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Ligand-free Suzuki coupling reaction with highly recyclable ionic palladium catalyst, $Ti_{1-x}Pd_xO_{2-x}$ (x = 0.03)

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ABSTRACT

We synthesized a recyclable palladium ionic catalyst, $Ti_{0.97}Pd_{0.03}O_{1.97}$, using a solution combustion method (SCM), and characterized by XRD and Rietveld refinement. The synthesized Pd ionic catalyst is stable, insensitive to moisture and air, and easy to handle. The new catalyst has exhibited a phenomenal result for the Suzuki-Miyaura cross-coupling reaction with a broad substrate scope, and the reaction proceeds in an aqueous medium. The new catalyst proved beneficial and produced excellent yields irrespective of aryl halide used in the reaction (electron-rich or electron-poor or heterocyclic compounds) and shown a turnover frequency (TOF) of 14–25 h^{-1} for different reactions. The catalyst was coated on a cordierite monolith ($Mg_2Al_4Si_5O_{18}$), which enhanced the applicability of the catalyst, and made the handling and recycling of the catalyst very easy. Suzuki Miyaura reaction was carried out using both Pd-powder catalysts as well as the Pd-coated honeycomb, which gave almost similar results. We have demonstrated the recyclability of Pd coated cordierite monolith and shown the superiority of the catalyst over the other Pd catalysts for the Suzuki-Miyaura reaction.

1. Introduction

Suzuki coupling reaction is an important tool for synthesizing biaryl compounds, that are found in many natural products [1,2], drug molecules [3,4], and advanced materials [5–7]. The palladium-catalyzed Suzuki coupling reaction is very well-known from time memorial [8], which is well exploited [9–12]. Generally, the Suzuki reactions are performed using palladium-catalyst in the presence of phosphine ligands [13,14], and *N*-heterocyclic carbene ligands [15–17], which proceeds through a well-known palladacycle [18–21]. Synthesizing biaryl compounds by employing heterogeneous Pd-catalysts leads to a sustainable method and offers the advantage of recovery and recyclability of the catalyst [22–26]. Suzuki coupling reaction without using ligands is advantageous [27,28], and Suzuki reaction in water or water/ organic co-solvents has received a considerable attention [25–35]. Although a few methods are designed to use homogeneous catalytic conditions, the costs, conditions, and limited substrate scope limit their applications. In a large-scale synthesis, a heterogeneous method has a definite advantage in terms of their practical utility and smooth operations.

Recent days, Pd nanoparticles catalyzed Suzuki Miyaura cross-coupling reactions are becoming more attractive as they offer advantages such as a high surface-to-volume ratio, ligand-free synthesis, simple workup procedure, easy separation of final products, easy recovery, and multiple recycling of the catalyst [36,37]. Dispersion of Pd on reducible oxide support on TiO_2 has enhanced the catalytic activity of CO oxidation several folds at a much lower temperature compared to the same amount of Pd on Al_2O_3. This is due to the dispersion of Pd^{2+} ion in TiO_2, which provides an enhanced active site for adsorption. In the catalyst, Pd-ion has been dispersed in TiO_2 as Pd^{2+} ion in stoichiometric ionic compounds of $Ti_{1-x}Pd_xO_{2-x}$ (x = 0.01-0.03) [38,39]. In $Ti_{1-x}Pd_xO_{2-x}$ catalytic system, Pd^{2+} ion, and O^{2-} vacancies are next to each other, and Pd^{2+} functions as an electrophilic site, whereas O^{2-} ion vacancy provides a nucleophilic site. Accordingly, CO has been adsorbed on Pd^{2+} ion, and O_2 has been adsorbed on oxide ion vacancy. Using this concept, a new class of noble metal ionic catalysts are developed [38–42]. In this direction, herein, we report a synthesis of a Pd^{2+} ionic catalyst on TiO_2 and demonstrate the utility of Pd^{2+} ionic catalyst for the Suzuki-Miyaura reaction (Scheme 1). The catalyst shows higher Suzuki-Miyaura coupling rates and a wide substrates scope compared to other Pd-ionic catalyst or Pd-metal catalyst.

