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Suzuki–Miyaura cross-couplings of arenediazonium tetrafluoroborate salts with arylboronic acids catalyzed by aluminium hydroxide-supported palladium nanoparticles†

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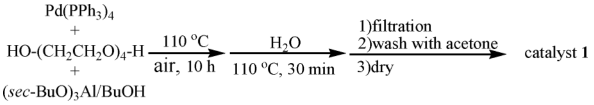
Suzuki–Miyaura cross-couplings of arenediazonium salts with arylboronic acids catalyzed by highly active aluminium hydroxide-supported palladium nanoparticles catalyst have been investigated for the first time. The reactions are performed at 25 °C in MeOH without any base and ligand to afford biaryls in good to excellent yields under non-anhydrous and non-degassed conditions.

The palladium-catalyzed Suzuki–Miyaura cross-coupling reactions have evolved as a reliable method[1] to synthesize biaryls, which are widely present in numerous classes of organic compounds, such as advanced materials, ligands and molecules of medicinal interest.[2] A great number of studies have been devoted to this cross-coupling reaction since the pioneering work from Suzuki and Miyaura[3], the vast majority of which involve the use of halogenated or sulfonated electrophiles.[4] Recently, some attention has been focused on the reaction that incorporates arenediazonium tetrafluoroborate salts as aryl electrophilic components because they can be easily synthesized from the corresponding amine with high yield[5] and are more reactive than the corresponding aryl halides in the palladium-catalyzed Suzuki–Miyaura reaction.[6] In addition, numerous kinds of palladium catalysts have been extensively investigated and some new catalysts are gradually being developed which have enabled this transformation to be applied with a broad substrate scope, a wide functional group tolerance, and low catalyst loadings.[6b,7,8] Among these palladium catalysts, nanoparticles catalysts are more promising, efficient and practical because of their advantages and have made some progress, showing enhanced reactivity with low catalyst loading under mild conditions. At the same time, tremendous attention and efforts have been devoted to the potential applications of them in various coupling reactions. Despite these creative efforts and significant progress, the design and synthesis of new nanoparticles palladium catalysts that are cheaper and more efficient and the development of new methods that are more effective remain considerable challenges and are highly desirable. Herein, we wish to disclose in this paper an efficient, and highly active Suzuki cross-coupling reaction of aryldiazonium salts with arylboronic acids catalyzed by heterogeneous palladium nanoparticles catalyst which was prepared by a simple one-pot three-component method with as low as 0.3 mol% Pd under base-free, non-anhydrous and non-degassed conditions in methanol at 25 °C.

We initiated our optimization studies by selecting benzenediazonium tetrafluoroborate and phenylboronic acid as partners for the Suzuki–Miyaura cross-coupling in the presence of the aluminium hydroxide-supported palladium catalyst **1** which was prepared and purified according to Min Serk Kwon's reported procedure (Scheme 1).[9] In the course of the preparation of this catalyst **1**, 110 °C was used as the reaction temperature instead of 120 °C (in the literature).[10] Firstly, the catalytic activity of the catalyst **1** was tested, and the results are summarized in Table 4 (see ESI†). High yields were observed for the coupling reaction when using the catalyst **1** for 4 h, whereas in the presence of the catalyst **2**, 26% yield was obtained after 24 h. Only 31% yield of biphenyl was isolated after 32 h if Pd $(PPh_3)_4$ was used as the catalyst. The catalyst **1** proved to be exceptionally active for Suzuki Miyaura reaction.



Scheme 1

Subsequently, the effect of catalyst loading on the cross-coupling reaction was investigated under air atmosphere at room temperature and the results are shown in Table 1. The yields were improved apparently and gradually with the increase of the catalyst (Table 1, entries 1–3). 92% of yield was obtained when as low as 0.3 mol% Pd was utilized (Table 1, entry 3). Unfortunately, 0.4 mol% gave a moderate 72% yield (Table 1, entry 4). The investigation of some solvents usually used in Suzuki–Miyaura cross-coupling, such as MeOH, EtOH, *i*-PrOH, H_2O, THF, and so on, revealed that the yields were significantly influenced by the sorts of the solvents and the results clearly highlighted the beneficial effect of MeOH as the best solvent (Table 1, entry 3).[11] In sharp contrast, EtOH and *i*-PrOH gave no product (Table 1, entries 5 and 6). The impact

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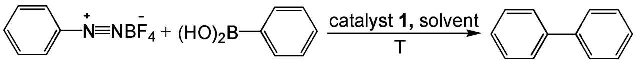
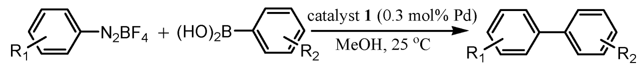
Table 1 Optimization of the cross-coupling reaction with catalyst **1**[a]

