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ARTICLE TYPE

A Protocol for Ligand Free Suzuki–Miyaura Cross-Coupling Reactions in WEB at Room Temperature

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A highly efficient green protocol for palladium acetate-catalysed ligand-free Suzuki–Miyaura cross-coupling reactions in neat ‘Water Extract of Banana (WEB)’ was developed. This method offers a mild, efficient and highly economic alternative to the existing protocols since the reaction proceeds in WEB at room temperature in air at very short reaction times (5–90 min) under ‘ligand/ external base/ external promoters/ organic media’ free condition.

The biaryl moiety is a common structural framework found mainly in pharmaceuticals, agrochemicals and biologically active natural compounds.¹ The Suzuki–Miyaura (SM) cross-coupling reaction of aryl halides with arylboronic acids is one of the most powerful carbon–carbon bond forming methodologies for constructing biaryl compounds in organic chemistry.² Among cross-coupling processes, SM reaction is particularly widely used, due to attractive attributes such as the commercial availability, the air and water stability, functional-group compatibility and the nontoxic nature of boronic acids. Generally, the palladium catalyst is a unique choice for the Suzuki–Miyaura reaction for the reason that it shows excellent catalytic activity and stability. Over the past few years, extensive efforts have been devoted toward the development of new ligands with the ability to provide excellent levels of catalytic generality and activity in palladium-catalyzed cross-coupling processes.³ A survey of the recent chemical literature revealed that many examples for Nickel⁴ and Copper⁵ complexes as catalysts exist for this cross-coupling reactions, but their inherent scopes and reaction efficiencies were found to be limited. In this context, to get highly satisfactory results, the properties of many catalysts had to be tuned using some unique ligands, such as phosphine complexes. However, phosphine ligands are sensitive to air and moisture with conversion to phosphine oxide.⁶ Again, the synthetic procedure for preparing these Pd-ligand complexes is quite complicated because the synthesis of the ligands requires time consuming multi-step sequences and thus it is expensive.⁷ In addition, most of the Pd-ligand complexes usually take place under an inert atmosphere or harsh conditions and also have a limited substrate scope. Keeping all these factors in mind researchers have modified those initially utilized palladium catalyst by using bulky or electron rich phosphine ligands,⁸ nitrogen containing ligands,⁹ N-heterocyclic carbenes,¹⁰ oximes,¹¹ and imines.¹² In general, these catalysts are air and moisture sensitive and are often difficult to prepare. Meanwhile, recent

studies demonstrated that, for the reduction of chemical waste, the number of synthetic steps and safer as well as more efficient reaction conditions- in short to fulfil green chemistry protocols, one of the most important aspects is the application of environmentally friendly solvents such as water, ionic-liquids or supercritical carbon dioxide. Water, in contrast to common organic reaction media, is particularly favourable as it is cheap, non-flammable, nontoxic and readily available and significance to environmentally benign processes.¹³ However, most efficient protocols for SM cross-coupling reactions in aqueous medium suffer from high catalyst loadings,¹⁴ elevated reaction temperatures,¹⁵ addition of promoters/additives,¹⁶ complex workup procedures or require the addition of hazardous organic solvents. Consequently, there is a need to design a very simple, highly economic, commercially feasible as well as environmentally sustainable route of synthesis of biaryls in order to meet its growing demand in diverse sectors.

Herein, we present a highly novel protocol with broad applicability regarding the range of substrates and functional group tolerance for SM cross-coupling reaction. In this communication, WEB was chosen as reaction media without using any external promoters, external base, phosphine ligands and organic co-solvents or biphasic media. To the best of our knowledge, this is the first report of base/ligand/organic solvent free environment friendly protocol for Suzuki cross-coupling reactions carried out in WEB at room temperature. Here, we have prepared the aqueous extract of banana (Scientific Name: *Musa balbisiana* Colla; Family: Musaceae; Species: *Musa balbisiana*) by first drying the banana peels followed by burning to ash. Water was added to the ash, mixed well and then filtered. The filtered is termed as WEB here (Figure 1).¹⁷ The resulting system shows superior catalytic activity in comparison to a variety of reported catalyst systems. There is no doubt that WEB has very great potential in green chemical processes from the economic and environmental points of view in the near future. The main objectives of this protocol are to develop an efficient synthetic process for the facile conversion of Suzuki–Miyaura reaction in oxygen atmosphere at room temperature. Furthermore, the present method developed for the Suzuki–Miyaura reaction offers many advantages including high conversion, short duration, highly economic and the involvement of non-toxic green substrate *etc.* The operational simplicity of the process without the need of special handling is also noteworthy. This new Suzuki

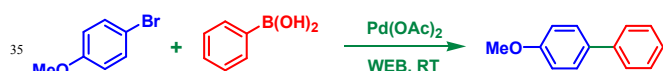
variant can be accomplished with excellent yields for a broad range of arylhalides and arylboronic acids.