We performed the Suzuki-Miyaura coupling reaction with the Pd-
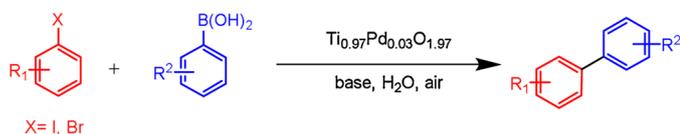
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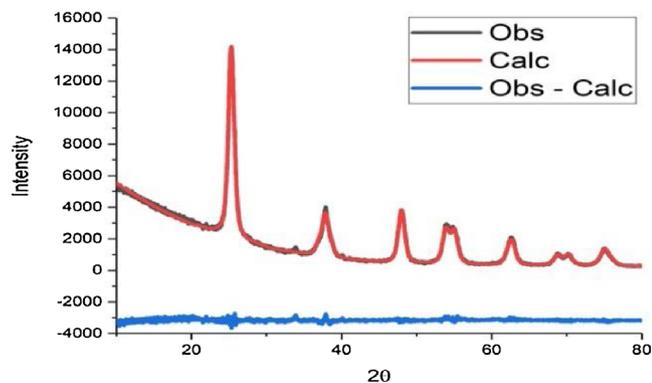**Scheme 1.** Suzuki-Miyaura-Coupling Reaction.

Fig. 1. Rietveld refinement of the XRD profile of freshly prepared catalyst.

powder catalyst as well as the Pd-coated on cordierite. The advantages of the new catalyst for the Suzuki-Miyaura coupling reaction are, (i) the catalyst is less expensive, (ii) air and moisture stable, (iii) the catalyst is coated on cordierite monolith, which is easy to handle and easy to recycle. Besides, the reaction was performed in ligand-free conditions, the reaction proceeds smoothly in an aqueous medium, and the reaction is compatible with heterocyclic molecules.

2. Results and discussion

The catalyst, $Ti_{0.97}Pd_{0.03}O_{1.97}$, which is Pd^{2+} ion substituted TiO_2, was synthesized based on earlier reports and confirmed by XRD, XPS and EXAFS study [38]. XRD pattern and Rietveld refinement of the XRD profile of freshly prepared catalyst is shown in Fig. 1. As confirmed by the X-ray pattern, the catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$ is a single-phase catalyst [38]. From the X-ray pattern, the average crystallite size of the catalyst was found to be 8 ± 2 nm, which was calculated using the Scherrer formula ($0.95 \lambda/\beta \cos\theta$), wherein β is FWHM of diffraction lines of the X-ray pattern. The color of the catalyst is brown.

The catalyst was coated on a cordierite monolith by solution combustion method [43]. Cordierite monolith is a ceramic material with a cylindrical structure made up of many parallel channels of square shape. The composition of cordierite monolith is $Mg_2Al_4Si_5O_{18}$. Wash coating of cordierite was performed to obtain coated cordierite with γ–Al_2O_3 [43]. This operation has increased the surface area of cordierite as γ–Al_2O_3 is one of the oxides with a high surface area. Then the catalyst, $Ti_{1-x}Pd_xO_{2-x}$, was coated over γ–Al_2O_3 to obtain a "ready to use catalyst" coated over a cordierite monolith.

Having a pure catalyst in hand, we focused our attention on the applicability of the catalyst for the Suzuki-Miyaura coupling reaction. First, the screening studies were started to find optimal reaction conditions for the reaction using 4–iodoanisole (**1c**, 0.4 mmol, 1 equiv.) and phenylboronic acid (**2a**, 0.8 mmol, 2 equiv) as model substrates (Table 1). The optimization studies were carried out using the powder catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$. The reaction of **1c** with **2a** using K_2CO_3 (2 equiv.) as a base, water (2 mL) as a solvent, and a powder catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$ (10 % by weight) at 100 °C for 15 h furnished the corresponding coupled product **3c** in 92 % yield (entry 1, Table 1). A similar reaction at 100 °C for 6 h afforded the product **3c** in 93 % yield (entry 2, Table 1). However, the reaction at 70 °C furnished **3c** in 68 % (entry 3, Table 1). Although water is a preferred solvent, as it is non-

toxic, highly abundant, and environmentally benign, we conducted a reaction in DMF/H_2O in 3:1 ratio (2 mL) as a solvent system at 100 °C, which furnished a slightly low yield of **3c** (72 %, entry 4, Table 1), whereas the reaction in the absence of base was unsuccessful (entry 5, Table 1). Reaction using Cs_2CO_3 furnished 87 % of **3c** (entry 6, Table 1). Increasing the catalyst loading from 10 wt% to 20 wt%, resulted in the formation of **3c** in 88 % yield (entry 7, Table 1), whereas reducing the catalyst loading to 5% afforded the 85 % of **3c** (entry 8, Table 1). Decreasing the reaction time to 3 h (entry 9, Table 1) or employing the phenylboronic acid in 1.5 equiv. (entry 10, Table 1) furnished the **3c** in 74 and 81 % yields, respectively. The best result (entry 2, Table 1) was obtained with the use of K_2CO_3 (2 equiv.) as a base, 10 wt percentage of catalyst, and water (2 mL) as the solvent at 100 °C for 6 h (See the Supporting Information for the optimization studies were also performed using iodobenzene (**1a**) and phenyl boronic acid (**2a**)).

