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Striking Effects of a Titania Support on the Low-Temperature Activities of Ir Catalysts for the Dehydrogenative Synthesis of Benzimidazole and Indole

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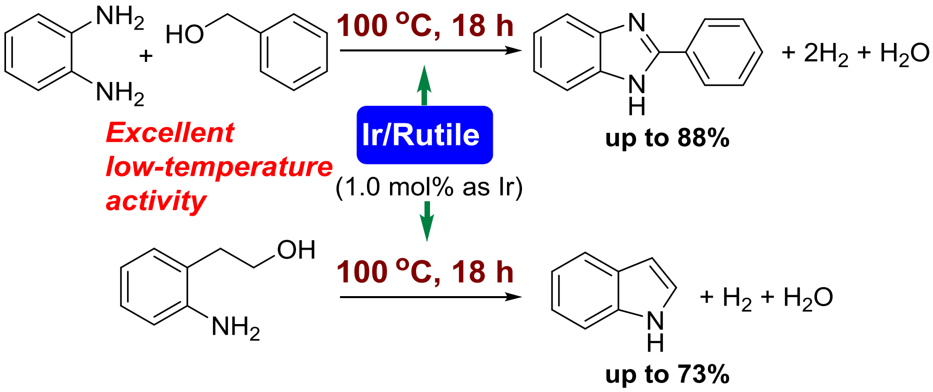
TOC/Abstract Graphic:



Highlights

> Rutile-supported iridium catalysts showed excellent activity.

> A correlation between CO uptake by iridium and the activities was observed.

> Well-reduced iridium nanoparticles would be responsible for the excellent activities.

ABSTRACT:

The crystalline structure of titania supports for iridium catalysts markedly affected their low-temperature activity for the dehydrogenative synthesis of *N*-containing heteroaromatics, namely benzimidazole and indole. While solid iridium catalysts supported on anatase showed moderate to poor activity for the synthesis of 2-phenylbenzimidazole (**3**) from *o*-phenylenediamine (**1**) and benzyl alcohol (**2**) at 100 °C, the reaction in the presence of rutile-supported catalysts proceeded smoothly to give **3** in high yields of up to 88%. Similar results were observed for the dehydrogenative conversion of 2-(2-aminophenyl)-ethanol (**4**) to indole (**5**). The reaction at 100 °C for 18 h in the presence of 1.0 mol% iridium on rutile gave **5** in a yield of 73%, while the use of anatase-supported catalysts resulted in significantly lower yields. TEM analysis showed the formation of small (*ca*. 2 nm in diameter), homogeneously-dispersed iridium nanoparticles on rutiles, while the inhomogeneous loading of iridium species was observed on anatase supports. CO pulse experiments revealed that there is a strong correlation between CO uptake by iridium nanoparticles and the activities at 100 °C. These results suggest that the predominant formation of small, well-reduced iridium nanoparticles is one major reason for the excellent activities of rutile-supported catalysts at low temperatures.

Keywords: supported catalyst; iridium; titania; rutile; benzimidazole; indole

1. Introduction

The development of environmentally benign organic synthesis is one of the most important issues in modern chemistry [1]. While homogeneous catalysts often play a significant role in organic syntheses, the development of heterogeneous catalysts, particularly solid oxide-supported catalysts, that enable highly efficient organic synthesis has attracted much attention [2,3], since these solid catalysts can overcome the practical and environmental disadvantages of homogeneous catalysis, such as the difficulty of separation and recovery of the catalysts from the reaction mixture as well as contamination of the products by metallic species. In this context, we have developed various supported catalysts, namely ceria-supported ruthenium catalysts, which are effective for various highly atom-efficient organic transformations [3,4].

