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ARTICLE

Dehydrogenative Synthesis of Benzimidazoles under Mild Conditions with Supported Iridium Catalysts

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Solid supported iridium catalysts, which show excellent activity for the dehydrogenative synthesis of benzimidazoles from primary alcohols and phenylenediamine derivatives under mild reaction conditions, were developed. Among the catalysts examined, titania-supported iridium catalyst showed the highest activity, and benzimidazole derivatives were selectively produced at temperatures of 80 °C or higher: for example, the reaction of phenylenediamine (**1a**) with benzyl alcohol (**2a**) in the presence of Ir (1.0 wt%)TiO_2 (1.0 mol%, towards **1a**) at 120 °C selectively gave 2-phenylbenzimidazole (**3aa**) in 80% yield after 6 h and over 90% yield after 18 h. A high turnover number (TON) of more than 800 was achieved in the reaction at a higher substrate-to-catalyst ratio. Reduction of the catalysts under a hydrogen atmosphere at around 500 to 600 °C is essential for their significant activity. Characterization of the catalysts by gas adsorption , XRD, XPS, H_2-TPR, TEM, and XAFS revealed that highly-dispersed nanoparticles of iridium(0) species (*ca.* 1 to 2 nm in diameter) formed on TiO_2 are responsible for the catalysis. The catalysts could be recycled without a significant loss of activity, and the leaching of iridium species into the solution during the catalytic runs was negligible, which suggests that the present catalysts would be excellent from both environmental and practical perspectives.

Introduction

The development of novel catalysts that can realize environmentally-benign organic syntheses is an important topic. [1,2] The use of heterogeneous catalysts, especially supported catalysts, is attractive from both environmental and practical points of view, since these solid catalysts are advantageous in terms of ease of preparation and handling, high thermal and chemical stability, excellent reusability or recyclability, and minimal contamination of the products by heavy metals. Therefore, the development of solid catalysts that are applicable for various reactions has attracted much attention.[2,3] We previously developed Ru/CeO_2 catalysts that are effective for organic transformations[4,5] including the synthesis of indole via the dehydrogenative *N*-heterocyclization of 2-(2-aminophenyl)ethanol.[5]

On the other hand, benzimidazoles are important compounds, particularly in pharmaceutical chemistry, because of their antiarrhythminic, antihistaminic, antiulcer, anticancer, inotropic, fungicidal, anthelmintical, and antiviral activities.[6] Among the methods used for the synthesis of benzimidazole derivatives,[7] dehydrogenation between primary alcohols and derivatives of 1,2-phenylenediamine[8-10] is one of the most efficient synthetic routes, since the only byproducts are molecular hydrogen and water. An initial example catalyzed by ruthenium phosphine complexes required harsh conditions such as a high reaction temperature of over 200 °C.[8a] Resent successful examples of homogeneous catalysis, which are operated at lower temperatures, require a stoichiomeric amounts of hydrogen acceptors[8b] or strong bases.[8c,e,f] On the other hand, the development of solid catalysts are limited.[9,10] Oxidative reactions at 80 °C in O_2 or air in the presence of a supported ruthenium catalyst have been shown to give benzimidazole.[9a] A photo-assisted dehydrogenative route with a Pt/TiO_2 catalyst has recently been demonstrated.[9b] Very recently, dehydrogenative reactions catalyzed by a simple Pt/TiO_2 have been reported, which are operated in refluxing mesitylene (b.p. 164.7 °C).[10b] However, the development of simple solid catalysts that can realize the dehydrogenative reaction under much mild conditions without any oxidant, UV-irradiation, or strong bases are highly desirable because of the advantages in atom efficiency, operating costs, scalability, and safety.

Here, we report the development of very simple solid catalysts that are effective for the selective synthesis of benzimidazole derivatives via a dehydrogenative route under significantly mild conditions, i.e. at 80–120 °C. Among the catalysts examined, titania-supported iridium ones are the

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most effective. These catalysts could be recycled without a significant loss of activity, and the leaching of iridium species was negligible, which indicates that the present catalysts are advantageous from both environmental and practical perspectives.

Experimental

Materials

Tris(acetylacetonato)iridium(III) (Ir(acac)$_3$, Wako), Di-μ-chloro-bis[chloro(pentamethylcyclopentadienyl)iridium(III) ([Cp*IrCl$_2$]$_2$, Aldrich), tris(acetylacetonato)ruthenium(III) (Aldrich), tris(acetylacetonato)rhodium(III) (Aldrich), bis(acetylacetonato)palladium(II) (Nacalai Tesque), tetrahydrofuran (THF, dehydrated, stabilizer-free, Wako), 1,2-phenylenediamine (Wako), mesitylene (Nacalai Tesque), biphenyl (Wako), silica (Cabot, Cab-O-Sil), and alumina (Sumitomo Chemical Co., Ltd, AKP-G015; JRC-ALO-8 equivalent) were obtained commercially and used without further purification. Titania (JRC-TIO-4) and zirconia (JRC-ZRO-3) were obtained from the Catalysis Society of Japan. Ceria and magnesia were prepared by the precipitation method with the use of cerium(III) nitrate hexahydrate and magnesium nitrate hexahydrate, respectively.[4f]

