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Advance Publication on the web November 1, 2017 doi:10.1246/bcsj.20170296

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# Effective Heterogeneous Catalyst for Suzuki-Miyaura Cross-Coupling in Aqueous Media: Melamine Cyanurate Complex Containing Pd Species

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#### Abstract

A melamine cyanurate complex catalyst containing Pd(II) ions (denoted Pd/M-CA) was effective for Suzuki-Miyaura cross-coupling reactions in environmentally benign aqueous media at room temperature. The reaction conditions, such as the type of Pd species in Pd/M-CA, loading amounts of Pd, solvent, and substrate concentration, were investigated for optimization. In the presence of Pd/M-CA under the optimal conditions, crosscoupling reactions of a wide range of structurally diverse aryl halides and arylboronic acids containing functional groups proceeded smoothly to provide the corresponding products in high yields. In addition, the Pd/M-CA could be reused at least 5 times while maintaining high yields. The reduction of Pd(II) ions in Pd/M-CA to Pd(0) by NaBH<sub>4</sub> enhanced the catalytic activity to provide a high turnover number (TON) of 17600 and turnover frequency (TOF) of 880 h<sup>-1</sup>.

#### 1. Introduction

The Suzuki-Miyaura cross-coupling reaction is an important carbon-carbon bond-forming reaction in organic synthesis.<sup>1-7</sup> Its broad use for synthesis of natural products,<sup>8</sup> pharmaceuticls,<sup>9</sup> agrochemicals,<sup>10</sup> and polymers<sup>11</sup> demonstrates its broad impact on the chemical sciences. A transition metal such as Pd often is used as a catalyst because of its efficiency. However, homogeneous catalytic systems usually require cumbersome and costly workup procedures to obtain pure products, and the recovery of precious and toxic metals is timeconsuming. Therefore, development of metal-immobilized heterogeneous catalysts is desirable because they can be separated easily by filtration and reused in subsequent reactions.<sup>12-14</sup> These advantages make heterogeneous catalysts suitable for continuous flow systems in large-scale industrial syntheses. However, heterogeneous catalysts must be prepared by heterogeneous coordination of the supports to the metal ions, causing aggregation of metal ions, which reduces catalytic activity.

Investigation into recovery of precious metals (*e.g.*, Pd, Au, Pt) using organic materials led to the development of highly efficient and selective processes for precious metal recovery based on the complexation of melamine (M) with cyanuric acid (CA).<sup>15</sup> Melamine is a water-soluble ligand that associates with CA through hydrogen bonding, affording a 1:1 supramolecular complex (melamine cyanurate, M-CA).<sup>16,17</sup> The addition of M to an aqueous solution of metal ions results in rapid and highly efficient homogenous coordination between M and metal ions. After coordination, subsequent addition of CA to the metal/M

complex results in precipitation of a metal/M-CA complex, which can be separated by filtration. The system operates efficiently, providing the third largest Pd(II) recovery amount (0.596  $g_{Pd}/g_{M-CA}$ ) among reported adsorbents.<sup>18,19</sup>

To isolate the metals from metal-recovered materials, the organic components generally need to be burned. However, this requires energy and can produce environmental pollutants, and it also produces low-purity metals due to carbonization. Therefore, the development of effective utilization of metalrecovered materials is important from the viewpoints of environment and material sciences. The M-CA complex was selected as a candidate for an effective heterogeneous catalyst because the M-CA system coordinates to the metal ions homogeneously, which means that the metal ions should be uniformly dispersed in the M-CA complex. In addition, the M-CA complex contains multiple hydrogen bonds, in contrast to heterogeneous catalysts formed by covalent bonds. The interatomic distance between M and CA is approximately 2.85-2.96 Å, which is 2 times greater than the general carbon-carbon covalent bond length (1.54 Å).<sup>17</sup> Seiche et al. reported that a rhodium complex with a bidentate ligand, prepared by selfassembly through hydrogen bonding of the two monodentate ligands, catalyzes hydroformylation of functional terminal alkenes with greater catalytic activity and regioselectivity than the rhodium complex with bidentate ligands containing covalent bonds.20 They demonstrated through molecular orbital calculations that the flexible hydrogen bonds of the ligands promoted the catalytic activity and regioselectivity.<sup>21</sup> In addition, M-CA is easily prepared through simple mixing of M and CA and metal ions, eliminating costly and troublesome procedures. These results prompted the use of Pd(II)-recovered M-CA (Pd/M-CA) as a heterogeneous catalyst for effective utilization of metal-recovered material. The present article describes the Pd/M-CA-catalyzed Suzuki-Miyaura coupling of various substrates in environmentally benign aqueous media at room temperature.