On the other hand, nitrogen-containing aromatics such as benzimidazoles and indoles are important pharmaceutical and agrochemical raw materials [5,6]. For example, angiotensin II receptor blockers (ARBs), which are used for the treatment of hypertension, often have benzimidazole-type core structures, and indole structures are found in many alkaloids, such as tryptophan and auxin. Dehydrogenative synthesis is one of the most efficient routes to these nitrogen-containing chemicals [4e,7,8]. We previously reported that ceria-supported ruthenium catalyst effectively catalyzed the synthesis of indole via dehydrogenative *N*-heterocyclization [4e]. In the initial report [8a] dehydrogenative synthesis of benzimidazoles from phenylenediamines and primary alcohols in the presence of ruthenium complex catalysts required temperatures as high as 200 °C, and the following homogeneous catalyses operated at lower temperature required the presence of strong bases [8b-d]. While the photo-assisted reactions [8f] proceeded at room temperature, the dehydrogenative reactions without irradiation using TiO_2 on organosilicon-supports [8g] or Pt/TiO_2 [8h] were operated at relatively high temperatures (above 160 ^{o}C). Recently, we have developed iridium catalysts supported on TiO_2 (JRC-TIO-4, Degussa P-25 equivalent), which realize the smooth dehydrogenative synthesis of benzimidazoles under significantly mild conditions, within 18 h at 120 °C [7,9].

However, further investigation revealed that the iridium species were not homogeneously loaded on the titania support, JRC-TIO-4. The formation of dense iridium nanoparticles was observed on some specific facets of the titania particles, but not on other facets. These findings encouraged us to investigate the effects of the crystalline structures of titania supports in detail to develop more active iridium catalysts. Herein, we describe the marked improvement of the activity of titania-supported iridium catalysts for the dehydrogenative synthesis of 2-phenylbenzimidazole and indole at a low reaction temperature through suitable selection of the titania support. Among those examined, the catalysts supported on rutile showed the highest activity at 100 °C even in the absence of any additives such as bases or hydrogen acceptors. On the other hand, the catalysts prepared using anatase titanias resulted in low activity regardless of their surface areas. Factors that govern the catalytic activity of iridium species are discussed based on a detailed characterization of the catalysts.

2. Experimental

2.1. General Information

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Tris(acetylacetonato)iridium(III) (Ir(acac)$_3$, $C_{15}H_{21}O_6Ir$), bis(1,5-cyclooctadiene)diiridium(I) dichloride ([(COD)IrCl]$_2$), mesitylene, tetrahydrofuran (THF), methanol, biphenyl, *o*-phenylenediamine, and benzyl alcohol were obtained from Wako and used as received. 2-(2-Aminophenyl)ethanol (TCI) was obtained commercially and used without further purification. JRC (Japan Reference Catalyst) titanias (JRC-TIO-4, 6, 7, 8, 9) were obtained from the Catalysis Society of Japan. Other titanias (F-1, F-1R, F-2, F-4, F-6) were obtained from Showa Denko Ceramics Co. Ltd. XRD patterns of F-series titanias are shown in Figure S1 of the Supplementary content.

Physical and Analytical Measurements

The organic products of catalytic runs 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 °C) and gas-liquid chromatography (Shimadzu GC-14A; Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 °C).

Solid catalysts were analyzed by X-ray photoelectron spectroscopy (XPS), X-ray diffraction (XRD), transmittance electron microscopy (TEM), nitrogen gas adsorption, thermogravimetric analysis (TG-DTA), wavelength-dispersive X-ray spectrometry (WDX), and CO adsorption. XP spectra of the catalysts were recorded 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 N_2. Samples just after reduction in a H_2/Ar stream (see below), without passivation, were mounted in a glove box (Korea Kiyon) with an O_2 level below 0.5 ppm. 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. The residual gas pressure during data acquisition was less than 1 x 10^{-8} Torr (1 Torr; 133.3 N m^{-2}). Binding energies were referenced to the C 1s level of residual graphitic carbon [10]. Powder XRD patterns were recorded using Cu $K\alpha$ radiation (40 kV, 40 mA) and a carbon monochromator (Shimadzu XRD-6100). TEM photographs were obtained using a JEOL JEM-3010 microscope at the Faculty of Engineering, Kagawa University or a JEOL JEM-200EX at the Hanaichi Ultrastructure Research Institute, Okazaki, Japan. Nitrogen adsorption/desorption isotherms of catalysts were recorded with a computer-controlled automatic gas sorption system (Quantachrome NOVA 4200e). Samples were degassed at 300 °C for 2 h just before the measurements.TG-DTA analyses were performed using a RIGAKU TG8120 in a stream (40 cm^3min^{-1}) of synthetic air. The composition of supported iridium catalysts was confirmed by a wavelength dispersive X-ray fluorescence spectrometer (Panalytical Axios system equipped with a 4 kW rhodium anode X-ray tube) at the Kagawa Prefectural Industrial Technology Center. The amount of adsorbed carbon monoxide was measured at 50 ℃ using a home-made pulse titration analyzer connected to a TC detector on a Shimadzu 8AIT gas chromatograph. Before measurement, a sample was reduced at 500 ℃ for 30 min in a flow of H_2 (2vol.%)/Ar at atmospheric pressure.