Physical and Analytical Measurements

The products of the catalytic reactions were analyzed by GC-MS (Shimadzu GC-MS Parvum 2, Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 $^{\circ}$C) and gas liquid chromatography (GLC, Shimadzu GC-14APF, Zebron ZB-1701 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 $^{\circ}$C). The amount of evolved hydrogen gas was measured by gas chromatography (GC, Shimadzu GC8AIT, Porapak-Q, i.d. 3 mm, length 2 m, at 70 $^{\circ}$C). The composition of titania-supported iridium catalysts after calcination were confirmed by a wavelength dispersive X-ray fluorescence spectrometer (Panalytical Axios system equipped with a 4 kW rhodium anode X-ray tube). Nitrogen adsorption/desorption isotherms of the catalysts were obtained with a computer-controlled automatic gas sorption system (Quantachrome NOVA 4200e). Samples were degassed at 300 $^{\circ}$C for 2 h just before the measurements. The amount of carbon monoxide adsorbed was measured using a semi-automatic pulse titration analyzer (Ohkura Riken BP-2) at 298 K. Before measurement, a sample was reduced at 500 $^{\circ}$C for 30 min in a flow of H_2 (5 vol%)/Ar at atmospheric pressure. The sample was then exposed to air at room temperature, and reduced again at 150 $^{\circ}$C for 1 h. The dispersion (D(%); percentage of metal atoms exposed to the surface) of the supported metal was evaluated from the amount of chemisorbed carbon monoxide and adsorption stoichiometry (CO/surface metal atom = 1). X-ray powder diffraction (XRD) analysis was performed using Cu $K\alpha$ radiation and a carbon monochromator (Rigaku Ultima IV). X-ray photoelectron spectroscopy (XPS) of the catalysts was performed using an ULVAC-PHI 5500MT system equipped with a hemispherical energy analyzer. Samples were mounted on indium foil and then transferred to an XPS analysis chamber under Ar. The residual gas pressure during data acquisition was less than 1 x 10^{-8} Torr (1 Torr; 133.3 N m^{-2}). The spectra were measured at room temperature using Mg $K\alpha$ radiation (1254 eV) generated by an X-ray tube operating at 15 kV, 400 W. The electron take-off angle was set at 45 deg. Binding energies were referenced to the C 1s level of residual graphitic carbon.[11] Temperature-programmed reduction (TPR) was carried out with a flow-type reactor. Hydrogen (1.9 vol.% in Ar; atmospheric pressure; 30 cm^3 min^{-1}) was passed through a reaction tube containing the catalyst. The tube was heated with an electric furnace at 2 °C min^{-1}, and the amount of H_2 consumed was monitored with a TC detector on a Shimadzu 8AIT gas chromatograph. Transmission electron microscope (TEM) photographs were taken using a JEOL JEM-200EX by the Hanaichi Ultrastructure Research Institute, Okazaki, Japan. Iridium K-edge XAFS measurements of the supported catalysts were performed at the BL01B1 in the SPring-8 operated at 8 GeV using a Si(311) two-crystal monochromator. The Ir/TiO_2 catalyst was pressed into a pellet (10 mm in diameter) and mounted on an *in situ* measurement cell equipped with a heating unit and aluminum windows. After heating the samples in a flow of H_2(5.0 vol%)/He (50 cm^3/min) at 150 $^{\circ}$C or 500 $^{\circ}$C for 30 min, XAFS spectra were taken in a He flow. Leaching of ruthenium species from the catalysts during the reaction was investigated by an inductively coupled plasma atomic emission spectroscopy (ICP-AES) using a Thermo Scientific iCAP6300 analyzer.

Preparation of an Ir/support catalyst

Supported catalysts were prepared by the impregnation method. To a solution of Ir(acac)$_3$ (51 mg, 0.104 mmol) in 10 cm^3 of methanol was added 1.0 g of a support in air at 80 $^{\circ}$C. After impregnation, the resulting powder was dried at 80 $^{\circ}$C in air for a day and calcined in air at 300 $^{\circ}$C for 30 min. The thus-prepared calcined catalysts (*ca.* 150 mg) were reduced in a H_2 (2.0 vol%)/Ar flow (180 cm^3 min^{-1}) at the prescribed temperature (ramping rate; 10 $^{\circ}$C/min) for 30 min by the use of a conventional flow reactor to give Ir(2.0 wt%)/support-XX catalysts, where XX is the reduction temperature in degrees Celsius. For titania-supported catalysts, JRC-TIO-4 was used as a support unless otherwise noted. Supported Ru-, Rh-, and Pd-catalysts were prepared using Ru(acac)$_3$, Rh(acac)$_3$ and Pd(acac)$_2$, respectively.