Fig. 1

The efficiency of the catalytic system was evaluated by the coupling of 4-bromoanisole and phenylboronic acid in WEB in the absence of ligand or additives (Table 1, Entries 1-6).¹⁸ To optimize the reaction conditions, the effect of the amount of Pd(OAc)₂ on the coupling reaction was studied. From the results in table 1, we can see that an excellent yields of the desired product was obtained in the presence of 1 mol% Pd(OAc)₂ for 5 min (Table 1, Entry 1). Even with 0.5 mol% of Pd(OAc)₂, furnished the cross-coupled product in 99% yields within a very short reaction time (Table 1, Entry 2). Decreasing the catalyst loading to 0.25 mol% gave a respectable 93% yields of the product in 30 min (Table 1, Entry 3). Pd(OAc)₂ in the amount of 0.1 mol% was found to be sufficient to give a moderate conversion with a 72% isolated yields of the product after 30 min (Table 1, Entry 4). A further decrease in catalyst loading (to 0.02 mol%) resulted in poor conversion even after increasing the reaction time up to 24 h (Table 1 Entry 5). No further increase in yields was observed on increasing the reaction time. In the absence of palladium acetate, the reaction did not proceed at all in WEB (Table 1, Entry 6). Pd(OAc)₂ in WEB catalyzed the reaction very efficiently producing excellent yields of products at room temperature in a very short reaction time. After exploring a wide array of conditions, 0.5 mol% Pd(OAc)₂ in WEB was found to be optimal (Table 1, Entry 2) for SM reaction.

Table 1. Effects of catalyst quantity in the Suzuki–Miyaura reaction of 4-bromoanisole with phenylboronic acid in water extract of banana (WEB) at room temperature^a



Entry	Catalyst (mol%) Pd(OAc) ₂	Time	Yield ^b (%)
1	1	5 min	99
2	0.5	5 min	99
3	0.25	30 min	93
4	0.1	30 min	72
5	0.02	24 h	50
6	-	24 h	No reaction

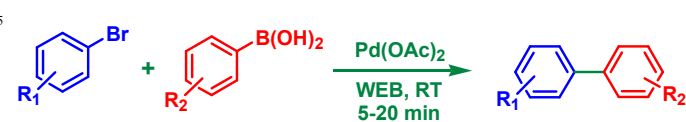
^a Reaction conditions: arylhalide (1 mmol), arylboronic acid (1.2 mmol), catalyst, in WEB (3 mL) at room temperature.

^b Isolated yields.

To explore the scope of this reaction, a series of aryl bromides was allowed to react with arylboronic acids under identical

conditions. Both the electron-rich and the electron-deficient aryl bromides showed an excellent reactivity and furnished the products in high yields in short reaction times (Table 2, Entries 1-7) at room temperature. It is worth noting that the catalytic system was tolerant to a broad range of functional groups, such as –OMe, –CH₃, –NO₂, –CN, –CHO and –COMe. Interestingly, both the electron-rich and the electron-deficient arylboronic acids delivered the products with high yields at room temperature in aerobic condition (Table 2, Entries 4, 5 & 8). We are quite satisfied to see that the formation of undesired homo-coupling product was very negligible under this reaction condition. The ability to operate for a range of substrates at low catalyst loading is of great importance in metal-catalyzed processes. Thus, our present result is quite significant as the desired biaryls could be achieved at room temperature using neat aqueous extract of banana as a reaction medium and with relatively low catalyst loading (0.5 mol%) without using any additives, external base, ligand and organic co-solvents.