3. Substrate scope using $Ti_{0.97}Pd_{0.03}O_{1.97}$ powder catalyst

First, we explored the scope of the Suzuki reaction using $Ti_{0.97}Pd_{0.03}O_{1.97}$ powder catalyst (Table 2). As can be seen, the reaction proceeded well with a variety of aryl halides and arylboronic acid derivatives. The reaction of iodobenzene with phenylboronic acid and *m*-tolylboronic acid was facile furnishing the corresponding biaryl derivatives **3a** and **3b** in 90 and 96 % yields, respectively. Similarly, the reaction of *para*-methoxyiodobenzene, *para*-methyliodobenzene, and *para*-fluoroiodobenzene with phenylboronic acid afforded the corresponding biaryl derivatives **3c**, **3d**, and **3e** in 92, 83, and 96 % yields, respectively. The reaction of *para*-methoxyiodobenzene with (4-acetylphenyl)boronic acid was also facile, affording the product **3f** in almost quantitative yield. The reaction of halo substituted arylboronic acids such as (4-fluorophenyl)boronic acid, (3-chlorophenyl)boronic acid, and (4-chlorophenyl)boronic acid proceeded smoothly furnishing the products **3 g**, **3 h**, and **3i** in 99, 96, and 98 % yields, respectively. (4-(Methylthio)phenyl)boronic acid and (4-*tert*-butyl)phenyl)boronic acid underwent a smooth Suzuki-Miyaura coupling with *para*-methoxyiodobenzene forming the coupled products **3 j** and **3k** in 76 and 98 % yields, respectively. These experiments reveal that the reactions of the substrates with the electron-withdrawing or electron-donating groups lead to the corresponding coupled products in good to excellent yields.

The reaction of aryl bromides with arylboronic acids were also facile furnishing the corresponding biaryl derivatives in good to excellent yields. A few examples have been presented in Table 2. The reaction of 2-bromonaphthalene with phenylboronic acid and 1-bromonaphthalene with *p*-methoxy phenylboronic acid proceeded smoothly, furnishing the corresponding biaryl derivatives **3 l** and **3 m** in 97 and 99 % yields, respectively. The reaction of phenylboronic acid with *para*-bromoacetophenone and *meta*-bromoprophiophenone proceeded smoothly, affording the coupled products **3n** and **3o** in 85 and 85 % yields, respectively. Similarly, the reaction of *meta*-methoxy-bromobenzene with phenylboronic acid afforded the product **3p** in 84 % yield. The reaction of bromobenzene with 3-cyanophenylboronic acid furnished coupled product **3q** in 64 % yield.

For broadening the scope of the reaction, the reactions were carried out with heterocyclic aromatic halides and heterocyclic aromatic boronic acids. As can be seen, the reaction of phenylboronic acid with 6-bromoindole and 5-bromoindole proceeded well and furnished the corresponding Suzuki-Miyaura coupled products **6 t** and **6 u** in 99 and 90 % yields, respectively. The reaction of 6-bromoindole with 3,4-methylenedioxyphenylboronic acid was also facile, providing the coupled product **6v** in 98 % yield. The reactions of heterocyclic bromides, such as 3-bromopyridine with phenylboronic acid, also proceeded well furnishing the corresponding coupled products **6 w** in 89 % yields. Our attempt of using alkyl halides and alkylboronic acids for the Suzuki-Miyaura coupling reactions using developed conditions were not successful.