General procedure for the synthesis of 2-phenylbenzimidazole (3aa) from 1,2-phenylenediamine (1a) and benzyl alcohol (2a) by the Ir/TiO_2 catalyst

All of the reactions were performed using hot stirrers equipped with cooling blocks to reflux the solution. The Ir(2.0 wt%)/support-XX catalyst (96 mg, 0.010 mmol as Ir) was mounted in a glass Schlenk tube (20 cm^3): Since the catalyst was exposed to open air at room temperature during mounting, the catalyst was again heated at 150 $^{\circ}$C for 1 h in the Schelenk tube filled with H_2 gas (1 atm) just before use, and subjected to the catalytic run without any contact with air or moisture. A typical reaction procedure is as follows: 1,2-phenylenediamine (**1a**) (1.0 mmol), benzyl alcohol (**2a**) (2.0 mmol), and mesitylene (1.0 cm^3) were added to the Schlenk tube containing the reduced catalyst. The reaction mixture was stirred at 120 $^{\circ}$C for 18 h under an argon atmosphere, and

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then rapidly cooled in an ice bath. The solid catalyst was removed by passing the mixture through a 0.45 µm polytetrafluoroethylene (PTFE) filter (Millipore Millex LH), and the products were quantified by GC using biphenyl as an internal standard. For isolation of the products, the remaining solution was concentrated under reduced pressure, and the products were then purified by Kugelrohr distillation.

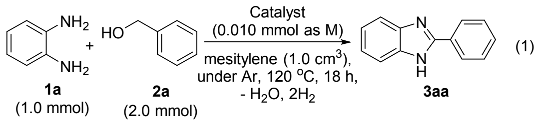
Hot filtration tests

A 20 cm^3 Schlenk tube was charged with **1a** (1.0 mmol), **2a** (2.0 mmol), and the Ir(2.0 wt%)/TiO_2-500 catalyst (0.010 mmol as Ir) in mesitylene (1.0 cm^3) together with an internal standard (biphenyl, *ca*. 30 mg) under an argon atmosphere. After the reaction was allowed to proceed for 3 h at 120 °C, the mixture was filtered through a 0.45 µm PTFE syringe filter (Millipore Millex LH) into another preheated Schlenk tube. The filtrate was stirred at 120 °C, and the conversion of **1a** was followed by GLC.

Results and Discussion

Effect of the catalysts on the synthesis of 2-phenylbenzimidazole

The effects of metal oxide-supported transition metal catalysts on the synthesis of benzimidazole (**3aa**) from 1,2-phenylenediamine (**1a**) and benzyl alcohol (**2a**) were examined at 120 °C for 18 h (eq. 1). Entries 2–6 in Table 1 compare the effects of various transition metal catalysts (2.0 wt%) supported on titania. Among these catalysts, the iridium catalyst showed the highest activity: **3aa** was obtained in 97% yield by the reaction in the presence of Ir (2.0 wt%)/TiO_2-500. Only a trace amount of benzaldehyde and benzyl benzoate was observed, indicating an excellent selectivity of the present catalysis. Note that the formation of a stoichiometric amount of H_2 (2.1 mmol) was confirmed by GC. The use of $[Cp^*IrCl_2]_2$ instead of $Ir(acac)_3$ as a source of the titania-supported iridium catalyst slightly decreased the activity of the resulting catalyst (entry 3). While a titania-supported palladium catalyst showed moderate activity, ruthenium and rhodium catalysts were not very effective.



(1)

As shown in entries 2, 7–11 in Table 1, the activity of the solid iridium catalyst is significantly affected by the support: Of the supports examined, titania exhibited the highest performance (entry 2). The alumina- and zirconia-supported catalysts gave **3aa** in moderate yields, whereas ceria-, magnesia-, and silica-supported catalysts were ineffective. $Ir(acac)_3$, which was used as an iridium precursor of the supported iridium catalysts, did not give **3aa** at all (entry 12). $[Cp^*IrCl_2]_2$ with or without a suitable base such as $NaHCO_3$ has been reported to be an effective catalyst for the dehydrogenative oxidation of alcohols and related reactions in the presence[12] or absence[13,14] of hydrogen acceptors, but did not show catalytic activity under the present conditions (entry 13). The results clearly show that the present titania-supported iridium catalysts are extremely effective.

Table 1 Effects of metallic species and supports on the activity of the catalysts

Entry	Catalyst^a	Yield of **3aa** (%)^b
1	None	Trace
2	Ir(2.0 wt%)/TiO_2-500	97
3	Ir(2.0 wt%)/TiO_2-500^c	81
4	Pd(2.0 wt%)/TiO_2-500	73
5	Rh(2.0 wt%)/TiO_2-500	19
6	Ru(2.0 wt%)/TiO_2-500	5
7	Ir(2.0 wt%)/ZrO_2-500	74
8	Ir(2.0 wt%)/Al_2O_3-500	69
9	Ir(2.0 wt%)/CeO_2-500	13
10	Ir(2.0 wt%)/MgO-500	13
11	Ir(2.0 wt%)/SiO_2-500	1
12	$Ir(acac)_3$	0
13	$[Cp^*IrCl_2]_2$^{d}	6
14	$[Cp^*IrCl_2]_2$ + $NaHCO_3$^{e}	trace

^{a}For supported Ir catalysts, $Ir(acac)_3$ was used as an Ir precursor. For the preparation of titania-supported catalysts, JRC-TIO-4 was used. ^{b}Determined by GLC. ^{c}Prepared using $[Cp^*IrCl_2]_2$ as an Ir source. ^{d}160 °C, 18 h. ^{e}$NaHCO_3$ 0.020 mmol.

