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Homogeneous Catalytic System for Reversible Dehydrogenation−Hydrogenation Reactions of Nitrogen Heterocycles with Reversible Interconversion of Catalytic Species

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Catalytic dehydrogenation and hydrogenation reactions of organic molecules are fundamental and important processes in catalytic organic transformations.[1] In addition, these reactions have recently attracted considerable attention from the viewpoint of organic hydride hydrogen storage systems, i.e., storing hydrogen in organic hydrides containing chemically bonded hydrogen atoms.[2] Along this line, recent experimental and computational studies of the potential ability of nitrogen heterocycles to serve as the organic hydrides have indicated that incorporation of a nitrogen atom into the cyclic system facilitates the dehydrogenation process by decreasing the endothermicity of the reaction.[3,4] However, to the best of our knowledge, all of these systems reported to date have employed conventional heterogeneous metal catalysts, and therefore, fine-tuning of the catalysts and mechanistic investigations would generally be more difficult than for homogeneous catalysts. It should be also noted that the reversibility of and selectivity between the dehydrogenation and hydrogenation reactions were still insufficient in these heterogeneous catalytic systems.[5] Thus, the development of an efficient homogeneous catalytic system for the reversible dehydrogenation−hydrogenation reactions of nitrogen heterocycles is of great current interest.[6]

Recently, we have reported the oxidant-free catalytic oxidation of secondary alcohols to ketones with concomitant evolution of hydrogen, in which Cp*Ir complexes **1** and **2a** containing 2-hydroxypyridine and 2-pyridonate, respectively, as functional ligands (Figure 1) have proven to be effective catalysts.[7−9] Thus, it would be challenging to explore the catalytic performance of these catalysts for the dehydrogenation and hydrogenation reactions of nitrogen heterocycles. In this paper, we report the first homogeneous catalytic system for the efficient reversible and repetitive dehydrogenation−hydrogenation reactions of nitrogen heterocycles using a single complex as the catalyst.

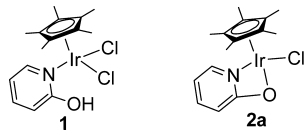
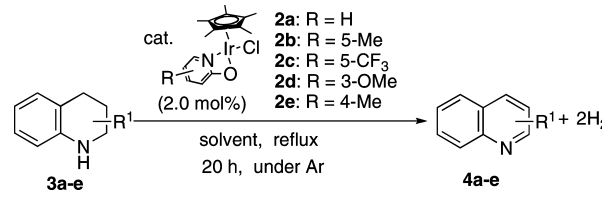


Figure 1. Cp* Iridium complexes containing (left) 2-hydroxypyridine and (right) 2-pyridonate ligands.

We started to investigate the catalytic performance of the Cp*Ir complexes for the dehydrogenation of 1,2,3,4-tetrahydroquinoline to form quinoline (Table 1, entries 1−7).[10] When the dehydrogenation reaction of 1,2,3,4-tetrahydroquinoline (**3a**) was carried out in the presence of the Cp*Ir catalyst **1** (2.0 mol %) under reflux in toluene, quinoline (**4a**) was formed in only 7% yield (entry 1). The reaction using the catalyst **2a** gave **4a** in 13% yield (entry 2), exhibiting the higher activity of the chelating 2-pyridonate ligand. The yield of **4a** was increased to 69% by conducting the reaction under reflux in *p*-xylene (entry 3), though it was still unsatisfactory. Next, we modified the 2-pyridonate ligand by introducing electron-donating and -withdrawing groups in the pyridine ring. New Cp*Ir complexes containing 5-methyl- and 5-trifluoromethylpyridonate ligands (**2b** and **2c**, respectively) were synthesized, and complex **2c** exhibited superior activity and selectivity compared with **2a** and **2b** (entries 4 and 5).[11] Other Cp*Ir complexes containing 3-methoxy- and 4-methylpyridonate ligands (**2d** and **2e**, respectively) gave rather low yields and selectivities (entries 6 and 7).

