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## ARTICLE TYPE

**Pd(OAc)<sub>2</sub> in WERSA: A novel green catalytic system for Suzuki–Miyaura cross-coupling reactions at room temperature**

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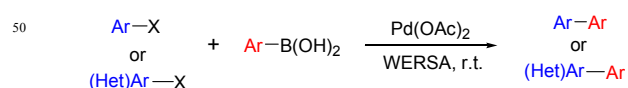
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A recyclable/reusable Pd(OAc)<sub>2</sub> catalysed Suzuki–Miyaura cross-coupling reaction condition in neat “Water Extract of Rice Straw Ash” (WERSA) at room temperature was developed. This is a ligand/base/promoter/additive/organic media free protocol.

Nowadays, the development of greener, efficient and simple reaction methodologies has become a key driving force of synthetic organic chemistry in industry as well as in academic world.<sup>1</sup> It is very important to note that the attempt to find environmentally sustainable methods in modern chemical synthesis led to an enormous increase of research activities in the field of green chemistry. Palladium catalyzed Suzuki–Miyaura (S–M) cross-coupling<sup>2,3</sup> reactions have been recognized as a very dominant and indispensable method for biaryl synthesis because of the inherent advantages of organoboron reagent, such as its air and moisture stability, good functional group tolerance, low toxicity as well as its wide availability.<sup>4</sup> Over the 30 years of research history on S–M cross-coupling reaction, predominantly the palladium-based catalysts have been the most frequently investigated ones.<sup>5</sup> Nowadays, many S–M reactions can be carried out under very mild reaction conditions and in a short reaction time, within only several minutes.<sup>6</sup> Recent literature report reveals that S–M reactions in the absence of ligands, additives/promoters and organic co-solvents are very much limited by the substrate solubility and their reactivity in aqueous media and therefore, “greening-up” the Suzuki–Miyaura cross-coupling reaction is a very urgent and challenging issue for chemists in modern era.<sup>7</sup> In this regard, the design of a catalyst system using truly nontoxic and biodegradable/recyclable medium is a very challenging and promising direction for establishing greener S–M cross-coupling reactions.

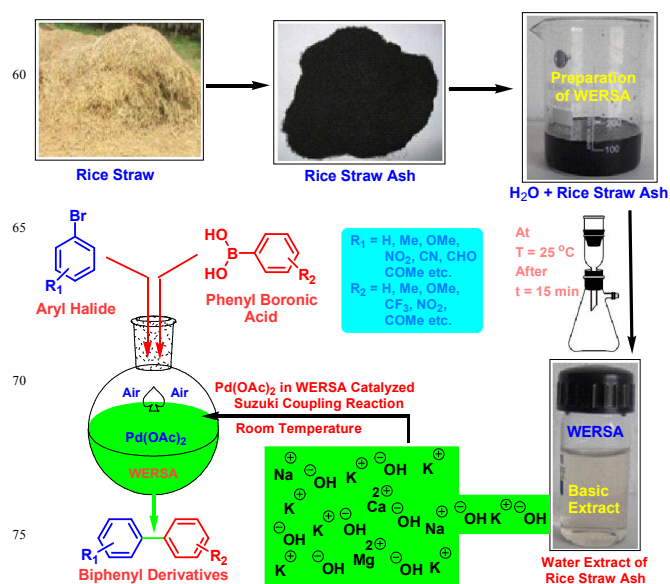
We present here a novel and highly green protocol of S–M cross-couplings carried out in neat water extract of rice straw ash (WERSA). Herein, we demonstrate that a range of substrates, including heterocycles, participate in the Pd(OAc)<sub>2</sub> catalyzed S–M cross-coupling reaction in WERSA and we thought that this method would be highly attractive for industrial applications in near future (Scheme 1). Rice straw is a highly abundant natural organic synthesis will catch tremendous interest from the point of environmental issue. From the practical point of view, these conditions are very appealing, especially considering the use of

an inexpensive and environmentally friendly natural feedstock extract without purification or characterization.



Scheme 1

We have prepared the WERSA by burning the rice straw into ashes. After that the ash was suspended in distilled water in a glass beaker and stirred for few minutes at room temperature. The mixture was then filtered and the filtrate was termed as WERSA (Figure 1).<sup>8</sup>