#### 2. Experimental

**Materials.** Melamine (M, Tokyo Kasei Kogyo, >98.0%) and cyanuric acid (CA, Tokyo Kasei Kogyo, >98.0%) were commercially available and used as received. Sodium tetrachloropalladate (II) (Na<sub>2</sub>PdCl<sub>4</sub>, Tokyo Kasei Kogyo, >98.0%), palladium acetate (II) [Pd(OAc)<sub>2</sub>, Wako Pure Chemical, 46.5–49.5%], tris(dibenzylideneacetone)dipalladium (0) (ALDRICH, 97.0%) were purchased commercially and used as received. Iodobenzene (Tokyo Kasei Kogyo, >98.0%), 1-

iodo-4-nitrobenzene (Tokyo Kasei Kogyo, >99.0%), 4iodoanisole (Tokyo Kasei Kogyo, >99.0%), bromobenzene (Tokyo Kasei Kogyo, >99.0%), 4-bromonitrobenzene (Wako Pure Chemical, 98.0%), and 4-bromotoluene (Wako Pure Chemical, 98.0%) were purchased commercially and used as received. Phenylboronic acid (Tokyo Kasei Kogyo, >97.0%), 4tolylboronic acid (Aldrich, 97.0%), 2-tolylboronic acid (Aldrich, 97.0%), and 4-(trifluoromethyl)phenylboronic acid (Tokyo Kasei Kogyo, >97.0%) were purchased commercially and used as received. Sodium acetate (Wako Pure Chemical, >98.5%), potassium acetate (Wako Pure Chemical, >97.0%), sodium hydrogen carbonate (Wako Pure Chemical, >98.5%), potassium hydrogen carbonate (Wako Pure Chemical, >99.5%), sodium carbonate (Kanto Chemical, >99.8%), potassium carbonate (Kanto Chemical, >99.5%), cesium carbonate (Kanto Chemical, >98.0%), sodium hydroxide (Wako Pure Chemical, >97.0%), and potassium hydroxide (Wako Pure Chemical, >85.0%) were purchased commercially available and used as received. Undecane (Tokyo Kasei Kogyo, >99.5%) was purchased commercially and used as received. Ethanol (Wako Pure Chemical, 99.5%) was distilled before use.

**Instruments.** Gas chromatographic analysis was conducted using a Shimadzu GC-2014ATF/SPL instrument equipped with an ULBON-HR-1 capillary column and flame ionization detector (FID), with helium as the carrier gas. Flame atomic absorption spectrometry was conducted using a Hitachi polarized Zeeman atomic absorption spectroscopy (XPS) spectra were obtained using a Kratos AXIS-NOVA instrument. Scanning electron microscopy (SEM) was performed using a Hitachi S3000N instrument at an acceleration voltage of 1.5 kV. Energy dispersive X-ray analysis (EDX/SEM) measurements were obtained with a Horiba EX-200K/Hitachi S3000N instrument.

**Preparation of Pd/M-CA.** Melamine (23.8 mg, 0.189 mmol) was added to a 0.200 mM aqueous solution of sodium tetrachloropalladate(II) (Na<sub>2</sub>PdCl<sub>4</sub>, 400 mL), and the mixture was stirred at room temperature for 1 h. Subsequent addition of a 10.4 mM aqueous solution of cyanuric acid (20.0 mL) to the mixture resulted in instant precipitation. The precipitate was separated by filtration, and the concentration of Pd(II) in the filtrate was measured by atomic absorption spectrometry (AAS). The loading amount was calculated based on the following equation:

Loading amount  $(g_{Pd}/g_{M-CA}) =$  atomic weight (g/mol) of metal  $\times$  loading amount (mol) / weight of melamine and cyanuric acid used (g)