The reduction of supported iridium catalysts under suitable conditions is essential for the present reaction. The effects of the reduction conditions for the Ir/TiO_2 catalysts on the yield of **3aa** are shown in entries 1–6 in Table 2. While the catalyst without reduction showed very low activity (entry 1), **3aa** was obtained in a yield of over 90% after the reactions for 18 h with Ir/TiO_2 catalysts reduced above 150 °C. To examine the effects of the reduction temperature more precisely, the yields of **3aa** in the reactions for 6 h were compared. With an increase in the reduction temperature of the catalyst to above 300 °C, the yield of **3aa** markedly increased. The Ir/TiO_2 catalyst reduced at 500 °C or 600 °C showed enhanced activity: As shown below, the spectroscopic studies have revealed that the reduction of surface iridium species are promoted with increasing reduction temperature, and low-valent iridium species are considered to be responsible for the excellent activity. The reaction conditions were optimized by the use of the catalyst reduced at 500 °C in the following study.

Table 2 also shows the effects of the iridium loadings. As shown in entries 6, 8, 9, the optimum loading was found to be around 1.0 wt% as iridium metal: Catalysts with higher and lower levels of iridium loading showed lower activities. The present result suggests that the formation of surface iridium clusters of a suitable size is important for the present dehydrogenative synthesis of 2-phenylbenzimidazoles (vide infra). In the previous study on the related reactions, namely the direct synthesis of quinolines from nitroarenes and aliphatic alcohols, Ir/TiO_2 catalysts with ultralow iridium loading (*ca.* 0.05 wt%) showed excellent activities, and the formation of surface iridium sub-nano-sized clusters was reported to be responsible.[3a]

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Table 2 Effects of the reduction temperature and loading level of the Ir/TiO_2 catalysts on the reaction of **1a** with **2a**[a]

Entry	Catalyst[b]	Yield of **3aa** (%) after 18 h[c]	Yield of **3aa** (%) after 6 h[c]
1	Ir(2.0 wt%)/TiO_2[d]	9	-
2	Ir(2.0 wt%)/TiO_2-150[e]	90	35
3	Ir(2.0 wt%)/TiO_2-200	97	41
4	Ir(2.0 wt%)/TiO_2-300	98	37
5	Ir(2.0 wt%)/TiO_2-400	99	43
6	Ir(2.0 wt%)/TiO_2-500	97	55
7	Ir(2.0 wt%)/TiO_2-600	-	60
8	Ir(0.50 wt%)/TiO_2-500	-	77
9	Ir(1.0 wt%)/TiO_2-500	91	80

[a] **1a** 1.0 mmol, **2a** 2.0 mmol, catalyst 0.010 mmol as Ir, mesitylene 1.0 cm^3, under Ar, at 120 °C. [b] Ir/TiO_2 catalysts were prepared using $Ir(acac)_3$ and JRC-TIO-4. [c] Determined by GLC. [d] Without the reduction of the catalyst. [e] The catalyst was heated in H_2 (1 atm) at 150 °C for 1 h just before the catalytic run.

The effect of the reaction temperature on Ir(2.0 wt%)/TiO_2-500-catalyzed reactions is shown in Table 3. The present supported iridium catalysts realized the synthesis of **3aa** at significantly lower temperatures than those required for the Ru complex-catalyzed reactions:[8a] the reactions were completed within 18 h at 120 °C with Ir(2.0 wt%)/TiO_2-500. At 100 °C, **3aa** was obtained in a satisfactory yield after a prolonged reaction. Remarkably, even the reaction at 80 °C gave **3aa** in a moderate yield after 72 h.

Table 3 Effects of the reaction temperature on the reaction of **1a** with **2a** catalyzed by Ir(2.0 wt%)/TiO_2-500[a]

Entry	Temp. (°C)	Reaction time (h)	Yield of **3aa** (%)[b]
1	120	6	55
2	120	18	97
3	110	18	67
4	100	18	51
5	100	40	66
6	100	72	92
7	90	72	56
8	80	72	48
9[c]	80	72	47
10	70	72	25

[a] **1a** 1.0 mmol, **2a** 2.0 mmol, Ir(2.0 wt%)/TiO_2-500 catalyst (prepared using $Ir(acac)_3$ and JRC-TIO-4) 0.010 mmol as Ir, mesitylene 1.0 cm^3, under Ar. [b] Determined by GLC. [c] Ir(1.0wt%)/TiO_2-500 catalyst was used.