2.2. Preparation of supported iridium catalysts

Supported catalysts were prepared by an impregnation method as shown in Scheme 1. To a solution of $Ir(acac)_3$ or $[(COD)IrCl]_2$ (0.10 mmol as Ir) in 10 mL of methanol (THF for $[(COD)IrCl]_2$), 1.0 g of titania support was added in air at room temperature. After impregnation, the sample was dried overnight in air at 80°C. Unless otherwise noted, the resulting powder was calcined in air at 400 °C for 30 min in a box furnace (ramp rate 10 °C min^{-1}). About 600 mg of the resulting powder was mounted in a quartz tube (o.d. 12 mm) and reduced in a H_2 (2vol.%)/Ar flow (40 cm^3 min^{-1}) at 500 °C (ramp rate; 10 °C min^{-1}) for 30 min by the use of a conventional flow reactor. After reduction, the catalysts were passivated in an O_2 (*ca*. 2%)/N_2 flow (40 cm^3 min^{-1}) at 50 °C for 5 min. The loading level of iridium speceies was finally checked by WDX.

2.3. General procedure for the catalytic runs

The procedure was slightly modified from that in our previous study [7]. All of the reactions were performed using hot stirrers equipped with cooling blocks to reflux the solution. The Ir/titania catalyst (0.010 mmol as Ir) was mounted in a glass Schlenk tube (20 cm^3). As noted above, all the catalysts were used just after the reduction at 500 °C and following passivation without additional *in-situ* reduction treatment, while such treatment might increase the initial activities of the catalysts to some extent. A typical reaction procedure for the synthesis of 2-phenylbenzimidazole (**3**) is as follows: 1,2-phenylenediamine (**1**) (1.0 mmol), benzyl alcohol (**2**) (2.3 mmol), and mesitylene (1.0 cm^3) were added to the Schlenk tube containing the reduced catalyst. The reaction mixture was stirred at 100 °C for

18 h under an argon atmosphere. 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 (*ca*. 50 mg) as an internal standard. For the synthesis of indole (**5**), 2-(2-aminophenyl)ethanol (**4**, 1.0 mmol) and mesitylene (1.0 cm^3) were placed in a glass Schlenk tube (20 cm^3) under an argon atmosphere together with the reduced catalyst (0.010 mmol as Ir), and the reaction mixture was stirred at 120 or 100 °C for 18 h. Biphenyl (*ca*. 50 mg) was used as an internal standard for the GC analysis.

3. Results and discussion

3.1. Effects of titania supports of iridium catalysts for the dehydrogenative synthesis of benzimidazole

The activities of iridium catalysts supported on various titanias for the dehydrogenative synthesis of 2-phenylbenzimidazole (**3**) from *o*-phenylenediamine (**1**) and benzyl alcohol (**2**) were compared. The supported iridium catalysts were prepared by the procedure shown in Scheme 1, and used after the reduction at 500 °C in a stream of hydrogen. A chlorine-free iridium complex, $Ir(acac)_3$ (acac = acetylacetonate), was used as an iridium source. Note that a composition analysis of the catalyst using a WDX analyzer revealed that some of the iridium species loaded with the catalyst might be lost during calcination in the preparation of the catalysts, probably by the sublimation of $Ir(acac)_3$ due to its relatively high volatility (see Experimental and Table 1). Such a loss of iridium species was highly significant for catalysts supported on titania with low surface areas such as F-series titanias. Therefore, in the following study, the activities were compared under the same molar amount of iridium species by adjusting the weight of the catalysts used.