Table 1
Optimization studies[a].
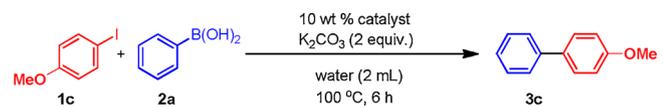
entry	catalyst (wt %)	base	solvent	temp (°C)	time (h)	yield (%)
1	10	K_2CO_3	H_2O	100	15	92
2	**10**	**K_2CO_3**	**H_2O**	**100**	**6**	**93**
3	10	K_2CO_3	H_2O	70	6	68
4	10	K_2CO_3	DMF/H_2O (3:1)	100	6	72
5	10	none	H_2O	100	20	n.r
6	10	Cs_2CO_3	H_2O	100	6	87
7	20	K_2CO_3	H_2O	100	6	88
8	5	K_2CO_3	H_2O	100	6	85
9	10	K_2CO_3	H_2O	100	3	74
10	10	K_2CO_3	H_2O	100	6	81[b]

Reaction conditions: 4-Iodoanisole (**1c**, 0.4 mmol, 1 equiv.), phenylboronic acid (**2a**, 0.8 mmol, 2 equiv.), K_2CO_3 (0.8 mmol, 2 equiv.), 10 wt% of Pd catalyst (3.02 μg of Pd^{2+} ion), 2 ml of water.
[b] Phenylboronic acid (**2a**,1.5 equiv.). All are isolated yield, n.r = no reaction.

Table 2
Substrate scope using Ti0.97Pd0.03O1.97 powder catalyst.
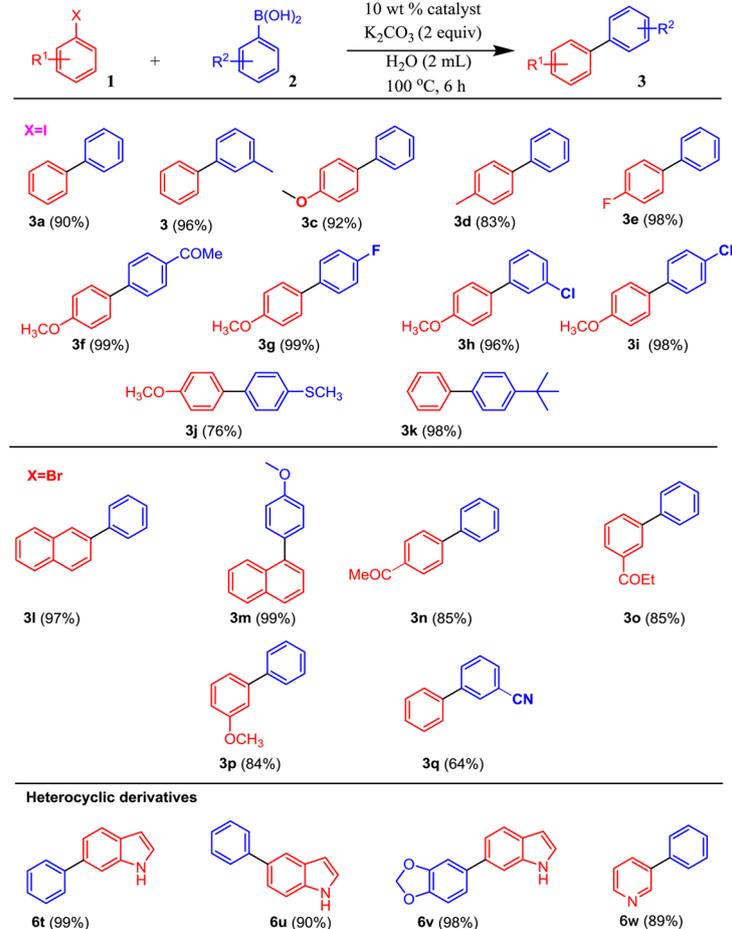
Reaction conditions: Aryl halides (0.4 mmol), arylboronic acid (0.8 mmol), K_2CO_3 (0.8 mmol), $Ti_{0.97}Pd_{0.03}O_{1.97}$ (10 wt percentage), H_2O (2 mL), 100 °C, 6 h, the values presented in the parenthesis are isolated yields.

4. Suzuki coupling reactions using catalyst coated on the monolith

After successfully showcasing the utility of the catalyst ($Ti_{0.97}Pd_{0.03}O_{1.97}$) for the Suzuki coupling reactions, we continued our expedition on the applicability of the catalytic system. From past decades, the palladium-catalyzed reactions became part of the large-scale synthesis and adopted by many industries. Having this in mind, we continued the investigation employing the catalyst coated over cordierite monolith (Table 3). Therefore, the reaction of bromobenzene (1