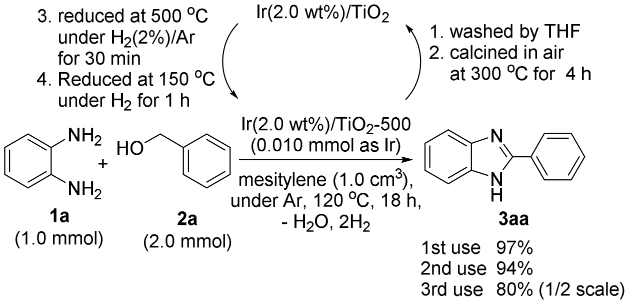
Table 4 Effects of the amounts of subtrates and mesitylene on the reaction of **1a** with **2a** catalyzed by Ir(2.0 wt%)/TiO_2-500[a]

Entry	**1a** (mmol)	**2a** (mmol)	Mesitylene (cm^3)	Yield of **3aa** (%)[b]
1	1.0	2.0	1.0	97
2	1.0	1.0	1.0	94
3	1.0	2.0	-	39
4	1.0	5.0	-	84
5[c]	5.0	10	1.0	87
6[d]	5.0	10	1.0	81

[a] Ir(2.0 wt%)/TiO_2-500 catalyst (prepared using $Ir(acac)_3$ and JRC-TIO-4) 0.010 mmol as Ir, under Ar, at 120 °C for 18 h. [b] Determined by GLC. [c] The reaction at 150 °C for 18 h. [d] Ir(1.0 wt%)/TiO_2-500 (0.0050 mmol as Ir) was used as a catalyst, at 150 °C for 18 h.

As shown in Table 4, the reaction of equimolar amounts of **1a** and **2a** proceeded smoothly to give **3aa** in 94% yield (entry 2), which indicates that the present catalysis prevents the formation of unnecessary wastes. Whereas the reaction of **1a** with two equivalents of **2a** in the absence of mesitylene resulted in a low yield of **3aa** (entry 3), the reaction without solvent gave **3aa** in high yield when a large excess of **2a** was added (entry 4), indicating that the use of solvent is not essential for the present catalysis. The reaction also proceeded smoothly at a higher substrate to catalyst ratio: The reaction of **1a** (5.0 mmol) and **2a** (10 mmol) in the presence of Ir(2.0 wt%)/TiO_2-500 (0.010 mmol as Ir) in 1.0 cm^3 of mesitylene at 150 °C for 18 h gave **3aa** in 87% GLC yield (TON 430, entry 5). A higher TON of 810 was achieved by the reaction with the use of the Ir(1.0 mol%)/TiO_2-500 catalyst (0.0050 mmol as Ir, entry 6).

Scheme 1 Recycle use of Ir/TiO_2 catalyst.



The present Ir/TiO_2 catalysts could be recycled without a significant loss of activity. After the reaction was performed at 120 °C for 18 h using the Ir(2.0 wt%)/TiO_2-500 catalyst (see Table 1, entry 2), the solid catalyst was separated from the reaction mixture by centrifugation and washed three times with THF (10 cm^3). The resulting solid was calcined at 300 °C for 4 h and then reduced under a hydrogen atmosphere. The thus-recycled catalyst afforded **3aa** in 94% yield (Scheme 1), which shows that the present catalyst exhibits excellent recyclability.

To investigate whether the reaction actually proceeds on the surface of the solid catalyst,[15,16] the catalysts was removed by hot filtration through a PTFE filter (pore size 0.45 μm) after the reaction had been allowed to proceed for 3 h (Fig. 1): Because of poor solubility of **3aa** in mesitylene, changes of the yield of **3aa** were not monitored. The further conversion of **1a** was completely stopped after removal of the solid catalyst, indicating that the solid catalyst acts heterogeneously. ICP-AES analysis also revealed that the leaching of iridium species into the reaction mixture after the catalytic run shown in Table 1, entry 2, was very slight: 0.000022 mmol (0.22 mol% of the iridium species in the fresh catalyst). These results indicate that the reaction of **1a** with **2a** requires the presence of solid catalysts.

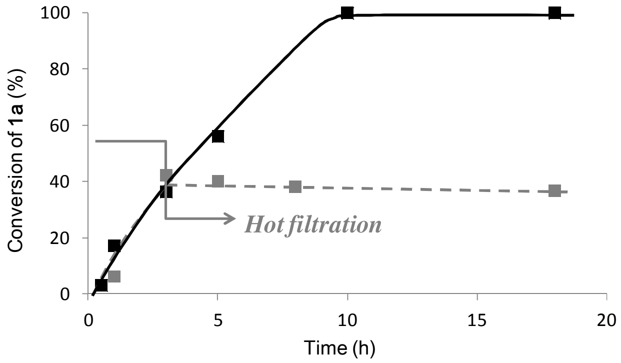
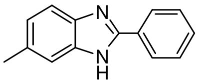
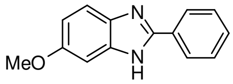
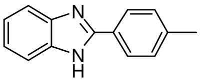
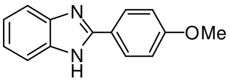
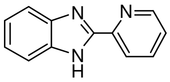
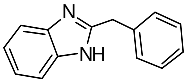
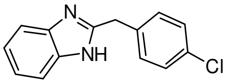
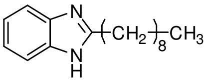


Fig. 1 Time-course of the conversion of **1a** over Ir(2.0 wt%)/TiO_2-500 (*a*) without filtration of the catalyst and (*b*) with removal of the catalyst by hot filtration after 3 h. Reaction conditions: **1a** 1.0 mmol, **2a** 2.0 mmol, Ir catalyst 0.010 mmol as Ir, mesitylene 1.0 cm^3, under Ar, 120 °C.

