris, R. H. *Inorg. Chem.* **1993**, 32, 2236. (c) Sellmann, D.; Gottschalk-Gaudig, T.; Heinemann, F. W. *Inorg. Chem.* **1998**, 37, 3982. (d) Sellmann, D.; F  rsattel, A. *Angew. Chem., Int. Ed.* **1999**, 38, 2023. (e) Sellmann, D.; Geipel, F.; Moll, M. *Angew. Chem., Int. Ed.* **2000**, 39, 561. (f) Sellmann, D.; Prakash, R.; Heinemann, F. W.; Moll, M.; Klimowicz, M. *Angew. Chem., Int. Ed.* **2004**, 43, 1877. (g) Matsumoto, T.; Nakaya, Y.; Tatsumi, K. *Angew. Chem., Int. Ed.* **2008**, 47, 1913.
- (5) (a) Schlaf, M.; Lough, A. J.; Morris, R. H. *Organometallics* **1996**, 15, 4423. (b) Sellmann, D.; Rackelmann, G. H.; Heinemann, F. W. *Chem.–Eur. J.* **1997**, 3, 2071. (c) Ohki, Y.; Sakamoto, M.; Tatsumi, K. *J. Am. Chem. Soc.* **2008**, 130, 11610.
- (6) Ohki, Y.; Takikawa, Y.; Sadohara, H.; Kesenheimer, C.; Engendahl, B.; Kapatina, E.; Tatsumi, K. *Chem.–Asian J.* **2008**, 3, 1625.
- (7) (a) Takagi, F.; Seino, H.; Hidai, M.; Mizobe, Y. *Organometallics* **2003**, 22, 1065. (b) Seino, H.; Yoshikawa, T.; Hidai, M.; Mizobe, Y. *Dalton Trans.* **2004**, 3593. (c) Nagao, S.; Seino, H.; Hidai, M.; Mizobe, Y. *Dalton Trans.* **2005**, 3166. (d) Kajitani, H.; Seino, H.; Mizobe, Y. *Organometallics* **2005**, 24, 6260. (e) Misumi, Y.; Seino, H.; Mizobe, Y. *J. Organomet. Chem.* **2006**, 691, 3157. (f) Saito, A.; Seino, H.; Kajitani, H.; Takagi, F.; Yashiro, A.; Ohnishi, T.; Mizobe, Y. *J. Organomet. Chem.* **2006**, 691, 5746.
- (8) (a) Bullock, R. M.; Voges, M. H. *J. Am. Chem. Soc.* **2000**, 122, 12594. (b) Magee, M. P.; Norton, J. R. *J. Am. Chem. Soc.* **2001**, 123, 1778. (c) Bullock, R. M. *Chem.–Eur. J.* **2004**, 10, 2366. (d) Guan, H.; Iimura, M.; Magee, M. P.; Norton, J. R.; Zhu, G. *J. Am. Chem. Soc.* **2005**, 127, 7805. (e) Namorado, S.; Antunes, M. A.; Veiros, L. F.; Ascenso, J. R.; Duarte, M. T.; Martins, A. M. *Organometallics* **2008**, 27, 4589.
- (9) Addition of MeCN also retarded the catalysis by **5**.
- (10) (a) Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, R. K.; Kavana, M. *J. Am. Chem. Soc.* **2001**, 123, 1090. (b)   berg, J. B.; Samec, J. S. M.; B  ckvall, J.-E. *Chem. Commun.* **2006**, 2771. (c) Shirai, S.; Nara, H.; Kayaki, Y.; Ikariya, T. *Organometallics* **2009**, 28, 802.
- (11) (a) Ng Cheong Chan, Y.; Meyer, D.; Osborn, J. A. *J. Chem. Soc., Chem. Commun.* **1990**, 869. (b) Ng Cheong Chan, Y.; Osborn, J. A. *J. Am. Chem. Soc.* **1990**, 112, 9400. (c) Gross, T.; Seayad, A. M.; Ahmad, M.; Bellier, M. *Org. Lett.* **2002**, 4, 2055.
- (12) (a) Shima, S.; Thauer, R. K. *Chem. Rec.* **2007**, 7, 37. (b) Shima, S.; Pilak, O.; Vogt, S.; Schick, M.; Stagni, M. S.; Meyer-Klaucke, W.; Warkentin, E.; Thauer, R. K.; Ermiler, U. *Science* **2008**, 321, 572. (c) Hiromoto, T.; Ataka, K.; Pilak, O.; Vogt, S.; Stagni, M. S.; Meyer-Klaucke, W.; Warkentin, E.; Thauer, R. K.; Shima, S.; Ermiler, U. *FEBS Lett.* **2009**, 583, 585.
- (13) (a) Royer, A. M.; Rauchfuss, T. B.; Gray, D. L. *Organometallics* **2009**, 28, 3618. (b) Yang, X.; Hall, M. B. *J. Am. Chem. Soc.* **2009**, 131, 10901.

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