Table 3

Suzuki coupling reactions using catalyst coated on the monolith.
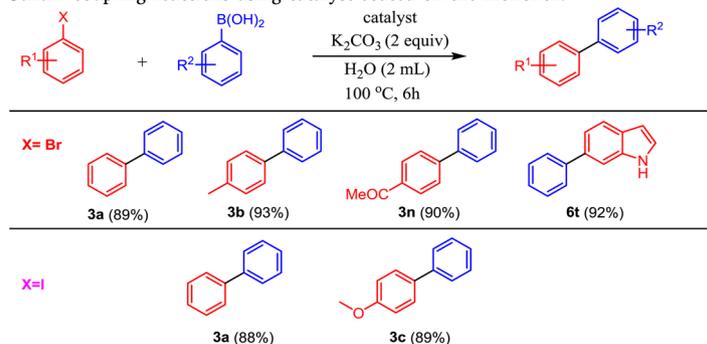
Reaction conditions: Aryl halides (1 equiv., 300 mg), phenylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), $Ti_{0.97}Pd_{0.03}O_{1.97}$ coated on monolith (30 mg), H_2O (6 mL), 100 °C, 6 h, the values presented in the parenthesis are isolated yields.

equiv.) with phenylboronic acid (2 equiv.) was performed using catalyst coated on monolith (30 mg), base K_2CO_3 (2 equiv.), at 100 °C for 6 h. To our delight, the reaction proceeded smoothly to afford the corresponding coupled product **3a** in an 89 % yield. The advantage of this reaction is that after the reaction, the catalyst (coated over cordierite monolith) is removed from the reaction flask, washed with hexane to remove the organic phase, and washed with distilled water to remove solvent and base. After washing, the monolith is heated in a furnace for about 2 h at 300 °C, and the monolith is ready to reuse for another cycle. To demonstrate the generality of this protocol, a few more selected examples are illustrated in Table 3 by employing the same procedure. Thus, the reaction of *para*-methylbromobenzene and 4-bromo acetophenone with phenylboronic acid proceeded very well to afford the coupled products **3b** and **3n** in 93 and 90 % yields, respectively. Similarly, the reaction of 6-bromoindole with phenylboronic acid, under similar conditions, afforded the coupled product **6 t** in 92 % yield. The reactions of iodobenzene and *para*-methoxyiodobenzene with phenylboronic acid were also facile, yielding the corresponding coupled products **3a** and **3c** in 88 % and 89 %, respectively. All these examples show that the catalyst coated on the monolith is equally efficient as the powder catalyst ($Ti_{0.97}Pd_{0.03}O_{1.97}$). Each time, a separate monolith was used for the reaction. The amount of substrate used in these reactions is corresponding to the amount of catalyst coated on the monolith. In every reaction, we maintained a 10 wt percentage catalyst to the substrate.

5. Comparison of $Ti_{0.97}Pd_{0.03}O_{1.97}$ catalyst with other palladium catalysts

To demonstrate the advantage of using the catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$, we performed the Suzuki reaction of *para*-methoxyiodobenzene with phenylboronic acid using Pd-catalysts such as $Pd_2(dba)_3$, $Pd(OAc)_2$, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, and $PdCl_2(dppf)$ (Table 4). For the sake of convenience, we performed the reaction in *N, N*-dimethyl formamide at 100 °C for 6 h using K_2CO_3 as a base. The Suzuki reaction of *para*-methoxyiodobenzene with phenylboronic acid in the presence of $Pd_2(dba)_3$, $Pd(OAc)_2$, $Pd(PPh_3)_4$, and $PdCl_2(dppf)$ furnished the coupled product in 60, 70, 10, and 65 % yields, respectively (entries1-4, Table 4). A similar reaction using catalyst $PdCl_2(PPh_3)_2$ tuned out to be an unsuccessful (entry 5). As can be seen in entry 6, the reaction of *para*-methoxyiodobenzene with phenylboronic acid using $Ti_{0.97}Pd_{0.03}O_{1.97}$ catalyst under similar conditions (employed for the other palladium catalysts, as seen in Table 4), furnished a better yield of Suzuki product in 74 % yield. To our delight, the same reaction in water furnished almost quantitative yield of the coupled product (entry 7). Besides, the present method employs only 3% of Pd, whereas other methods (entries 1–5, Table 4) require a higher percentage of Pd-catalysts. More importantly, the TOF for the present method is quite high. For comparison sake, we also performed the reaction using conditions in DMF as well as water. In both the solvents, the yield and TOF are higher than other known methods, and the reaction in water turned out to be very good.