Table 1 shows the yield of **3** in the presence of 1.0 mol% (as Ir) of supported iridium catalysts at 120 °C and 100 °C for 18 h. Anatase-rich and rutile-rich titanias are denoted as (A) and (R), respectively. As reported in our previous study [7], JRC-TIO-4-supported catalyst showed excellent activity at 120°C. The desired product was obtained in 96% yield after 18 h reaction under the present conditions. On the other hand, different kinds of titanias had different effects on the yield of **3** in the reactions at 100 °C. Catalysts supported on rutile titanias, namely JRC-TIO-6 and F-1R, showed excellent activities (see entries 2 and 7), whereas the yields of **3** in the presence of anatase-supported catalysts were not satisfactory (see entries 1, 4-6, 8-11). No significant correlation was found between surface area and the activity of the catalysts, and catalysts supported on titanias with high surface areas, such as JRC-TIO-7, -8, or -9, did not show significant activities. The yield of JRC-TIO-6-supported iridium catalyst further improved to 88% when the catalyst was prepared without calcination (entry 3, see below).

The loss of iridium species during preparation of the catalysts could be avoided by the use of chlorine-containing iridium complexes such as $[(COD)IrCl]_2$ (COD = 1,5-cyclooctadiene). However, the resulting catalysts showed lower activities than that prepared using $Ir(acac)_3$ at 100 °C, as shown in Table S1. XPS analyses of these catalysts revealed the presence of a larger amount of chlorine atoms on the surface of the catalysts prepared using $[(COD)IrCl]_2$ (see Table S2), which suggests that the presence of chlorine decreases the catalytic activity at a relatively low temperature (100 °C).

3.2. *Ir/TiO$_2$-catalyzed dehydrogenative synthesis of indole*

The effects of various titania supports on the synthesis of indole (**5**) via a dehydrogenative route were examined. The results are summarized in Table 2. While previously-reported Ru/CeO$_2$ catalysts (2.0 mol% as Ru) required a relatively high temperature of around 140 °C for the reaction to be complete within 18 h [4e], iridium catalysts supported on JRC-TIO-6 successfully gave **5** in an excellent yield (86 %) at lower temperature (120 °C). As in the dehydrogenative synthesis of 2-phenylbenzimidazole, rutile-supported catalysts generally showed activities at lower temperature. Again, anatase titanias with high surface areas were not good supports for this reaction. At 100 °C, **5** was obtained in the highest yield (52%) in the presence of the F-1R (rutile)-supported catalyst .

3.3. *Optimization and characterization of iridium catalysts supported on various titanias*

The activities of Ir/TiO$_2$ catalysts greatly depend on the calcination procedure during their preparation. Note that all the catalysts were reduced under H$_2$ at 500 °C just before the catalytic runs (see Scheme 1). As shown in Figure 1, the yield of **5** at 100 °C greatly improved when the catalyst was calcined below 240 °C, and **5** was obtained in the highest yield of 73% in the presence of the catalyst without calcination. The Ir/JRC-TIO-6 catalyst without calcination was also effective for the synthesis of 2-phenylbenzimidazole (see Table 1, entry 3). A TG-DTA study showed that surface Ir(acac)$_3$ on JRC-TIO-6 oxidatively decomposed at around 230 °C (Fig. S2). Since CO uptake by the reduced catalysts without calcination, followed by the reduction at 500 °C, was greater than that with catalysts calcined at 400 °C (see below), calcination at a high temperature would promote the formation of aggregated iridium oxide species. The BET surface area of the catalyst without calcination (63 m^2g^{-1}) was slightly greater than that of the catalyst calcined at 400 °C (53 m^2g^{-1}). Our previous study [7] revealed that the calcination of spent catalysts is required to maintain excellent activities in repeated uses to completely remove strongly-adsorbed carbonaceous materials. The present results suggest that calcination should be performed at a temperature lower than the decomposition temperature of the surface complex, namely 230 °C.

Figure 2 shows TEM images of several Ir/TiO_2 catalysts after the reduction at 500 °C. A photograph of Ir/JRC-TIO-4 (1 wt% as Ir) is shown for comparison ([7] - Reproduced by permission of The Royal Society of Chemistry). As previously reported [7,11], iridium species of all the catalysts examined were very small, less than 2.5 nm. While the formation of homogeneously-dispersed iridium particles was confirmed on JRC-TIO-6, the effects of calcination temperature on the particle size were ambiguous, as shown in Figure 2 (a) and (b). Slightly larger particles were formed on F-1R(R). Much smaller particles of iridium species were formed on JRC-TIO-7, whereas the catalytic activity was low and CO-uptake by this catalyst was limited (see Table 1 and Figure 3). On F-2, inhomogeneous loading of iridium species was observed, while the particle size was small. Some facets of titania particles were thickly covered by small iridium nanoparticles, while other facets had no iridium particles. This could be due to differences in the surface energies between facets of anatase [12]. Such inhomogeneous formation of transition metallic species has been reported previously [13].