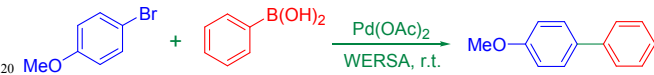


**Figure 1:** Preparation of WERSA and their catalytic activity for the Suzuki–Miyaura cross-coupling reaction.

To evaluate the efficiency of this system for the S–M cross-coupling reaction, we chose 4-bromoanisole and phenylboronic acid as model substrates. The S–M reaction proceeds very smoothly in the Pd(OAc)<sub>2</sub>–WERSA system without the use of any ligand/base/promoter/additive and organic media and therefore, undoubtedly, this result is very promising and encouraging from the practical point of view. All these advantages make the Pd(OAc)<sub>2</sub>–WERSA system a competitive catalyst and thus can be a clean and highly convenient alternative

for other industrially important methods. At the beginning, we checked the catalyst loading and time on the S–M cross-coupling reaction and best results have been obtained using 1 mol% Pd(OAc)<sub>2</sub> in WERSA at room temperature. In order to demonstrate the effect of WERSA in this reaction, we performed a reaction of 4-bromoanisole and phenylboronic acid in neat H<sub>2</sub>O at room temperature using only Pd(OAc)<sub>2</sub>, but no reaction progress was observed and the starting materials were fully recovered (Table 1, entry 6). Similarly, to ascertain the requirement of Pd(OAc)<sub>2</sub> in this cross-coupling reaction, a controlled experiment was performed by carrying out the reaction of 4-bromoanisole with phenylboronic acid in presence of neat WERSA without using Pd(OAc)<sub>2</sub>, but no cross-coupling product was observed (Table 1, entry 7).

**Table 1.** Effects of catalyst quantity, temperature and time in the Suzuki–Miyaura reaction of 4-bromoanisole with phenylboronic acid in WERSA at room temperature<sup>a</sup>



Entry	Pd(OAc) <sub>2</sub> (mol%)	Time (h)	Yield <sup>b</sup> (%)
1	0.02	2 h	10
2	0.1	2 h	30
3	0.25	2 h	35
4	0.5	2 h	50
5	1.0	2 h	88
6	1.0	12 h	No reaction <sup>c</sup>
7	–	12 h	No reaction <sup>d</sup>

<sup>a</sup> Reaction conditions: 4-bromoanisole (1 mmol), phenylboronic acid (1.2 mmol), Pd(OAc)<sub>2</sub> (1 mol%) in WERSA (3 mL) at room temperature.

<sup>b</sup> Isolated yields.

<sup>c</sup> Without WERSA

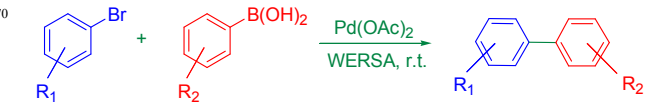
<sup>d</sup> Without Pd(OAc)<sub>2</sub>

With the optimized catalyst loading and reaction time in hand, we investigated the catalytic activity of Pd(OAc)<sub>2</sub>–WERSA for various substrates. All the reactions were carried out at room temperature in air and aqueous extract of rice straw ash as reaction medium and the results are summarized in Table 2. A set of aryl halides with various phenylboronic acids was used in order to test the activity and tolerance of the catalytic system to various functional groups. As shown in Table 2, all reactions afforded the corresponding coupling products in moderate to high yields irrespective of the presence of electron donating groups or electron withdrawing groups in the substrates (Table 2, entries 1–22). For aryl halides bearing an electron-donating group, yields up to 89% were obtained in a very shorter reaction time (Table 2, entries 8 & 11). The catalytic performance is excellent considering the fact that these reactions are carried out at room temperature and require such short reaction times. It is noteworthy that in the case of aryl halides bearing electron-withdrawing groups, a maximum of 67% yield was obtained after 4 h (Table 2, entry 12). However, longer reaction (12 h) times did not lead to further conversion to product. In our study the scope of the reaction was successfully expanded to a range of aryl halides. Furthermore, to test the limits of compatibility of different functionalities using our protocol, various boronic acids containing both electron withdrawing and electron donating groups were also tested for activity and the results obtained are

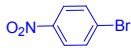
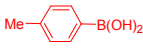
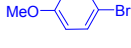
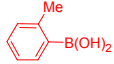

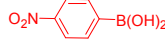

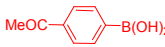

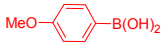

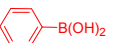
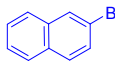


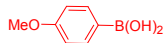

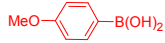

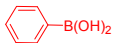
discussed in Table 2 (Table 2, entries 8–11, 13–17 & 19–21).

This interesting finding led us to the exploration of using WERSA in the coupling of heteroaryl halides. Therefore, we further tested the catalytic performances for the couplings of arylboronic acids with heteroaryl halides. Heterocyclic moieties are of great importance because they are generally present in pharmaceutically active compounds.<sup>9</sup> Despite their importance, the cross-coupling reaction of hetero aryl halides remains a challenge, especially at room temperature. Interestingly, heterocyclic systems also show identical reactivity towards aryl boronic acids under this catalytic condition (Table 2, entries 17 & 18) with cross-coupling yields ranging from 50 to 80%. The capability of this system to achieve cross-coupling of aryl/heteroaryl halides without using any ligand, base, promoters/additives and organic media in air is noteworthy.<sup>10</sup>

**Table 2.** Substrate scope for Suzuki–Miyaura cross-coupling reaction using Pd(OAc)<sub>2</sub> in WERSA at room temperature<sup>a</sup>