Table 1. Dehydrogenation of 1,2,3,4-Tetrahydroquinolines Catalyzed by Various Cp*Ir Complexes[a]



entry	catalyst	substrate	solvent	conv. (%)[b]	yield (%)[b]
1	**1**	**3a** (R^1 = H)	toluene	8	7
2	**2a**	**3a** (R^1 = H)	toluene	13	13
3	**2a**	**3a** (R^1 = H)	*p*-xylene	70	69
4	**2b**	**3a** (R^1 = H)	*p*-xylene	61	57
5	**2c**	**3a** (R^1 = H)	*p*-xylene	73	73
6	**2d**	**3a** (R^1 = H)	*p*-xylene	67	66
7	**2e**	**3a** (R^1 = H)	*p*-xylene	63	59
8	**2c**	**3b** (R^1 = 2-Me)	*p*-xylene	100	100
9	**2c**	**3c** (R^1 = 3-Me)	*p*-xylene	86	86
10	**2c**	**3d** (R^1 = 4-Me)	*p*-xylene	76	76
11	**2c**	**3e** (R^1 = 6-Me)	*p*-xylene	82	82

[a] The reaction was carried out with **3** (1.0 mmol) and the catalyst (2.0 mol % Ir) under reflux in solvent (3 mL) for 20 h. [b] Determined by GC.

Having the preferred dehydrogenation catalyst **2c** in hand, we next investigated the dehydrogenation reactions of substituted 1,2,3,4-tetrahydroquinoline derivatives in order to find a more effective substrate. Among methyl-substituted 1,2,3,4-tetrahydroquinolines (Table 1, entries 8−11), 2-methyl-substituted **3b** was dehydrogenated quite smoothly to give **4b** quantitatively with complete selectivity (entry 8).[12,13] The dehydrogenations of 3-, 4-, and 6-methyl-substituted substrates (**3c**−**e**, respectively) were relatively slow (entries 9−11).

In order to obtain unambiguous experimental evidence that the evolved gas is hydrogen and that it can be used in another reaction, we undertook the following dual reactions (Scheme 1). The dehydrogenation reaction of **3b** using the catalyst **2c** was conducted in a flask that was connected through a rubber tube to another flask in which

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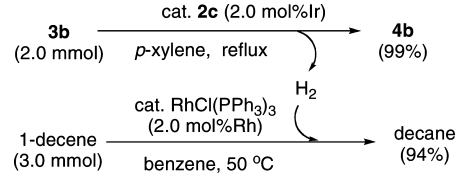
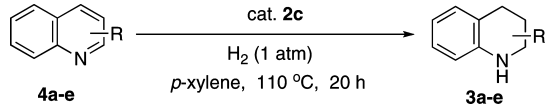
1-decene and a catalytic amount of $RhCl(PPh_3)_3$ in benzene were placed. After the dehydrogenation was almost completed, decane was produced in 94% yield in the latter flask, demonstrating that the hydrogen gas generated in the former flask was transferred through the tube to reduce 1-decene in the latter.[14] Thus, it is apparent that hydrogen gas generated in the present dehydrogenation is pure enough to be utilized in other reactions.

Scheme 1. Dual Reactions Involving Dehydrogenation of **3b** and Hydrogenation of 1-Decene



Since the 5-trifluoromethylpyridonate Cp*Ir complex **2c** was found to be the most efficient catalyst for the dehydrogenation of 1,2,3,4-tetrahydroquinolines, we next examined whether the reverse reaction, i.e., hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline,[15] could be accomplished using the same catalyst **2c**. The hydrogenation reactions of quinolines using **2c** were conducted under almost the same conditions as those of the above dehydrogenation reactions, except for an atmosphere of hydrogen. The results are summarized in Table 2.[16] The reaction of quinoline **4a** itself under hydrogen (1 atm) in the presence of **2c** at 110 °C in *p*-xylene gave **3a** in almost quantitative yield (entry 1). Under similar conditions, 2-methylquinoline **4b** was also completely converted to **3b** (entry 2). When the reaction was carried out under 3 atm H_2, the smooth hydrogenation occurred at the lower temperature of 80 °C (entry 3). Even a higher pressure of hydrogen (10 atm) remarkably reduced the reaction time to only 2 h (entry 4). The hydrogenations of other substituted quinolines were less effective, except for the reaction of 6-methylquinoline **4e**, which gave **3e** quantitatively (entry 7). The hydrogenations of **4c** and **4d** resulted in low to moderate yields (entries 5 and 6).