Anal. Found for Pd/M-CA: C, 27.99; H, 3.73; N, 48.43

Suzuki-Miyaura cross-coupling reaction catalyzed by Pd/M-CA complex (typical procedure). Pd/M-CA (7.10 mg, 0.500 mol% to iodobenzene), phenylboronic acid (146 mg, 1.20 mmol), K<sub>2</sub>CO<sub>3</sub> (415 mg, 3.00 mmol), 1/1 (v/v) H<sub>2</sub>O/ethanol solvent (3.00 mL), iodobenzene (0.110 mL, 1.00 mmol), and undecane (0.300 mL) were added to a test tube under nitrogen atmosphere. After stirring for 20 h at room temperature, the Pd/M-CA was separated by filtration, and diethyl ether (30 mL) was added to the filtrate. The filtrate was washed with water (10 mL) three times. The organic phase was analyzed by GC (internal standard; undecane), which indicated an 80% yield of the product.

#### 3. Results and Discussion

**Preparation of Pd/M-CA complex.** The Pd/M-CA catalyst was initially prepared by adding melamine (M, 0.189 mmol) to an aqueous solution of sodium tetrachloropalladate(II) (Na<sub>2</sub>PdCl<sub>4</sub>, 400 mL), and the mixture stirred at room temperature. Subsequent addition of 10.4 mM

aqueous cyanuric acid (CA, 20 mL) to the mixture resulted in instant precipitation. The precipitate was separated by filtration, and the concentration of Pd(II) in the filtrate was measured by atomic absorption spectrometry (AAS), resulting in a load amount of 80 mg<sub>Pd</sub>/g<sub>M-CA</sub>. Elemental analysis of the complex showed that the ratio of M to CA was 1:1. Based on these results and the amount of Pd(II) loaded, as determined by AAS, the ratio of Pd/M/CA was 1/5/5. To examine the coordination site, IR spectra of Pd/M-CA with different loading amounts (48 mgPd/gM-CA; 81 mgPd/M-CA; 122 mg<sub>Pd</sub>/g<sub>M-CA</sub>) were obtained (see Supporting Information, Table S1). The absorption peak corresponding to C=N (1537 cm<sup>-1</sup>) shifted to a higher wavenumber, while those corresponding to C=O (1782 cm<sup>-1</sup>) and NH<sub>2</sub> (1741 cm<sup>-1</sup>) did not change position significantly. These results indicate that the imine group in M coordinated predominantly to Pd(II). This tendency is consistent with the nucleophilicity of the imine group in M, which is greater than those of the primary amine group in M and the carbonyl group in CA. The XPS analysis of the Pd/M-CA complex showed Pd3d5/2 and Pd3d<sub>3/2</sub> peaks at 337.7 and 343.0 eV, respectively, which were assigned to Pd(II) species (Figure 1a).<sup>22,23</sup> The EDX/SEM analysis showed the presence of Pd and Cl species (Figure 1b). The Cl species originated from Na<sub>2</sub>PdCl<sub>4</sub>; therefore, Pd(II)Cl<sub>2</sub> is contained in the complex. The SEM images showed a needle-type structure, suggesting a high surface area (Fig. 1c). In addition, EDX/SEM mapping images showed that the Pd species (red dots) were uniformly dispersed on the M-CA, indicating the potential high catalytic activity of Pd/M-CA (Fig. 1d). Therefore, we examined the utility of Pd/M-CA as a heterogeneous catalyst for Suzuki-Miyaura cross-coupling, which is a favorable and versatile method for carbon-carbon bond formation.



Figure 1. (a) XPS spectrum, (b) EDX spectrum, (c) SEM image, and (d) EDX/SEM mapping of Pd (red dos) of Pd/M-CA complex (loading amount =  $81 \text{ mg}_{Pd}/\text{g}_{M-CA}$ ).

**Suzuki-Miyaura cross-coupling reaction catalyzed with Pd/M-CA complex catalyst.** To examine the efficacy of the Pd/M-CA catalysts, the Suzuki-Miyaura crosscoupling reaction of iodobenzene and phenylboronic acid catalyzed with Pd/M-CA (0.5 mol% of Pd to iodobenzene) was carried out in the presence of K<sub>2</sub>CO<sub>3</sub> in H<sub>2</sub>O/EtOH. After reaction, the catalyst was separated by filtration and the yield was monitored by GC because the loss of workup is overlooked, which gave biphenyl in 43% yield (GC yield) (Scheme 1, Table 1, entry 1). Investigation of other reaction conditions, such as the type of palladium species in the M-CA complex, loading amounts of Pd, the base selected, and solvent used, was carried out to determine the optimal conditions.