Table 4

Comparison $Ti_{0.97}Pd_{0.03}O_{1.97}$ catalyst with other palladium catalysts[a].

entry	Pd-catalyst	percentage of Pd	yield (%)	TOF (h^{-1})
1	$Pd_2(dba)_3$	21.5	60	4.6
2	$Pd(OAc)_2$	45.9 – 48.4	70	2.48
3	$Pd(PPh_3)_4$	9	10	1.85
4	$PdCl_2(dppf)$	53.62 – 58.04	65	1.67
5	$PdCl_2(PPh_3)_2$	14	n.r.	–
6	$Ti_{0.97}Pd_{0.03}O_{1.97}$	3	74	14
7	$Ti_{0.97}Pd_{0.03}O_{1.97}$	3	99[b]	18[b]

[a] Reaction conditions: 0.4 mmol of 4-iodoanisole, 0.8 mmol of phenylboronic acid, 0.8 mmol of K_2CO_3, 10 mol% of Pd catalyst, 2 ml of DMF as a solvent, temperature of the reaction is 100 °C.

[b] Water (2 mL) as a solvent. n. r. = no reaction.
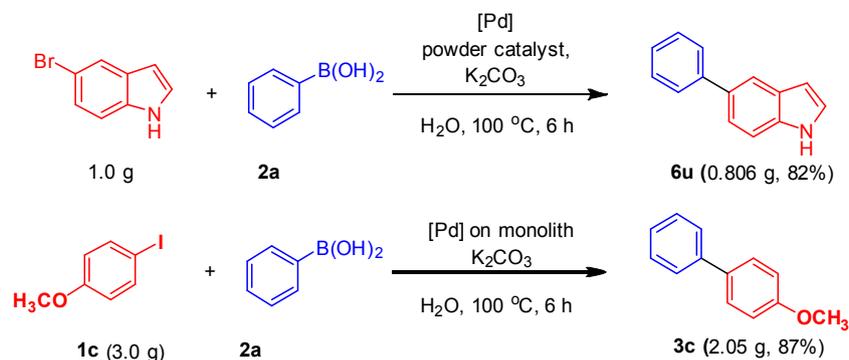
Scheme 2. Scale-up reactions [a,b].
[a] Reaction conditions: Aryl halide (1 equiv.), phenylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), $Ti_{0.97}Pd_{0.03}O_{1.97}$ (10 wt percent), H_2O, 100 °C, 6 h. [b] Isolated yield
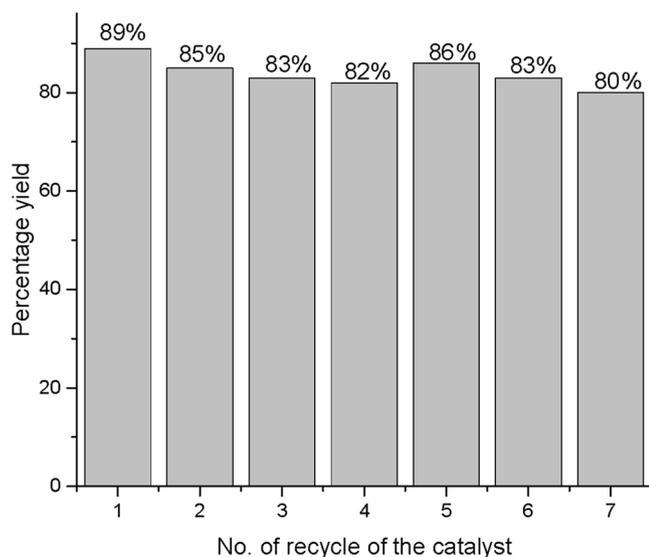

Fig. 2. Recycling the catalyst coated on the monolith.
Reaction conditions: 4-Iodoanisole (1 equiv. 300 mg), phenylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), $Ti_{0.97}Pd_{0.03}O_{1.97}$ coated on monolith (30 mg), H_2O (6 mL), 100 °C, 6 h, all products are isolated yield.

6. Scale-up reaction

We performed a preparative scale reaction of 5-bromoindole with phenylboronic acid (**2a**) for demonstrating the usefulness of the method. Thus, we carried out a reaction of 5-bromoindole (5.1 mmol, 1 g) with phenylboronic acid (2 equiv., 10.2 mmol, 1.24 g) using $Ti_{0.97}Pd_{0.03}O_{1.97}$ (nanoparticles. 10 wt percent) in H_2O (15 mL) at 100 °C for 6 h. This reaction afforded the coupled product **6 u** in 82 %

yield (Scheme 2). Similarly, we carried out another scale-up reaction of 4-iodoanisole (**1c**, 12.8 mmol, 3 g) with phenylboronic acid (**2a**, 25.6 mmol, 3.1232 g) using catalyst coated monolith (300 mg) in H_2O (25 mL) at 100 °C for 6 h. This reaction afforded the coupled product **3c** in 87 % yield (Scheme 2).