Table 2. Hydrogenation of Quinolines Catalyzed by Complex **2c**[a]

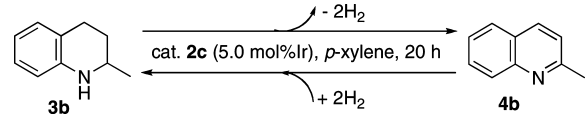


entry	cat. mol % Ir	substrate	conv. (%)[b]	yield (%)[b]
1	4.0	**4a** (R = H)	100	99
2	4.0	**4b** (R = 2-Me)	100	100
3[c]	4.0	**4b** (R = 2-Me)	100	100
4[d]	4.0	**4b** (R = 2-Me)	100	100
5	5.0	**4c** (R = 3-Me)	58	56
6	5.0	**4d** (R = 4-Me)	13	13
7	5.0	**4e** (R = 6-Me)	100	100

[a] The reaction was carried out with **4** (1.0 mmol) and catalyst **2c** in *p*-xylene (3 mL) at 110 °C for 20 h. [b] Determined by GC. [c] Carried out at 80 °C under 3 atm H_2. [d] Carried out under 10 atm H_2 for 2 h.

As mentioned above, it has been found that the 2-pyridonate Cp*Ir complex **2c** very efficiently catalyzes both of the dehydrogenation of **3b** and the hydrogenation of **4b**. Thus, we investigated the reversible and repetitive transformations between **3b** and **4b** in one flask via dehydrogenation−hydrogenation reactions using complex **2c** as the single catalyst (Table 3). At first, the dehydrogenation of **3b** was conducted under reflux in *p*-xylene under an atmosphere of argon to afford **4b** quantitatively. Next, the atmosphere of the flask was replaced with hydrogen (1 atm), and the solution was stirred at 110 °C. This simple procedure gave back **3b** quantitatively. Moreover, it should be noted that these reversible catalytic transformations between **3b** and **4b** could be nearly quantitatively repeated five times with almost no loss of efficiency.

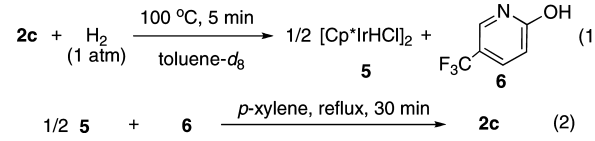
Table 3. Reversible and Repetitive Transformation between **3b** and **4b** in One Flask via Dehydrogenation−Hydrogenation Reactions Catalyzed by Complex **2c**[a]



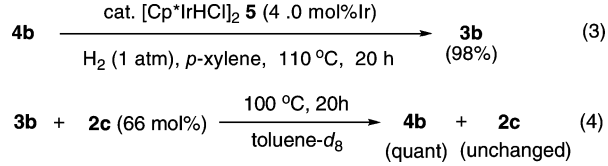
cycle	dehydrogenation yield (%)[b]	hydrogenation yield (%)[b]
1	100	100
2	100	100
3	100	99
4	99	98
5	98	98

[a] The dehydrogenation was carried out with **3b** (1.0 mmol) and catalyst **2c** (5 mol %) in *p*-xylene (3 mL) under reflux for 20 h under argon. Next, the atmosphere of the flask was replaced with hydrogen, and a balloon filled with hydrogen was connected to the flask. The mixture was stirred for 20 h at 110 °C. [b] Determined by GC.