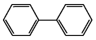
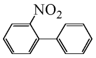
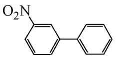
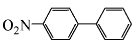
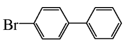
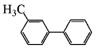
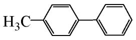
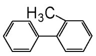
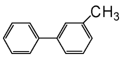
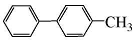
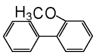
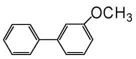
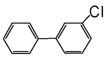
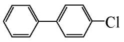
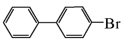
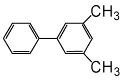
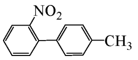
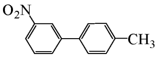
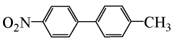
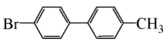
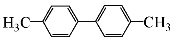


Entry	Pd (mol%)	Solvent	Solvent dose (mL)	T/°C	Equiv. of phenylboronic acid	t (h)	Yield (%)[b]
1	0.1	MeOH	1.8	25	1.2	5.5	56
2	0.2	MeOH	1.8	25	1.2	4	69
3	0.3	MeOH	1.8	25	1.2	4	92
4	0.4	MeOH	1.8	25	1.2	4	72
5	0.3	EtOH	1.8	25	1.2	4	ND
6	0.3	*i*-PrOH	1.8	25	1.2	4	ND
7	0.3	H_2O	1.8	25	1.2	4	ND
8	0.3	THF	1.8	25	1.2	4	trace
9	0.3	MeOH	1.5	25	1.2	4	70
10	0.3	MeOH	2	25	1.2	4	75
11	0.3	MeOH	1.8	13	1.2	10	85
12	0.3	MeOH	1.8	35	1.2	1	62
13	0.3	MeOH	1.8	25	1.1	2.2	55
14	0.3	MeOH	1.8	25	1.3	2.2	75
15[c]	0.3	MeOH	1.8	25	1.2	4	trace

[a] Unless otherwise specified, all reactions were performed on a 0.3 mmol scale of benzenediazonium tetrafluoroborate. [b] Isolated yield. [c] Reaction was performed without benzenediazonium.

Table 2 Cross-couplings of arenediazonium tetrafluoroborate salts and arylboronic acids catalyzed by palladium nanoparticles catalyst **1**[a]



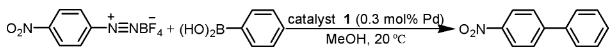
Entry	R_1	R_2	t (h)	Product	Yield (%)[b]
1	H	H	4		92
2	2-NO_2	H	11		94[c]
3	3-NO_2	H	3		92
4	4-NO_2	H	6		97[c]
5	4-Br	H	3.5		73
6	3-CH_3	H	3.5		45
7	4-CH_3	H	20 (7)[d]		73 (72)[d]
8[f]	H	2-CH_3	4		69
9[f]	H	3-CH_3	4		88
10	H	4-CH_3	4		74
11[f]	H	2-OCH_3	4		97
12	H	3-OCH_3	4		67
13[f]	H	3-Cl	4		80
14	H	4-Cl	4		85
15	H	4-Br	4		78
16[f]	H	3,5-$(CH_3)_2$	4		92
17	2-NO_2	4-CH_3	4.5		79
18	3-NO_2	4-CH_3	20		82[e]
19	4-NO_2	4-CH_3	12		73[e]
20	4-Br	4-CH_3	4		78[c]
21	4-CH_3	4-CH_3	10		70

[a] Reaction conditions: arenediazonium tetrafluoroborate (0.3 mmol), arylboronic acid (1.2 equiv, 0.36 mmol), catalyst (0.3 mol% Pd, 11.2 mg), MeOH (1.8 mL), 25 °C. [b] Isolated yield. [c] Reaction was conducted at 20 °C (See ref. 13). [d] 0.5 mol% Pd catalyst was used. [e] Reaction was conducted at 0 °C. [f] 0.4 mol% Pd catalyst and 2 mL MeOH were used.

of the solvent dosage on the yield was also studied. From that work, we noticed that the reaction was best conducted with a solvent dosage of 1.8 mL (Table 1, entry 3).[12] The yield dropped drastically to 70% and 75% when the solvent dosages were 1.5 mL and 2 mL, respectively (Table 1, entries 9 and 10). Temperature obviously influenced the reaction yield too. 25 °C was found to be suitable temperature (Table 1, entry 3). Decreasing or elevating the reaction temperature failed to increase the yield and an unwanted by-product formed at higher temperature (Table 1, entries 11–12). The amount of phenylboronic acid apparently affected the reaction yield. It was preferable to use 1.2 equiv. of phenylboronic acid with the yield of 92% (Table 1, entry 3). Lowering and increasing its quantity to 1.1 equiv. and 1.3 equiv. could sharply decrease the yields to 55% and 75%, respectively (Table 1, entries 13 and 14). After all these extensive experiments, it was discovered that the optimal conditions employed 0.3 mol% Pd and 1.2 equiv. of phenylboronic acid in 1.8 mL MeOH at 25 °C for 4 h, which provided biphenyl in 92% isolated yield. Note that biphenyl that may come from homocoupling of phenylboronic acid has been eliminated as supported by the fact that no biphenyl product is observed under the same experimental conditions except for the absence of benzenediazonium tetrafluoroborate. (Table 1, entry 15).