Entry	ArX	ArB(OH) <sub>2</sub>	Time (h)	Yield <sup>b</sup> (%)
1			2	88
2			2	88
3			4	55
4			4	60
5			2	55
6			4	60
7			4	60
8			2	89
9			2	88
10			2	70
11			2	89
12			4	67

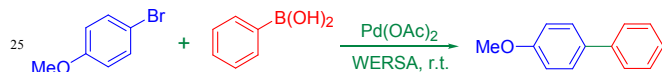
13			4	45
14			2	65
15			2	70
16			2	45
17			4	80
18			4	50
19			4	80
20			3	90
21			4	85
22			2	85

<sup>a</sup> Reaction conditions: aryl/heteroaryl halide (1 mmol), phenylboronic acid (1.2 mmol), Pd(OAc)<sub>2</sub> (1 mol%) in WERSA (3 mL) at room temperature.

<sup>b</sup> Isolated yields.

From the green chemistry point of view, recycling is a major concern, especially in metal catalysis. The recyclability of Pd(OAc)<sub>2</sub>-WERSA catalyst system was investigated with consecutive Suzuki–Miyaura couplings of 4-bromoanisole and phenylboronic acid. After the first reaction cycle diethyl ether was added to the system followed by centrifugation, the clearly separated diethyl ether layer has been removed from the system and dried to get the desired crude product. After washing and drying, the recovered catalyst system was directly used for the next reaction cycle followed by the addition of fresh reactants to that system. Identical results were obtained for the consecutive runs up to 6<sup>th</sup> cycle under our reaction conditions; yields are slightly lower in 5<sup>th</sup> and 6<sup>th</sup> cycles though. The results obtained in our experiment confirmed that it was possible to recycle and reuse the catalytic medium after extraction of products with diethyl ether for at least up to six times without losing significant catalytic activity (Table 3, entries 1–6).

**Table 3.** Recyclability of the catalytic system<sup>a</sup>



Entry	Run	Time (h)	Yield <sup>b</sup> (%)
1	1 <sup>st</sup>	2	88
2	2 <sup>nd</sup>	2	86
3	3 <sup>rd</sup>	2	86
4	4 <sup>th</sup>	2	80
5	5 <sup>th</sup>	2.5	74
6	6 <sup>th</sup>	3.5	65

<sup>a</sup> Reaction conditions: 4-bromoanisole (1 mmol), phenylboronic acid (1.2 mmol), Pd(OAc)<sub>2</sub> (1 mol%) in WERSA (3 mL) at room temperature.

<sup>b</sup> Isolated yields.

The reactivity of this catalytic medium is currently not well understood. However, chemical analysis reports of rice straw ash have revealed that it primarily consist of oxides of SiO<sub>2</sub> (74.31%), Al<sub>2</sub>O<sub>3</sub> (1.40%), Fe<sub>2</sub>O<sub>3</sub> (0.73%), TiO<sub>2</sub> (0.02%), CaO (1.61%), MgO (1.89%), K<sub>2</sub>O (11.30%), Na<sub>2</sub>O (1.85%), P<sub>2</sub>O<sub>5</sub> (2.65%) *etc.*<sup>11</sup> It is believed that alkali oxides of potassium, sodium, magnesium and calcium react with water to produce hydroxides of these metals. Therefore, we assume that these alkali metal hydroxides (KOH as major constituent) are acting as internal base here to facilitate the Suzuki–Miyaura cross-coupling reactions.

As a contribution towards a greener chemistry, we applied and studied this highly abundant natural feedstock extract as an alternative green media for the S–M cross-coupling reactions and found very exciting results. The capability of this system [Pd(OAc)<sub>2</sub>-WERSA] to achieve cross-coupling of activated aryl halides at room temperature is noteworthy. It is an easily prepared and effective catalytic system for S–M cross-coupling reactions, working at room temperature without the use of ligand, base, promoter/additive and organic media. The method greatly enhances the synthetic utility of biaryl compounds and adds a new dimension to the chemistry of cross-coupling reactions. Further work is in progress to explore the full scope of this useful natural feedstock extract and its synthetic applications.

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- 8 **Method of preparation of WERSA:** 10 g of rice straw ash was suspended in 100 mL of distilled water in a beaker and stirred it well for 15 min at room temperature. The mixture was then filtered through sintered glass crucible and the filtrate was used as WERSA.
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- 10 **General experimental procedure for Suzuki reaction:** A mixture of aryl/heteroaryl halide (1 mmol), arylboronic acid (1.2 mmol) and Pd(OAc)<sub>2</sub> (1 mol%) in WERSA (3 mL) was stirred for the indicated time (Table 2) at room temperature. Afterward, the reaction solution was extracted three times with diethyl ether (3 × 10 mL). The products were purified by column chromatography over silica gel using *n*-hexane/ethyl acetate (9:1 v/v) to get the desired cross-coupling products. The products were characterized by IR and NMR spectroscopy methods.
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