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Impregnated palladium on magnetite, a new catalyst for the ligand-free cross-coupling Suzuki–Miyaura reaction

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ABSTRACT

A new catalyst for the cross-coupling Suzuki–Miyaura reaction is reported. The impregnated palladium on magnetite catalyst is very easy to prepare using the standard impregnation methodology. This catalyst avoids the use of any type of expensive and difficult handle organic ligand, showing excellent yields, under mild reaction conditions, for the classical formation of biaryl compounds. The catalyst is very easy to remove from the reaction medium, only by using a simple magnet, and it could be re-used up to three times with only a slightly decrease of the chemical yield.

1. Introduction

Over the past years transition-metal-catalyzed cross-coupling reactions have matured to get an impressive level of generality and complexity.[1] They have been used in building bio-active molecules as drugs and agrochemicals, in the developing of new generation of ingeniously-designed organic materials with novel electronic, optical or mechanical properties, likely to play a significant role in the burgeoning area of nanotechnology.

Among the various transition-metal-catalyzed cross-coupling reactions known today, the so-called Suzuki–Miyaura reaction is one of the most applied and valuable, owing to its exceptionally broad functional group tolerance, as well as the use of readily available, non-toxic, and air- and water-stable reagents.[2] One of its most important drawback is the presence of homogenous palladium species on the final product, as well as the use of expensive, difficult to prepare and handle ligands, such as phosphanes or carbenes, and additives, such as organic ammonium salts. To avoid the first drawback, different heterogeneous systems have been proposed.[2g,3] However, many of them use different grafted-ligands to anchor the palladium atoms, maintaining the second drawback.

On the other hand, the old impregnation protocol has been used very recently in the preparation of magnetite catalysts[4] derived from titanium,[5] manganese,[6] iron,[7] cobalt,[8] copper,[9] ruthenium,[10] rhodium,[11] palladium,[11,12] and platinum[11] derivatives. However, their applications in organic chemistry have been quite limited. For instance, the magnetically separable impregnated palladium on magnetite system has catalyzed successfully the carbonylative Sonogashira coupling reaction between aryliodides, ethynylarenes and carbon monoxide.[12a] The presence of a chiral heterocyclic carbene ligand permitted the enantioselective α-arylation of α-substituted ketones using the above nanoparticles with enantioselectivities up to 61%.[12c] The reduction of palladium with hydrogen permitted its use in the selective dehalogenation of organic compounds from aqueous wastes.[12b]

Here, we report a simple, mild, and ligand-free protocol to perform the Suzuki–Miyaura reaction using the aforementioned impregnated palladium on magnetite catalysts.[13]

2. Results and discussion

2.1. Arylation process

In order to optimize the reaction conditions we studied the reaction between 1-iodo-4-methoxybenzene (**1a**) and phenylboronic acid **2a** to give the corresponding compound **3a**, as depicted in Table 1. The reaction was performed using an excess of boronic acid and equimolecular amounts of potassium carbonate. The formation of product **3a** was not detected after 5 days of reaction using DMF as

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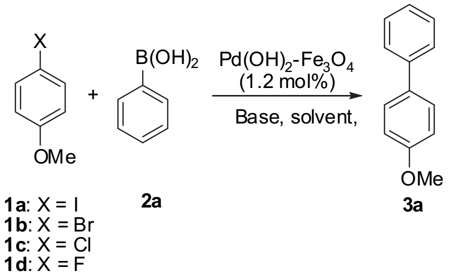
Table 1
Reaction condition optimization [a]