A question relating to the mechanism of the present reversible and repetitive catalytic transformations would be whether complex **2c** is the common catalytic species in both the dehydrogenation and hydrogenation reactions. To clarify this point, a solution of **2c** in toluene-d_8 was heated at 100 °C under hydrogen (1 atm) for 5 min. ^{1}H NMR analysis interestingly revealed that **2c** was completely converted to the hydride-bridged dinuclear Cp*Ir complex **5**[17] (83% by ^{1}H NMR analysis) with concomitant liberation of 5-trifluoromethyl-2-hydroxypyridine (**6**) in quantitative yield (eq 1). On the other hand, it was observed that heating a solution of dinuclear complex **5** and ligand **6** in *p*-xylene under reflux for 30 min without hydrogen regenerated complex **2c** (93% by ^{1}H NMR analysis) (eq 2).[18] These results evidently suggest reversible interconversion between **2c** and **5**, depending on the presence or absence of hydrogen.



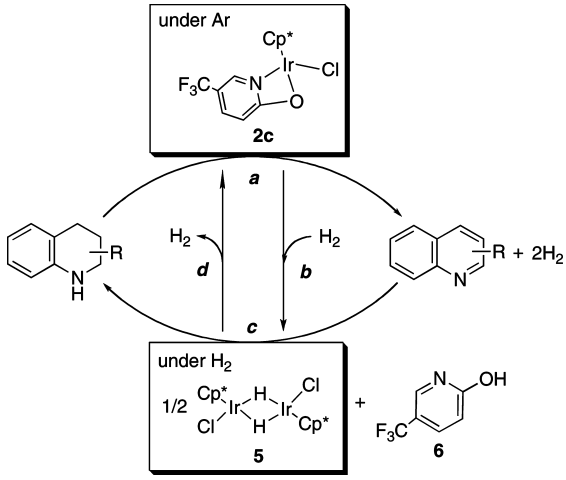
Furthermore, the hydrogenation of **4b** was conducted using the dinuclear complex **5** as the catalyst under reaction conditions similar to the above and gave **3b** in almost quantitative yield (eq 3), indicating that the catalytic species in the hydrogenation is **5** instead of **2c**.[19] ^{1}H NMR analysis also showed that the dehydrogenation of **3b** using a substoichiometric amount of **2c** (66 mol %) at 100 °C in toluene-d_8 gave **4b** quantitatively along with unchanged **2c** (eq 4), suggesting that the pyridonate complex **2c** was intact under the conditions without hydrogen.



On the basis of the above experimental evidence, it is highly probable that the present reversible catalytic dehydrogenation−hydrogenation proceeds with reversible interconversion of catalytic species between the pyridonate Cp*Ir complex **2c** and the hydride-bridged Cp*Ir dinuclear complex **5**. The overall processes for the

reversible catalytic transformations are summarized in Scheme 2. The catalytic dehydrogenation of 1,2,3,4-tetrahydroquinolines takes place by the pyridonate Cp*Ir complex **2c** to give quinolines with concomitant evolution of hydrogen (catalytic step ***a***). Under an atmosphere of hydrogen, complex **2c** is converted to the hydride-bridged Cp*Ir dinuclear complex **5**, accompanied by liberation of the ligand **6** (step ***b***). Next, complex **5** catalyzes the hydrogenation of quinolines to give 1,2,3,4-tetrahydroquiolines (catalytic step ***c***). Finally, removal of hydrogen results in combination of **5** and **6** to regenerate the original complex **2c** (step ***d***), returning the catalytic system to the starting point.[20]

Scheme 2. Overall Processes for the Reversible and Repetitive Catalytic Dehydrogenation−Hydrogenation



In summary, we have developed the first homogeneous catalytic system for the efficient reversible dehydrogenation−hydrogenation reactions of nitrogen heterocycles. The reversible catalytic transformations can be nearly quantitatively repeated five times with almost no loss of efficiency. Furthermore, the remarkable feature of the present catalytic system is that the reversible reactions proceed with reversible interconversion of the catalytic species, depending on the absence or presence of hydrogen. Further investigations of the development of more efficient homogeneous catalysts for the reversible dehydrogenation−hydrogenation reactions of nitrogen heterocycles as well as other organic molecules containing greater hydrogen content are in progress.[21]