There was a significant relationship between CO uptake and the activities of the reduced Ir/TiO_2 catalysts, as summarized in Figure 3. In general, the yields of both (a) **3** and (b) **5** via dehydrogenative routes increased with an increase in CO uptake, suggesting that fully-reduced, probably zero-valence, iridium species are the active sites of the present dehydrogenative reactions. Note that the catalysts supported on pure rutile such as JRC-TIO-6 or F-1R adsorbed much amount of CO, and the fraction of rutile phase in titania was generally correlated with CO uptake ability of the catalyst. Iridium catalysts prepared without calcination showed higher CO uptake than that calcined at 400 °C, implying that calcination at relatively high temperature might induce aggregation of the resulting iridium species, whereas this difference was not clear in TEM images (see above). Despite the formation of very fine nanoparticles, CO uptake of iridium catalysts supported on JRC-TIO-7 was low. Similar results were observed for JRC-TIO-8 or -9-supported catalysts. It has been reported that noble metals supported on reducible supports such as titanias often suffer from strong metal-support interaction (SMSI). Due to SMSI, the CO-adsorption ability of supported metallic catalysts has been reported to drastically decrease when the catalysts are reduced at high temperatures without aggregation of metallic species [14]. The lower CO uptake and the resulting lower activity of iridium catalysts supported on anatase titania with high surface areas could be attributed to SMSI, and the extent of SMSI would significantly depend on the titania support. As demonstrated in our previous study using Ir/JRC-TIO-4, the extent of the reduction of iridium species greatly affects the activity [7]. Therefore, the achievement of highly reduced states of iridium without SMSI could be one reason for the enhanced activity of JRC-TIO-6-supported catalysts.

The state of surface iridium species on various titanias just after reduction at 500 °C was investigated by XPS. The Ir 4f spectra are shown in Figure S3. The ratio of Ir^0 (60.7 eV) to Ir^0 + Ir^{VI} (62.0 eV) on the surface estimated by curve fitting was 55% for F-1R (R), 52% for JRC-TIO-6 (R), 45% for F-1 (A), 40% for F-2 (A), 43% for F-6 (A), and 41% for JRC-TIO-7 (A), indicating that, as a general trend, fully reduced iridium species are predominant on rutile titanias. The formation of well-reduced iridium species could be one reason of the predominant CO uptake by the rutile-supported catalysts

The results presented here clearly indicate that the predominant formation of highly reduced and highly dispersed iridium nanoparticles on rutile is important for the excellent activity in the dehydrogenative synthesis of *N*-containing chemicals. Kido and coworkers reported characteristic charge transfer between gold nanoclusters and a rutile support [15]. While an electronic charge transfer from gold nanoclusters to the O-rich TiO_2(110) played a crucial role in the enhancement of CO oxidation activity, the deposition of Au nanoclusters on reduced-TiO_2(110) surfaces resulted in a reverse electronic charge transfer from TiO_2. Therefore, one can expect the formation of more electron-rich iridium nanoparticles on rutile under a reductive atmosphere by such reverse electronic charge transfer, although comparative studies on such electronic effects are still required. In addition, further studies on why electron-rich iridium species promote these dehydrogenative reactions are now in progress.

4. Conclusion

The catalytic activities of titania-supported iridium catalysts for the dehydrogenative synthesis of benzimidazole and indole at relatively lowtemperature (100 °C) depended on the crystalline structure of titania. Of those examined, iridium catalysts supported on rutile titanias, such as JRC-TIO-6 and F-1R, selectively gave the desired products in high yields, while catalysts supported on anatase titanias with high surface areas, namely JRC-TIO-7, -8, and -9, did not show significant activity. TEM photographs showed that small nanoparticles (ca. 2 nm in diameter) were uniformly dispersed on JRC-TIO-6 and F-1R, while iridium particles are only found on specific facets or particles of several anatase supports. According to the results of CO pulse experiments and an XPS study, the formation of small, well-reduced iridium nanoparticles can be considered to be essential for excellent activities in dehydrogenative reactions. Further application of these catalysts for other dehydrogenative reactions is underway.