Table 5. Scope of substrates for the reactions catalyzed by Ir(2.0 wt%)/TiO_2-500[a]

 **3ba** >99%	 **3ca** 97%
 **3ab** 87%	 **3ac** >99%
 **3ad** 54% (150 °C)	 **3ae** 99% (150 °C)
 **3af** > 99% (150 °C)	 **3ag** 99%

[a] **1** 1.0 mmol, **2** 2.0 mmol, Ir(2.0 wt%)/TiO_2-500 catalyst (prepared using $Ir(acac)_3$ and JRC-TIO-4) 0.010 mmol as Ir, mesitylene 1.0 cm^3, under Ar, at 120 °C for 18 h. GLC yields are shown.

The Ir/TiO_2 catalyst could be used in the reactions of various primary alcohols and derivatives of 1,2-phenylenediamine, as shown in Table 5. 4-Methylbenzene-1,2-diamine (**1b**) and 4-methoxylbenzene-1,2-diamine (**1c**) could be used in the reaction. Similarly, the reaction of **2a** with benzyl alcohols bearing an electron-donating substituent proceeded smoothly to quantitatively afford the corresponding 2-arylbenzimidazoles. On the other hand, the reaction with 4-(trifluoromethyl)benzyl alcohol did not proceed well (data not shown). The reactions with pyridin-2-ylmethanol (**2d**) required a higher reaction temperature, 150 °C, to give **3ad** in a moderate yield. From 2-phenylethanol (**2e**) and 2-(4-chlorophenyl)ethanol (**2f**), the desired products **3ae** and **3af** were obtained quantitatively at 150 °C. An aliphatic alcohol (**2g**) gave the corresponding benzimidazole quantitatively. The present results indicate that these catalysts can be used with a wide range of substrates.

Characterization of supported iridium catalysts

To investigate the factors that govern the activity of the catalysts in the present reactions, we characterized the iridium catalysts by various methods. The results of a nitrogen gas adsorption study and XRD study of the fresh catalysts are summarized in Table S1 and Figure S1 of the Supporting Information. There is no significant correlation between the surface areas of the supports and the activities of the supported iridium catalysts.

The surface compositions of the freshly-calcined catalysts were investigated by an XPS study, and the results are summarized in Table 6. For titania-supported catalysts overlapping of Ti 3s peak (62.0 eV) on the Ir 4f peaks has been considered. The surface ratio of iridium species greatly depended on the support. Remarkably, the surface atomic ratio of iridium species of the Ir/TiO_2 catalyst was significantly greater than those of other catalysts, which suggests the formation of highly dispersed iridium species. The surface atomic composition was not changed by reduction under a hydrogen atmosphere (entries 1–3). The surface iridium ratios of 0.5 wt%- and 1.0 wt%-loaded catalysts were as those expected from the loading levels (entries 4, 5), which indicates the high dispersion of surface iridium species. On the other hand, the 5.0 wt%-loaded catalyst showed a surface iridium ratio similar to that of the 2.0 wt%-loaded catalyst (data not shown), suggesting the formation of aggregated surface iridium species. For 2.0 wt%-loaded catalysts (entries 1, 6–10), the order of the catalytic activities generally depended on the surface iridium compositions, except for the case of Ir/CeO_2, which showed a lower activity than Ir/ZrO_2 and Ir/Al_2O_3 despite a higher surface iridium ratio (entry 8).

Fig. 2 shows Ir 4f XP spectra of freshly-calcined Ir(2.0 wt%)/TiO_2 and Ir(2.0 wt%)/TiO_2-500. The Ir $4f_{5/2}$ binding energies reported for IrO_2 (62.0 eV) and metallic Ir (60.7 eV)[11] are also shown by vertical lines. As shown in Fig. 2a, the spectrum of freshly-calcined Ir(2.0 wt%)/TiO_2 shows a sharp $4f_{7/2}$ peak at around 62 eV, and a curve-fitting analysis suggests that 94% of surface iridium species are high-valent species such as Ir(IV), while the remaining 6% are considered to be Ir(0). On the other hand, Ir(2.0 wt%)/TiO_2-500 catalyst showed a broader band at 60 to 62 eV, and the ratio of Ir(0) to total iridium species further increased to 53%, as shown in Fig. 2b, suggesting that low-valent iridium species such as Ir(0) is responsible for the catalytic activity.