Table 2. Pd(OAc)₂ and WEB catalysed Suzuki–Miyaura cross-coupling reaction of aryl halides with aryl boronic acids at room temperature^a



Entry	R ₁	R ₂	Time (min)	Yield ^b (%)
1	4-OMe	H	5	99
2	3-OMe	H	10	98
3	4-Me	H	10	99
4	4-Me	4-OMe	10	99
5	4-Me	4-CF ₃	15	97
6	4-NO ₂	H	10	99
7	4-CN	H	10	98
8	H	4-OMe	10	99
9	4-CHO	H	15	96
10	3-CHO	H	15	95
11	2-CHO	H	20	92
12	4-COMe	H	15	97

^a Reaction conditions: arylhalide (1 mmol), arylboronic acid (1.2 mmol), Pd(OAc)₂ (0.5 mol%), in WEB (3 mL) at room temperature.

^b Isolated yields.

To check the efficiency of our catalytic system, we next employed some heterocyclic systems as Suzuki–Miyaura coupling partners (Table 3, Entries 1-3) and we found that heterocyclic systems also worked efficiently under this catalytic system.

In order to demonstrate the practical importance and wide application of the catalytic system consisting Pd(OAc)₂/WEB, it is essential to show the efficient recycling of the catalyst system. 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 but the yields obtained in successive steps were low (60% yields in 1st recycle). The lowering of yields is due to the solubility of Pd(II) or Pd(0) species in diethyl ether which is evidenced by the colour change of the ether fraction from colourless to little black.


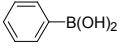

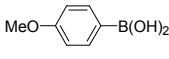

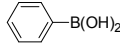
We extended our methodology to two more banana species [Banana peels, trunk and rhizome of 1. Dwarf Cavendish (Species: *Musa acuminata*) and 2. China (Manohar); *Musa*

sepientum] and we observed identical reactivity towards Suzuki-Miyaura cross coupling reactions.

The dramatic acceleration of SM reaction in WEB is currently not well understood. Literature reports reveal that banana peels contain potassium, sodium, carbonate and chloride as major constituents along with a host of other trace elements.¹⁹ Therefore, it is believed that carbonates of sodium and potassium of banana peels act as base here and chlorides of sodium and potassium act as promoters for SM reactions.

Table 3. Pd(OAc)₂ and WEB catalysed Suzuki–Miyaura cross-coupling reaction of (hetero)aryl halides with aryl boronic acids at room temperature^a



Entry	Ar-Br	Ar-B(OH) ₂	Time (min)	Yield ^b (%)
1			60	88
2			60	90
3			90	86

^a Reaction conditions: (hetero)aryl halide (1 mmol), arylboronic acid (1.2 mmol), Pd(OAc)₂ (0.5 mol%), in WEB (3 mL) at room temperature.

^b Isolated yields.

In summary, we have demonstrated the efficient Pd(OAc)₂-WEB catalyzed Suzuki–Miyaura cross-coupling of aryl halides and phenylboronic acids at room temperature in absence of organic co-solvents as well as other additives such as external base, external promoters, ligands *etc.* The scope of these reactions is broad with respect to both coupling partners, and we expect the methodology presented will find great utility in academic and industrial applications in near future.

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Notes and references:

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- Method of preparation of WEB:** 5 g of banana ash was suspended in 100 mL of distilled water in a beaker and stirred it well for 10 min.

The mixture was then filtered through sintered glass crucible and the filtrate was used as WEB.

- 18 **General experimental procedure for Suzuki reaction:** A mixture of
aryl halide (1 mmol), arylboronic acid (1.2 mmol) and Pd(OAc)₂ (0.5
5 mol%) in WEB (3 mL) was stirred for the indicated time at room
temperature. Afterward, the reaction solution was extracted four
times with diethyl ether (4 × 10 mL). The products were purified by
column chromatography over silica gel using n-hexane/ethyl acetate
10 (9:1 v/v) to get the desired coupling products. The products were
characterized by ¹H-NMR and GC-MS.
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Graphical Abstract:

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A highly efficient protocol for palladium acetate-catalysed ligand-free Suzuki–Miyaura cross-coupling reactions in neat 'Water Extract of Banana (WEB)' was developed. This method offers a mild, efficient and highly economic alternative to the existing protocols since the reaction proceeds in WEB at room temperature in air at very short reaction times (5-90 min) under 'ligand/ external base/ external promoters/ organic media' free condition.