7. Recycling of the catalyst coated on the monolith

To find the recyclability of the catalyst coated monolith, we carried out a few experiments using catalyst coated monolith (Fig. 2 and Table 5). The first set of the experiment (Fig. 2) was performed repeating the single reaction using the same monolith. The second experiment was carried out was using the same monolith for different substrates (Table 5). As can be seen in Fig. 2, in the first set of experiment, the reaction of 4-iodoanisole (**1c,** 1.28 mmol) and phenylboronic acid (**2a**, 2.56 mmol) was carried out with monolith coated with 30 mg of the catalyst, which accounts for 0.011 mmol of Pd^{2+} ion as an active catalyst. The reaction was repeated 7 times, reusing the same catalyst coated monolith. After each cycle, the monolith coated with the catalyst was removed from the reaction flask, washed with hexane to remove organic compounds, and washed with distilled water to remove solvent and base. After washing the monolith, it was heated in the furnace for about 2 h at 300 °C, cooled to room temperature, and reused for another reaction. The percentage of yields obtained in each cycle has been shown in Fig. 2. This result shows that there is a little loss of catalytic activity after 7 cycles of the same monolith. The total TOF of the reaction is $112.3 \, h^{-1}$.

In the second set of experiments (Table 5), the same catalyst (the same monolith) was recycled for the Suzuki-Miyaura reaction for three different substrates (Table 5). As seen, the reaction of phenylboronic acid (**2a**) was performed with iodobenzene, 4-methoxyiodobenzene, and 5-bromoindole, which afforded the corresponding Suzuki products **3a**, **3c**, and **6 u** in 88, 93, and 71 % yields, respectively.

Table 5
Recycling of catalyst for different substrates[a,b].

3a (88%)   **3c** (93%)   **6u** (71%)
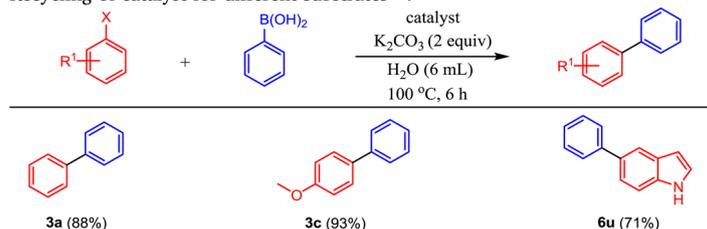
[a] Reaction conditions: Iodobenzene (300 mg, 1.47 mmol), 4-iodoanisole (300 mg, 1.28 mmol), 5-bromoindole (300 mg, 1.53 mmol), phenylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), $Ti_{0.97}Pd_{0.03}O_{1.97}$ (30 mg coated), H_2O (6 mL), 100 °C, 6 h.
[b] isolated yields.
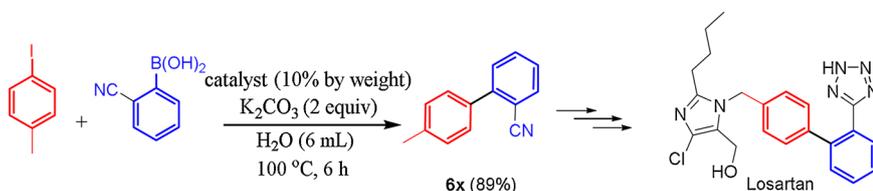
Scheme 3. Synthetic application[a,b].
[a]Reaction conditions: 1-Iodo-4-methylbenzene (0.68 mmol, 150 mg), 2-cyanophenylboronic acid (1.38 mmol, 202.04 mg), $Ti_{0.97}Pd_{0.03}O_{1.97}$ (nanoparticles; 10 wt %, 15 mg), K_2CO_3 (1.38 mmol, 190 mg) and water 6 ml (solvent) was stirred at 100 °C for 6 h. [b] isolated yield.

8. Synthetic application

By knowing the utility of palladium-catalyzed coupling reactions in pharmaceutical, agrochemical, and fine chemical industries, we have showcased the application of the methodology in synthesizing 4′-methyl-1,1′-biphenyl-2-carbonitrile **6x**, which is an intermediate for synthesizing angiostein II antagonists [44], using the developed method (Scheme 3). Thus, by reacting 1-iodo-4-methylbenzene with 2-cyno-phenylboronic acid, under optimal conditions, corresponding coupled product **6x** was obtained in 89 % yield.