Next, a variety of arenediazonium tetrafluoroborate salts and arylboronic acids were examined for the cross-coupling reactions using the optimized reaction conditions. As shown in Table 2, whatever the electronic and steric nature of the cross-coupling partners, most of the reactions gave biaryl products in good to excellent yields under mild conditions with as low as 0.3 mol% Pd. With regard to a series of salts, phenylboronic acid supplied better results than 4-Me-phenylboronic acid (Table 2, entries 1–5, 7 *vs.* 10, 17–21). As for phenylboronic acid and 4-Me-phenylboronic acid, the nitro-based diazonium salts gave good to excellent yields, better than the methyl-based diazonium salts (Table 2, entries 2–4 and 17–19 *vs.* 7, 21). Using a variety of arylboronic acids, benzene-

Table 3 Recycling and reuse of the catalyst **1**



Entry	Catalyst	Diazonium salts (mmol)	*t* (h)	Yield[a](%)	Recovery of the catalyst **1** (%)
1	Fresh	1.20	6	97	105[b]
2	First Reuse	0.86	22	81	78
3	Second Reuse	0.30	28	80	58

[a] Isolated yield. [b] Ref. 15.

diazonium tetrafluoroborate afforded the corresponding products with good yields (Table 2, entries 8–16). To our delight, the cross-coupling reactions of 2-nitrobenzenediazonium salt proceeded smoothly and showed good yields (Table 2, entries 2 and 17). It is also important to point out that good chemoselectivity was achieved in the coupling reactions using 4-bromophenyldiazonium tetrafluoroborate (Table 2, entries 5 and 20), suggesting potential utility in additional synthetic chemistry.

We further explored the catalyst recycling through the Suzuki–Miyaura cross-coupling of 3-nitrobenzenediazonium tetrafluoroborate and phenylboronic acid (Table 3).[14] The catalyst could be recovered and reused after separation, washing with CH_2Cl_2, and drying under vacuum under the same reaction conditions. Although it could be recycled and reused three times without a significant reduction in the yield, the catalyst activity obviously decreased after the first, second and third consecutive cycles, respectively. The significant decrease of the catalytic activity was probably due to some loss of the nanocomposite catalysts during the recovery process which was caused by the decrease of the recovery percent of this catalyst.

In summary, we have investigated for the first time the Suzuki–Miyaura cross-couplings of arenediazonium tetrafluoroborate salts and arylboronic acids catalyzed by this very highly active and easily synthesized palladium catalyst entrapped in aluminium hydroxide with as low as 0.3 mol% Pd. It is a practical, efficient and general protocol for cross-coupling with the advantages of good substrate generality, ease of experimental operation and mild conditions without inert-gas protection and any additional additives (base and ligand). More importantly, this palladium catalyst shows good to excellent yields towards a series of arenediazonium tetrafluoroborate salts.

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10 The boiling point of 1-butanol is 116 °C–118 °C. The reaction temperature could only reach 110 °C at the reflux under the local atmospheric pressure.

11 Among the solvents investigated, alcoholic solvents were the best. Especially, methanol was the most efficient in terms of yield and rate for the cross-coupling, which might be related to the solubility of arenediazonium tetrafluoroborate salts. Because EtOH and *i*-PrOH provided the worst solubility, EtOH could only provide the product with 61% yield and *i*-PrOH could still give no product after 28 h.

12 The amount of MeOH was related to the solubility of arenediazonium tetrafluoroborate salts. Although it was best that arenediazonium tetrafluoroborate salts were dissolved fully, which facilitated the proceeding of the reaction, too much MeOH would play a negative effect on the yield.

13 Side reactions would occur and the yields of the corresponding products decreased obviously when these reactions were performed at 25 °C, although the reaction time were shortened. The corresponding yields at 25 °C were 71%, 61%, 54%, respectively. For more details, see *Table 5* in the Supporting Information†.

14 For more details of a typical recycling procedure, see Supporting Information†.

15 It was confirmed that the results of the subsequent recovery experiments were best if the first recovery of the catalyst **1** was well beyond 100% and the solvent was used as little as possible when the catalyst **1** was recovered.