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[15] A. Visikovskiy, K. Mitsuhara, Y. Kido, J. Vac. Sci. Technol. A 31/ 6 (2013) 061404(1-9).

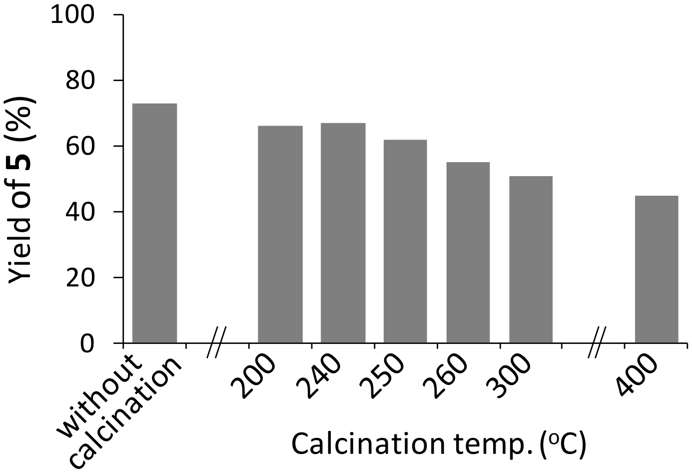


Fig. 1. Effects of calcination temperature of