At first, the catalytic activity of Pd/M-CA was compared with that of M-CA containing Pd(OAc)<sub>2</sub>, which is widely used as a catalyst for the Suzuki-Miyaura reaction.<sup>1-7</sup> The reaction of iodobenzene and phenylboronic acid catalyzed by Pd(OAc)<sub>2</sub>/M-CA was conducted under the above conditions, but gave a lower yield than that catalyzed by Pd/M-CA (entry 2). Examination of the Pd(OAc)2/M-CA complex using SEM revealed that the complex was spherical (Fig. S1), whereas Pd/M-CA was needle-shaped. These results indicate that the surface area of Pd(OAc)<sub>2</sub>/M-CA is smaller than that of Pd/M-CA, resulting in the lower yield.<sup>24</sup> Next, the effect of loading amount of Pd in Na<sub>2</sub>PdCl<sub>4</sub>/M-CA was examined. The yield of the product increased with loading amount (entries 3-6). A decrease in loading amount increased the amounts of M and CA in the Pd/M-CA complex, which disrupted progress of the reaction. From this table, a loading amount of 81 mgPd/gM-CA was selected for the subsequent experiments.

#### Scheme 1



**Table 1.** Effect of Pd species type and Pd loading amount on Suzuki-Miyaura reaction.<sup>a</sup>

| entry | Pd species                        | loading amount<br>(mgpd/gm-ca) | yield (%) <sup>b)</sup> |
|-------|-----------------------------------|--------------------------------|-------------------------|
| 1     | Na <sub>2</sub> PdCl <sub>4</sub> | 46                             | 43                      |
| 2     | Pd(OAc) <sub>2</sub>              | 35                             | 28                      |
| 3     | Na <sub>2</sub> PdCl <sub>4</sub> | 20                             | 37                      |
| 4     | Na <sub>2</sub> PdCl <sub>4</sub> | 46                             | 43                      |
| 5     | Na <sub>2</sub> PdCl <sub>4</sub> | 81                             | 66                      |
| 6     | Na <sub>2</sub> PdCl <sub>4</sub> | 121                            | 66                      |

<sup>*a*</sup>/Conditions: [iodobenzene]<sub>0</sub> = 0.33 M; [phenylboronic acid]<sub>0</sub> = 0.36 M; Pd/M-CA = 0.5 mol% of Pd to iodobenzene;  $[K_2CO_3]_0 = 1.0$  M; H<sub>2</sub>O/EtOH (v/v = 3/2); room temperature; reaction time = 20 h. <sup>*b*</sup>) Determined by GC analysis (internal standard: undecane).

Next, an appropriate base was identified for the Pd/M-CA system for the Suzuki-Miyaura cross-coupling reaction (Table 2). Nine widely available bases that have been used in Suzuki-Miyaura cross-coupling were considered. Reactions of iodobenzene and phenylboronic acid in the presence of weak bases, such as NaOAc and KOAc, and in the presence of strong bases, such as NaOH and KOH, gave low product yields (entries 1, 2 and 8, 9, respectively). In the Suzuki-Miyaura reaction, the base acts as an accelerator of transmetalation with phenylboronic acid by nucleophilic addition of the base to the Pd(II)-aryl halide complex. Since NaOAc and KOAc are weak bases, nucleophilic addition of acetate ion did not proceed effectively. In the presence of a

strong base such as NaOH and KOH, nucleophilic addition of hydroxide ion to phenylboronic acid also occurred, resulting in the formation of the phenylborate that was unreactive in transmetalation<sup>25</sup> (reaction mechanism for Suzuki-Miyaura coupling is shown in Scheme S1). The base  $K_2CO_3$  was chosen for the present system (entry 6).