9. Experimental

9.1. Synthesis of $Ti_{0.97}Pd_{0.03}O_{1.97}$

The catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$ was prepared using the solution combustion method. $Ti(OC_3H_7)_4$ and $PdCl_2$ were used as starting materials and glycine was employed as a fuel.

$TiO(NO_3)_2$ (2926 mg, 9.89 mmol), which was prepared from $Ti(OC_3H_7)_4$ (2810 mg, 9.89 mmol), $PdCl_2$, (54.8 mg, 0.31 mmol), and glycine (8242 mg, 10.99 mmol) were taken in a 300 ml capacity crystallizing dish. The mixture of compounds was completely dissolved in water (15 mL). The solution was kept in a preheated furnace at 350 °C (30 min). The combustion takes place after the dehydration, and the solid product was left behind. For the structural confirmation, powdered X-ray diffraction has been recorded. The absence of Pd-metal and PdO diffraction lines confirmed that the Pd ions are substituted in TiO_2.

9.2. Procedure for coating of the catalyst over the monolith

The commercially available cordierite monolith was dried in the oven for an hour. 0.05 mol of $Al(NO_3)_3$ and 0.083 mol of glycine were taken in a beaker. About 50–60 mL of water was added to dissolve the solids. A piece of a known mass of monolith was dipped in the solution and kept in the preheated furnace at 350 °C. The combustion takes place, and γ-Al_2O_3 will be coated over monolith. Repeated the procedure for 3–4 times and weighed the monolith each time. The amount of γ-Al_2O_3 was about 2–2.5 % of the monolith.

The same procedure has been repeated for the coating palladium catalyst over a γ-Al_2O_3 layer of the monolith. As mentioned in the synthesis of $Ti_{0.97}Pd_{0.03}O_{1.97}$, the solution of starting materials was made, and a known mass of the monolith is dipped in the solution and kept in a preheated furnace (30 min). Combustion takes place, and the catalyst will be coated over the monolith. The procedure has been repeated to get the desired weight of the catalyst.

9.3. Typical experimental procedure for the palladium-catalyzed suzuki cross-coupling reaction in water

A mixture of aryl halide **1** (0.4 mmol), arylboronic acid **2** (0.8 mmol), $Ti_{0.97}Pd_{0.03}O_{1.97}$ (nanoparticles; 10 wt %), K_2CO_3 (110 mg, 0.8 mmol) in water (2 mL) was stirred at 100 °C for 6 h. After the completion of the reaction, diethyl ether (15 ml x 3 times) was poured into the mixture, washed with water (15 mL), extracted with diethyl ether (3 × 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum; the residue was purified by column chromatography (petroleum ether or petroleum ether/ethyl acetate) to obtain the desired coupled product.

In the recycling of the catalyst, we used the monolith coated with the catalyst in the reaction. After the reaction, the monolith coated with the catalyst was removed from the reaction flask, washed with hexane to remove the organic compound, and again washed with distilled water to remove the solvent and base. After washing the monolith, it was heated in the furnace for about 2 h at 300 °C. Then it was reused for another reaction. The same procedure was repeated after every reaction.

10. Conclusions

In summary, we have developed a highly recyclable, non-toxic, catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$ and demonstrated its utility in the Suzuki-Miyaura cross-coupling reaction. The catalyst $Ti_{0.97}Pd_{0.03}O_{1.97}$, is very efficient and compatible with water and aerobic conditions. The utility of this catalyst has been enhanced in designing a coated catalyst on monolith and shown the coated monolith can be successfully used for several cycles. We have showcased the application of the methodology in synthesizing 4′-methyl-1,1′-biphenyl-2-carbonitrile, which is an intermediate for synthesizing angiostein II antagonists. The salient feature of using these catalysts in Suzuki reaction is, they are non-toxic, easy to handle, and show high TOF as compared to other Pd-catalysts.

Declaration of Competing Interest

The authors declare no competing financial interest.

CRediT authorship contribution statement

Shrikanth Bhat K: Data curation, Methodology. **Veeranjaneyulu Lanke:** Data curation, Methodology. **Jagadeesh Dasappa Prasad:** Writing - review & editing, Supervision. **Kandikere Ramaiah Prabhu:** Conceptualization, Formal analysis, Funding acquisition, Supervision, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.apcata.2020.117516.

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