The most of the iridium species on other oxide supports were also reduced to Ir(0) species after reduction, as shown by the Ir 4f XP spectra of reduced catalysts (see Fig. S2), while before reduction, the iridium species on all of the metal oxide supports were fully oxidized. The results of the H_2-TPR study indicate that a major part of iridium species on TiO_2 reduced below 100 °C under a hydrogen atmosphere (see Fig. S3). Iridium species on other supports were also fully reduced under a H_2 flow below 500 °C.

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Table 6 Surface atomic composition of supported iridium catalysts estimated by XPS analysis

Entry	Catalyst	Ir (%)	M (%)	C (%)	O(%)
1	Ir(2.0 wt%)/TiO_2	1.1	24.6	16.0	58.4
2	Ir(2.0 wt%)/TiO_2-150	1.0	24.7	16.8	57.5
3	Ir(2.0 wt%)/TiO_2-500	1.1	24.6	16.0	58.4
4	Ir(0.50 wt%)/TiO_2-500	0.2	25.7	15.5	58.5
5	Ir(1.0 wt%)/TiO_2-500	0.5	23.6	18.0	57.9
6	Ir(2.0 wt%)/ZrO_2	0.6	25.5	14.2	59.8
7	Ir(2.0 wt%)/Al_2O_3	0.5	31.8	8.6	59.2
8	Ir(2.0 wt%)/CeO_2	0.9	24.3	15.6	59.2
9	Ir(2.0 wt%)/MgO	0.3	34.7	8.6	56.5
10	Ir(2.0 wt%)/SiO_2	0.1	32.9	0.5	66.5

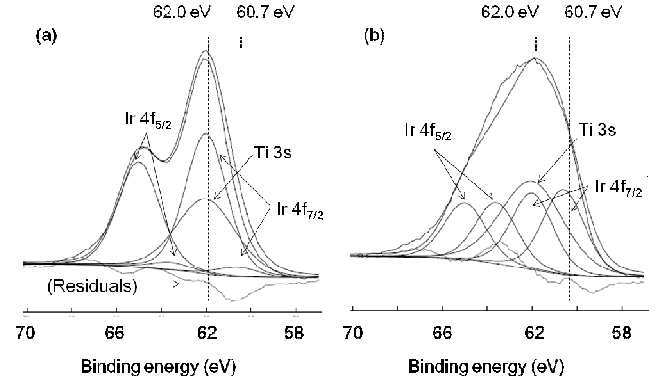

Fig. 2 Ir 4f spectra of (a) Ir(2.0 wt%)/TiO_2 and (b) Ir(2.0 wt%)/TiO_2-500.

To further examine the oxidation states of iridium species on ttania after the reduction, the X-ray absorption near-edge structure (XANES) spectra were recorded just after the reduction of the catalysts without any contact with air and moisture. As discussed earlier,[17] the Ir LIII-edge XANES is characterized by the white-line features, and the white line intensities are closely related to the oxidation state of iridium species. As shown in Fig. 3, the intensitiy of the white line of Ir(2.0 wt%)/TiO_2-500 was much smaller than that of Ir(2.0 wt%)/TiO_2-150, which indicate that the reduction of both bulk and surface iridium species further proceeded with increasing reduction temperature. Further detailed structural analyses of these catalysts by means of XAFS spectra are in progress.

Fig. 4 shows TEM images of the Ir/TiO_2-500 catalysts. As reported previously by He at al.[3a] and Yoshida et al.,[3b,c] the formation of very small iridium particles of around 1 to 2 nm was confirmed. The formation of such small iridium particles is also considered to contribute to the excellent activity of the Ir/TiO_2 catalysts. Note that the amounts of CO chemisorbed on Ir(2.0 wt%)/TiO_2-500 and Ir(1.0 wt%)/TiO_2-500 were 1.44 cm^3g^{-1} (D = 62%) and 0.77 cm^3g^{-1} (D = 66%), respectively. These results suggest that zero-valent iridium species are responsible for the present reactions, and that the amount of fully-reduced iridium species exposed on the surface govern the catalytic activity.

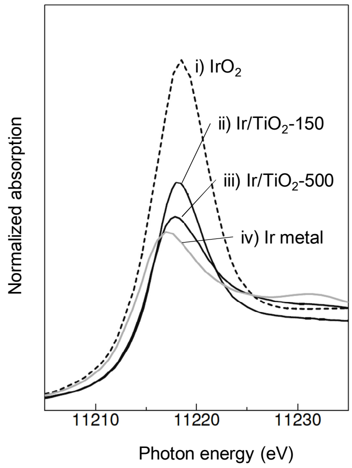

Fig. 3 Ir L3-edge XANES spectra of Ir/TiO_2 catalysts

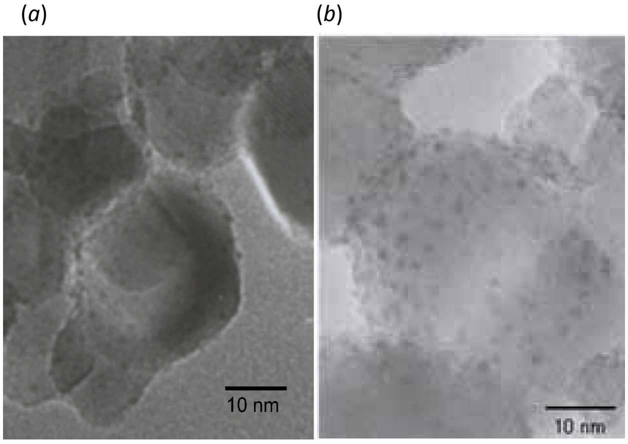

Fig. 4 TEM images of (a) Ir(2.0 wt%)/TiO_2-500 and (b) Ir(1.0 wt%)/TiO_2-500.