**Table 2.** Effect of base on Suzuki-Miyaura reaction.<sup>*a*</sup>

| entry | base                            | yield $(\%)^{b}$ | entry | base                           | yield (%) <sup>b)</sup> |
|-------|---------------------------------|------------------|-------|--------------------------------|-------------------------|
| 1     | NaOAc                           | 23               | 6     | K <sub>2</sub> CO <sub>3</sub> | 66                      |
| 2     | KOAc                            | 21               | 7     | $Cs_2CO_3$                     | 36                      |
| 3     | NaHCO <sub>3</sub>              | 46               | 8     | NaOH                           | 20                      |
| 4     | KHCO <sub>3</sub>               | 50               | 9     | КОН                            | 16                      |
| 5     | Na <sub>2</sub> CO <sub>3</sub> | 31               |       |                                |                         |

<sup>*a*</sup>/Conditions: [iodobenzene]<sub>0</sub> = 0.33 M; [phenylboronic acid]<sub>0</sub> = 0.36 M; Pd/M-CA = 0.5 mol% of Pd to iodobenzene;  $[K_2CO_3]_0 = 1.0$  M; H<sub>2</sub>O/EtOH (v/v = 3/2); room temperature; reaction time = 20 h. <sup>*b*</sup>) Determined by GC analysis (internal standard: undecane).

Finally, the effects of the H<sub>2</sub>O/EtOH ratio and reaction substrate concentration were examined (Table 3). When the reaction was conducted at various H<sub>2</sub>O/EtOH mixing ratios (entries 1-7), a ratio of 1/1 (v/v) H<sub>2</sub>O/EtOH gave the best results (entry 4) because H<sub>2</sub>O is a good solvent for K<sub>2</sub>CO<sub>3</sub> and EtOH promoted solubility of the substrates and the fast reduction of Pd(II) to Pd(0).<sup>26-28</sup> Reaction with 1/1 (v/v) H<sub>2</sub>O/EtOH at various concentrations of the substrate (entries 4 and 8-10), revealed that the best results were obtained when the substrate concentration was 0.33 M (entry 4). Therefore, the optimal conditions were: loading amount on Pd/M-CA: 81 mg<sub>Pd</sub>/g<sub>M-CA</sub>; base: K<sub>2</sub>CO<sub>3</sub>; H<sub>2</sub>O/EtOH (v/v) = 1/1; concentration of substrate: 0.33 M.

**Table 3.** Effect of  $H_2O/EtOH$  (v/v) mixing ratio and substrate concentration.<sup>*a*)</sup>

| entry | H <sub>2</sub> O/EtOH (v/v) | [iodobenzene]0 | yield $(\%)^{b}$ |
|-------|-----------------------------|----------------|------------------|
| 1     | H <sub>2</sub> O            | 0.33           | 44               |
| 2     | 4/1                         | 0.33           | 66               |
| 3     | 3/2                         | 0.33           | 66               |
| 4     | 1/1                         | 0.33           | 80               |
| 5     | 2/3                         | 0.33           | 74               |
| 6     | 1/4                         | 0.33           | 77               |
| 7     | EtOH                        | 0.33           | 47               |
| 8     | 1/1                         | 1.0            | 49               |
| 9     | 1/1                         | 0.50           | 74               |
| 10    | 1/1                         | 0.25           | 49               |

Conditions: [phenylboronic acid]<sub>0</sub> = 1.1 equivalent to [iodobenzene]<sub>0</sub>; Pd/M-CA = 0.5 mol% of Pd to iodobenzene;  $[K_2CO_3]_0 = 1.0$  M; room temperature; reaction time = 20 h.  $^{b)}$  Determined by GC analysis (internal standard: undecane).

To expand the scope of the reaction substrate, various aryl halides and arylboronic acids were used for Suzuki-Miyaura coupling. The results are summarized in Tables 4 and 5. The effect of the substitution group for aryl iodide was summarized in Table 4. Reactions of aryl iodides containing electron-withdrawing and -donating groups, such as -OMe and -NO2, with phenylboronic acid yielded the corresponding products in high yields (entries 2 and 3). When aryl bromides were used instead of aryl iodides, product yield decreased because the halogen-carbon bond energy of bromobenzene was stronger than that of iodobenzene, hindering progress of oxidative addition of Pd(0) to bromobenzene (entries 4-6). Contrary to expectation, the yield of the reaction of aryl bromide containing electron-donating group (-OMe) is higher than that of aryl bromide having electron-withdrawing group (-NO<sub>2</sub>) (entries 5 and 6). This is due to that 4bromonitrobenzene is insoluble in EtOH, resulting in the heterogeneous progress of reaction. Although the reaction was conducted in 1/1 (v/v) H<sub>2</sub>O/THF homogeneous system, the product was not obtained, suggesting the hindering of reduction of Pd(II) to Pd(0) without EtOH. Increasing the reaction temperature to 80 °C produced the greatest reactivity of the all reagents and the coupling products were obtained in high yields (entries 8-10).