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

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(5) In their patents, Pez and co-workers[3] described hydrogen storage systems by the reversible dehydrogenation−hydrogenation of N-heterocycles using conventional heterogeneous catalysts. Although these catalytic systems using N-heterocycles are more effective than those using cyclic hydrocarbons, these heterogeneous reactions have some disadvantages: (1) a small amount of hydrogenolysis products are always produced during the reactions; (2) in the repetitive dehydrogenation−hydrogenation cycles of *N*-ethylcarbazole, different metals (Ru and Pd) are employed as the hydrogenation and dehydrogenation catalysts; and (3) the hydrogenation must be carried out under a high pressure of hydrogen (>50 atm). Thus, the complete reversible and repetitive dehydrogenation−hydrogenation cycles using a single catalyst in one reactor has not been achieved to date.

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(9) We have also reported several organic transformations based on the high catalytic hydrogen-transfer activity of Cp*Ir complexes. See: (a) Fujita, K.; Yamaguchi, R. *Synlett* **2005**, 560, and references cited therein. (b) Fujita, K.; Asai, C.; Yamaguchi, T.; Hanasaka, F.; Yamaguchi, R. *Org. Lett.* **2005**, *7*, 4017. (c) Hanasaka, F.; Fujita, K.; Yamaguchi, R. *Organometallics* **2006**, *25*, 4643. (d) Yamaguchi, R.; Kawagoe, S.; Asai, C.; Fujita, K. *Org. Lett.* **2008**, *10*, 181. (e) Fujita, K.; Enoki, Y.; Yamaguchi, R. *Tetrahedron* **2008**, *64*, 1943.

(10) Several examples of the homogeneous catalytic transformation of 1,2,3,4-tetrahydroquinoline to quinoline are known. However, they require an oxidant such as molecular oxygen or *tert*-butylhydroperoxide, and therefore, hydrogen cannot be produced. See: (a) Murahashi, S.-I.; Naota, T.; Taki, H. *J. Chem. Soc., Chem. Commun.* **1985**, 613. (b) Yamaguchi, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 1480. (c) Yamaguchi, K.; Mizuno, N. *Chem.—Eur. J.* **2003**, *9*, 4353. (d) Choi, H.; Doyle, M. P. *Chem. Commun.* **2007**, 745. (e) Murahashi, S.-I.; Okano, Y.; Sato, H.; Nakae, T.; Komiya, N. *Synlett* **2007**, 1675.

(11) We think that the key step of the reaction would be ligand-promoted dehydrogenation of a hydridoiridium intermediate with the protic hydroxyl group on the pyridine ring (see ref 7). This step could be faster when the ligand contains an electron-withdrawing substituent such as a CF_3 group because the acidity of the hydroxyl group increases. Therefore, catalyst **2c** exhibited the highest activity.

(12) The dehydrogenation reactions presented in Table 1 were selective for the conversion of **3** into **4**. Formation of any isomers of dihydroquinolines or other hydrogenolysis products was not observed.

(13) At present, we have observed that a higher reaction temperature considerably reduces the reaction time: the dehydrogenation of **3b** in mesitylene (bp. 165 °C) gives **4b** quantitatively in less than 5 h.

(14) We also carried out the dual reaction in the absence of **3b**. The reaction resulted in no formation of decane, clearly indicating that **3b** was the only hydrogen source.

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(16) The hydrogenation reactions presented in Table 2 were selective for the conversion of **4** into **3**. Formation of dihydroquinolines, decahydroquinoline, or other hydrogenolysis products was not observed.

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(18) Small amounts of **5** (2%) and an unidentified complex (4%) were observed by ^{1}H NMR analysis.

(19) We carried out the stoichiometric reaction of **5** with **4b** in the absence of hydrogen at 100 °C. However, no iridium species coordinated with quinoline was observed, while **5** decomposed slowly and **4b** remained unchanged.

(20) The precise mechanisms for the dehydrogenation and the hydrogenation are under study. It should be noted that the present dehydrogenation is characteristic of nitrogen heterocycles, because dehydrogenation of tetrahydronaphthalene with catalyst **2a** or **2c** does not occur.

(21) The maximum hydrogen content of tetrahydroquinolines is 3.0%, which is lower than the DOE 2010 target value of 6%.

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