Possible reaction mechanisms

As shown in Scheme 2, the present reaction is considered to be initiated by the dehydrogenative oxidation of alcohol by the metallic catalyst to form corresponding aldehyde and metal hydride species. Note that the dehydrogenation of benzyl alcohol **2a** proceeded in the presence of Ir(2.0 wt%)/TiO_2-500 at 120 °C to give benzaldehyde (**4a**) together with a trace amount of benzyl benzoate.[18] Interestingly, the dehydrogenation of **2a** to **4a** after 3 h proceeded significantly slower than the reaction of **1a** and **2a** (see Fig. S4). To examined the possibility of the re-hydrogenation of benzaldehyde **4a** to benzyl alcohol **2a**, 2.0 mmol of **4a** was treated with Ir(2.0 wt%)/TiO_2-500 under H_2(2.0 vol%)/Ar at 120 °C for 18 h: This reaction, however, resulted in the formation of a very small amount of **2a** (8% yield, eq. 2), which rules out the contribution by re-hydrogenation of **4a**. On the other hand, the presence of 1.0 mmol of **4a** almost completely inhibited the dehydrogenation of **2a** to **4a** (see Fig. S5), which indicates that benzaldehyde **4a** had a strong poisoning effect on the

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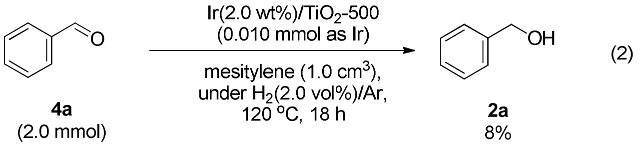
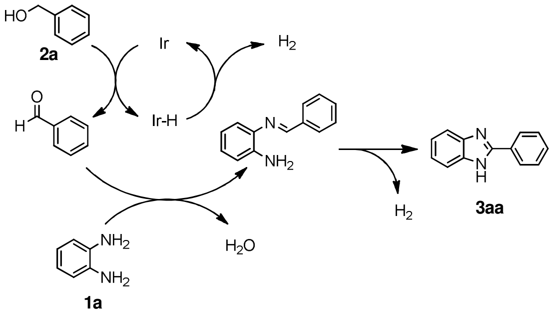
dehydrogenative reaction. In the present synthesis of benzimidazoles, the rapid transformation of **4a** to imine in the presence of **1a** would prevent the poisoning of the catalyst.



(2)

The successive reaction of the thus-formed aldehyde with 1,2-phenylenediamine proceeds even in the absence of any catalysts:[19] Heating of a mixture of **1a** (1.0 mmol) and **4a** (2.0 mmol) at 120 °C for 18 h in the absence of catalysts gave **3aa** in 28% yield, and the main by-product was *N*-benzylbenzimidazole. Since only small amounts of aldehydes were detected by GC analysis during the catalytic runs, the iridium-catalyzed dehydrogenation of alcohols is considered to be rate-determining. The formation of a stoichiometric amount of hydrogen (vide supra) also supports the mechanism shown in Scheme 2.

Scheme 2 Possible reaction pathways.



Conclusions

As discussed above, supported iridium catalysts that show excellent activity for the selective synthesis of benzimidazoles from primary alcohols and phenylenediamine derivatives have been developed. Among the catalysts examined, titania-supported iridium catalysts that were reduced at around 500 to 600 °C showed the highest activity and realized the formation of **3aa** under significantly mild reaction conditions, i.e., at 80 to 120 °C. A detailed characterization of the catalysts revealed that highly-dispersed zero-valent iridium nanoparticles of less than 2 nm in diameter were formed on the surface of titania, which would be responsible for the excellent catalytic activity. These solid catalysts are recyclable, and the leaching of iridium species was negligible. Due to these characteristic features, the present Ir/TiO$_2$ catalysts are quite attractive as highly efficient heterogeneous catalysts from synthetic, industrial, and environmental perspectives. Further application of the present catalysts to a wider range of dehydrogenative reactions is now in progress.

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Dehydrogenative Synthesis of Benzimidazoles under Mild Conditions with Supported Iridium Catalysts

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Text for Graphical Abstract

Recyclable Ir/TiO_2 catalysts enable the synthesis of benzimidazoles from primary alcohols and phenylenediamines under mild conditions, i.e. at 120 °C.