#### Scheme 2



**Table 4.** Suzuki-Miyaura reaction of aromatic halides and phenylboronic acid catalyzed with Pd/M-CA.<sup>*a*</sup>

| entry | Х  | R      | Pd (mol%) | T (°C)           | time (h) | yield (%) <sup>b)</sup> |
|-------|----|--------|-----------|------------------|----------|-------------------------|
| 1     | Ι  | Н      | 1.2       | rt               | 20       | 98                      |
| 2     | Ι  | OMe    | 1.2       | rt               | 20       | 92                      |
| 3     | Ι  | $NO_2$ | 1.2       | rt               | 20       | quant.                  |
| 4     | Br | Н      | 2.5       | rt               | 72       | 76                      |
| 5     | Br | Me     | 2.5       | rt               | 72       | 50                      |
| 6     | Br | $NO_2$ | 2.5       | rt               | 72       | 34                      |
| 7     | Br | $NO_2$ | 2.5       | rt               | 72       | 0 <sup>c)</sup>         |
| 8     | Br | Н      | 2.5       | 80 <sup>d)</sup> | 80       | quant.                  |
| 9     | Br | Me     | 2.5       | 80 <sup>d</sup>  | 80       | quant.                  |
| 10    | Br | $NO_2$ | 2.5       | 80 <sup>d)</sup> | 80       | 86                      |

Conditions: [iodobenzene]<sub>0</sub> = 0.33 M; [phenylboronic acid]<sub>0</sub> = 0.36 M;  $[K_2CO_3]_0 = 1.0 \text{ M}$ ;  $H_2O/EtOH (v/v = 1/1)$ . <sup>b)</sup> Determined by GC analysis (internal standard: undecane). <sup>C)</sup>  $H_2O/THF (v/v = 1/1)$  was used as a solvent. <sup>d)</sup>80 °C is the temperature of oil bath.

The results also demonstrated that the Pd/M-CA catalytic system could tolerate arylboronic acids with various substituents (Scheme 3, Table 5). Reaction of iodobenzene and 4-tolylboronic acid under similar conditions gave the product in quantitative yield (entry 1). In contrast, arylboronic acid containing an electron-withdrawing group (-CF<sub>3</sub>) exhibited lower reactivity (entry 2) because the electron density of the carbon bonded with boron decreased, hindering progress of nucleophilic addition of the carbon to Pd(II) during the transmetalation. Increasing the reaction temperature also was effective (entry 3). Substitution of methyl groups at the ortho position of arylboronic acid did not disrupt the reaction progress (entry 4).

#### Scheme 3



**Table 5.** Suzuki-Miyaura reaction of iodobenzene and various boronic acids catalyzed with Pd/M-CA.<sup>*a*</sup>

| entry | Х                 | T (°C) | yield (%) <sup>b)</sup> |
|-------|-------------------|--------|-------------------------|
| 1     | 4-Me              | rt     | quant.                  |
| 2     | 4-CF <sub>3</sub> | rt     | 15                      |
| 3     | 4-CF <sub>3</sub> | 80     | quant.                  |
| 4     | 2-Me              | rt     | quant.                  |

Conditions: [iodobenzene]<sub>0</sub> = 0.33 M; [phenylboronic acid]<sub>0</sub> = 0.36 M; Pd/M-CA = 1.2 mol% of Pd to iodobenzene;  $[K_2CO_3]_0 = 1.0$  M; H<sub>2</sub>O/EtOH (v/v = 1/1); reaction time = 20 h. <sup>b)</sup> Determined by GC analysis (internal standard: undecane).