Ir/JRC-TIO-6-supported catalysts on the synthesis of indole **5** at 100 °C for 18 h. All the catalysts were reduced under H_2 at 500 °C before use (see Scheme 1).

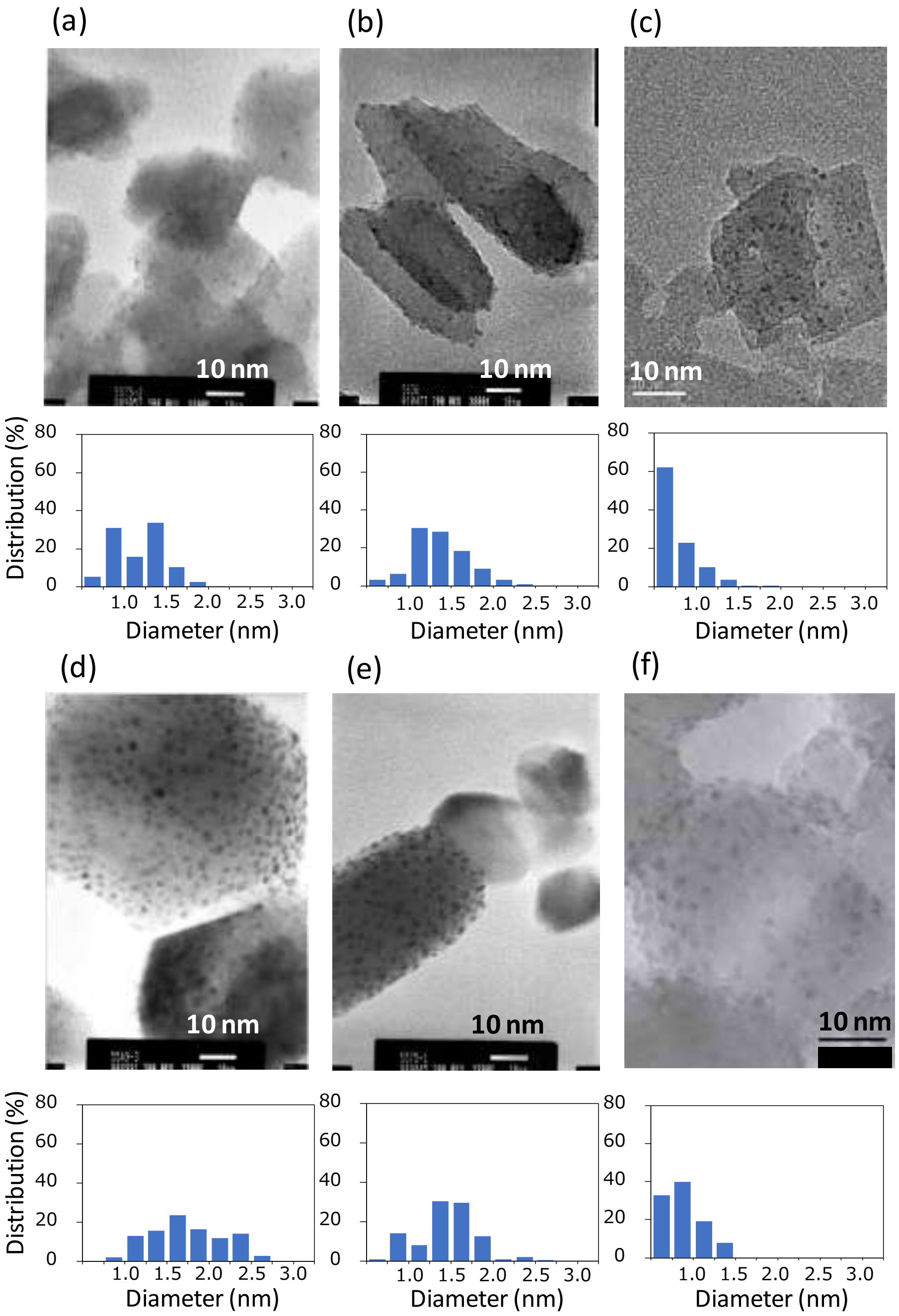
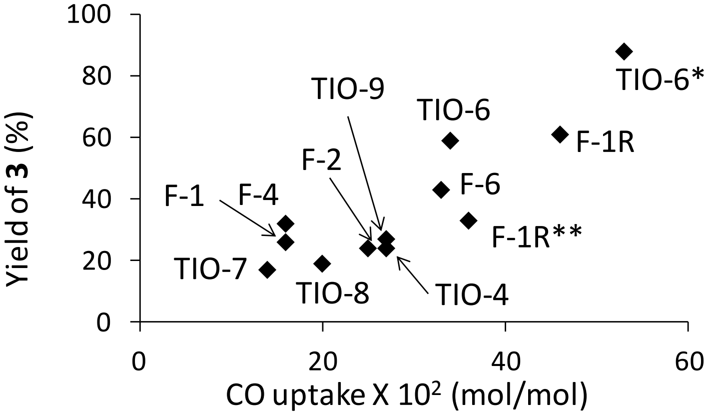


Fig. 2. TEM photographs and the particle size distribution histograms of iridium catalysts supported on (a) JRC-TIO-6 (R), (b) JRC-TIO-6 (R, calcined at 240°C), (c) JRC-TIO-7 (A), (d) F-1R (R), (e) F-2 (A), and (f) JRC-TIO-4 (A) [7]. Loading levels of iridium species are shown in Table 1. Catalysts were calcined at 400 °C and then reduced at 500 °C for 30 min unless otherwise noted.

(a)



(b)

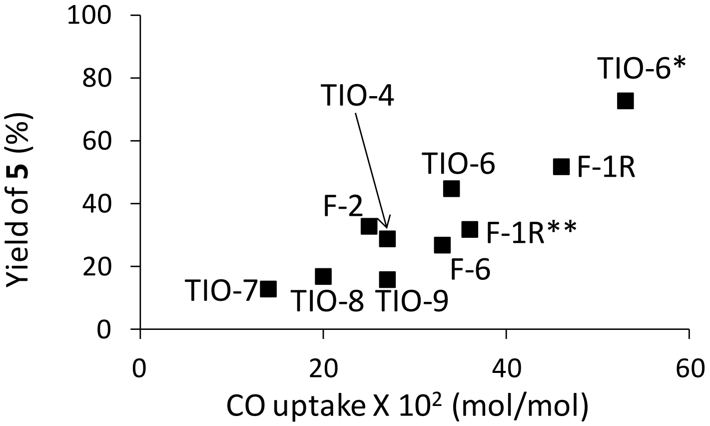
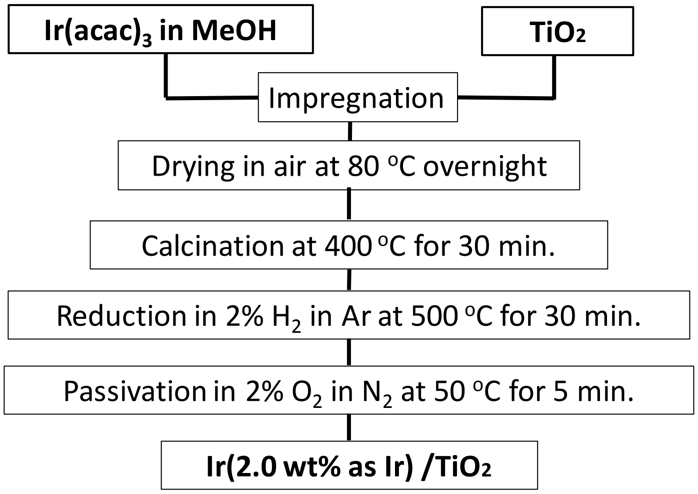
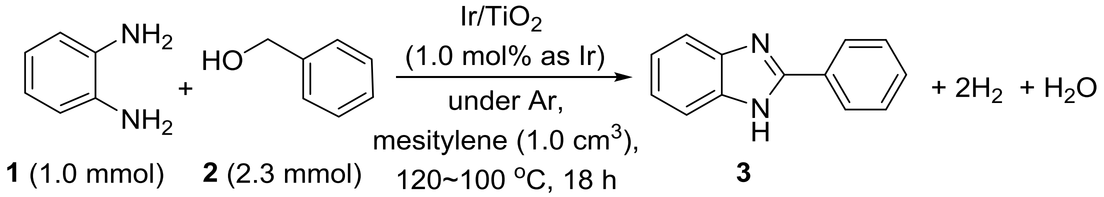


Fig. 3. Relationship between CO uptake of the catalysts and the yields of (a) **3** from **1** and **2** and (b) **5** from **4**. Reaction temperature 100 °C, reaction time 18 h. *Prepared without calcination. **Prepared using [(COD)IrCl]$_2$ as an iridium source.



Scheme 1. Preparation procedure of titania-supported iridium catalysts.

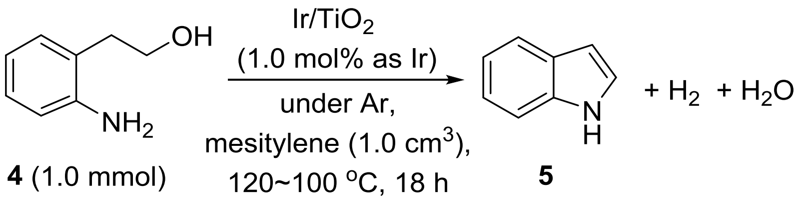
Table 1. Activities of Ir/TiO_2 catalysts for the synthesis of 2-phenylbenzimidazole



Entry	TiO_2 support[a]	BET S.A. of catalysts (m^2g^{-1})	Ir loading after calcination (wt%)	Yield of **3** at 120 °C 18 h (%)	Yield of **3** at 100 °C 18 h (%)
1	JRC-TIO-4 (A)[b]	51	2.0	96	24
2	JRC-TIO-6 (R)	53	2.0	96	59
3	JRC-TIO-6 (R)[c]	63	2.0	-	88
4	JRC-TIO-7 (A)	133	2.5	29	17
5	JRC-TIO-8 (A)	123	2.4	55	19
6	JRC-TIO-9 (A)	129	2.0	59	27
7	F-1R (R)	19	1.0	83	61
8	F-1 (A)	21	1.2	87	26
9	F-2 (A)	30	1.4	91	24
10	F-4 (A)	47	1.1	82	32
11	F-6 (A)	85	2.0	94	43

[a] (A): Anatase-rich and (R) rutile-rich titanias. [b] Containing *ca.* 20% of rutile. [c] Prepared without calcination.

Table 2. Activities of Ir/TiO2 catalysts for the synthesis of indole.



Entry	TiO2 support[a]	Yield of **5** at 120 °C 18 h (%)	Yield of **5** at 100°C 18 h (%)
1	JRC-TIO-4 (A)	50	29
2	JRC-TIO-6 (R)	86	45
3	JRC-TIO-7 (A)	15	13
4	JRC-TIO-8 (A)	22	17
5	JRC-TIO-9 (A)	23	16
6	F-1R (R)	80	52

[a] (A): Anatase-rich and (R) rutile-rich titanias.