In the reaction of iodobenzene and phenylboronic acid, a control experiment was conducted to confirm that the insoluble catalyst promotes the reaction under heterogeneous conditions. The reaction was performed under identical conditions as that in Table 3, entry 4 [1/1 (v/v) H<sub>2</sub>O/EtOH, 0.33 M iodobenzene, 0.36 M phenylboronic acid, 0.5 mol% of Pd to iodobenzene in Pd/M-CA, 1.0 M K<sub>2</sub>CO<sub>3</sub>, rt, 20 h reaction time]. After 1 h reaction (63% yield of product), the catalyst was subjected to membrane filtration (pore size = 0.45  $\mu$ m), and the filtrate stirred for additional 20 h. Gas chromatography showed that reaction did not proceed further, indicating that the reaction proceeded under heterogeneous conditions. In addition, AAS showed that only 0.05% of the original catalyst loading leached. To investigate the economy of the reaction, the reusability of Pd/M-CA was examined for Suzuki-Miyaura coupling of iodobenzene and phenylboronic acid in 3/2 (v/v) H<sub>2</sub>O/EtOH at room temperature for 20 h (Figure 2). After the first reaction, which gave 97% yield of the corresponding product, Pd/M-CA was recovered by filtration. The recovered Pd/M-CA was washed successively with tetrahydrofuran, water, and methanol, and dried in vacuo. The catalyst was subjected to 5 more reaction cycles under similar conditions, which gave the product in high yields,

indicating the reusability of Pd/M-CA. The slight decrease in the yield was due to loss of catalyst during workup.



**Figure 2.** Reusability of Pd/M-CA in Suzuki-Miyaura reaction of iodobenzene and phenyboronic acid. Conditions:  $[iodobenzene]_0 = 0.33$  M;  $[phenylboronic acid]_0 = 0.36$  M; Pd/M-CA = 0.5 mol% of Pd to iodobenzene;  $[K_2CO_3]_0 = 1.0$  M; H<sub>2</sub>O/EtOH (v/v = 1/1); room temperature; reaction time = 20 h. <sup>*a*</sup>/Determined by GC analysis (internal standard: undecane).

To further increase the catalytic activity of Pd/M-CA, the Pd(II) in Pd/M-CA was reduced to Pd(0) by NaBH<sub>4</sub>, because Pd(0) is the catalytically active species in the Suzuki-Miyaura cross-coupling reaction. The Pd/M-CA complexes were added to a dispersed aqueous solution of NaBH4 (4 equivalents to Pd) and stirred at room temperature. After reduction, the reduced Pd/M-CA [Pd(0)/M-CA] was separated by filtration and dried in vacuo. The XPS analysis confirmed the reduction of Pd(II) to Pd(0) (Fig. S2). Reaction of iodobenzene and phenylboronic acid catalyzed with Pd(0)/M-CA (0.005 mol% to iodobenzene) was performed in 1/1 (v/v) H<sub>2</sub>O/EtOH at room temperature to afford the product in 88% yield. The turnover number (TON) and turnover frequency (TOF) of the catalyst was 17600 and 880 h<sup>-1</sup>, respectively, demonstrating that the catalytic activity was improved by Pd(0)/M-CA over Pd(II)/M-CA. Examination of the conditions for enhancing catalytic activity of Pd(0)/M-CA, such as reduction and reaction conditions, is now under progress.

#### 4. Conclusions

In conclusion, a Pd/M-CA complex catalyzed Suzuki-Miyaura cross-coupling in an environmentally benign solvent at ambient temperature with good activity. The generality of this catalyst under these conditions was demonstrated for a wide range of structurally diverse aryl halides and arylboronic acid with many functional groups. The reduction of Pd(II) ions to Pd(0) in Pd/M-CA by NaBH<sub>4</sub> enhanced the catalytic activity to afford a high TON of 17600 and TOF 880 h<sup>-1</sup>. This research provides a novel approach to the effective utilization of metalrecovered materials for heterogeneous organometallic catalysts. Investigations to enhance the catalytic activity of Pd(0)/M-CA is now under investigation.

#### Acknowledgements

The authors would like to thank Professor Takeshi Yamanobe (Division of Molecular Science, Faculty of Science and Technology, Gunma University) for helpful suggestion. This work was financially supported by JSPS KAKENHI 17K059646.

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# **Graphical Abstract**

<Title>

Effective Heterogeneous Catalyst for Suzuki-Miyaura Cross-Coupling in Aqueous Media: Melamine Cyanurate Complex Containing Pd Species

<Authors' names>

Daisuke Nagai and Hiroki Goto

### <Summary>

A melamine cyanurate complex catalyst containing Pd(II) ions (denoted Pd/M-CA) was effective for Suzuki-Miyaura crosscoupling reactions in environmentally benign aqueous media at room temperature. The generality of this catalyst was demonstrated for a wide range of structurally diverse aryl halides and arylboronic acids with functional groups. Further, the Pd/M-CA could be reused at least 5 times while maintaining high yields.

<Diagram>