Entry	X	Solvent	Base (mol %)	T (°C)	t (h)	Yield (%)
1[b]	I	DMF	K_2CO_3 (120)	130	120	0
2	I	DMF	K_2CO_3 (120)	130	72	65
3[c]	I	DMF	K_2CO_3 (120)	130	72	50
4	I	—	K_2CO_3 (120)	130	144	64
5	I	PhMe	K_2CO_3 (120)	130	24	71
6	I	Dioxane	K_2CO_3 (120)	130	24	70
7	I	MeCN	K_2CO_3 (120)	130	24	68
8	I	PhMe	Na_2CO_3 (120)	130	0.5	89
9	I	PhMe	KOH (120)	130	4	65
10	I	PhMe	^{t}BuOK (120)	130	4	70
11	I	PhMe	Na_2CO_3 (50)	130	2	48
12	I	PhMe	Na_2CO_3 (300)	130	0.25	99
13	I	PhMe	Na_2CO_3 (300)	150	0.25	99
14	I	PhMe	Na_2CO_3 (300)	100	0.25	95
15	I	PhMe	Na_2CO_3 (300)	75	0.25	57
16	I	PhMe	Na_2CO_3 (300)	25	0.25	0
17[d]	I	PhMe	Na_2CO_3 (300)	130	3	5
18[e]	I	PhMe	Na_2CO_3 (300)	130	0.25	98
19	Br	PhMe	Na_2CO_3 (300)	130	72	50
20	Cl	PhMe	Na_2CO_3 (300)	130	72	0
21	F	PhMe	Na_2CO_3 (300)	130	72	0

[a] Reaction carried out using compounds **1** (1 mmol) and **2a** (3 mmol) in 2 mL of solvent, unless otherwise stated.
[b] Reaction performed without catalyst.
[c] Compound **2a** (1.2 mmol) was used.
[d] Reaction carried out using 0.24 mol % of catalyst.
[e] Reaction carried out using 2.4 mol % of catalyst.

solvent at 130 °C. However, the addition of the catalyst permitted to obtain the compound **3a** after only 3 days with a reasonable yield, with the decrease of the boronic reagent having a slightly negative impact on the yield (compare entries 1–3 in Table 1).

After these initial experiments, the role of the solvent was tested, finding practically no influence on the yield, except in the absence of solvent (Table 1, entries 4–7). Once toluene was chosen as possible solvent for the reaction, the nature of base was evaluated. The reaction using sodium carbonate gave the expected compound **3a** in only 30 min, meanwhile stronger bases, such as potassium hydroxide or *tert*-butoxide gave worse results (entries 9 and 10 in Table 1). However, the amount of base is a critic parameter since its increase up to 300 mol % (amount of boronic acid), permitted to obtain the expected compound in practically quantitative yield in only 15 min, with its decrease reducing the yield (compare entries 8, 11, and 12 in Table 1). The temperature of the reaction is also an important parameter in order to obtain compound **3a**, with temperatures higher than 100 °C producing practically quantitative yields (Table 1, entries 12–16), with the reaction failing at room temperature.

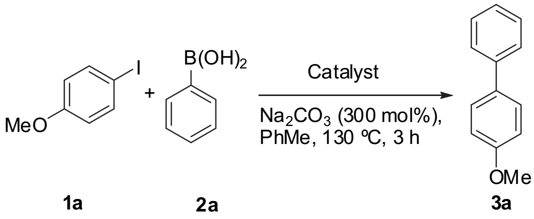
Whereas a 5% of compound **3a** was detected after 3 h when the reaction was performed using only 0.24 mol % of the heterogeneous palladium catalyst, the increase of this amount up to 2.4 mol % did not have any significant positive impact on the previous results (compare entries 12, 17, and 18 in Table 1).

The nature of the halogen atom in reagent **1** was also tested (Table 1, entries 19–21). The reaction gave a worse result using bromobenzene (**1b**) and failed after 3 days for the case of the corresponding chlorinated and fluorinated reagent (**1c**,**d**).

Once the optimal reaction conditions were established, the problem of recycling was faced. The catalyst recovered by a magnet from the reaction described in the entry 12 of Table 1 was washed with toluene and re-used under the same reaction conditions, obtaining the expected product **3a** in 82% yield. In the third re-use the yield was 72%, indicating that there is a small decrease in the activity of catalyst, probably due to the adsorption of Na_2CO_3 and boronic salts on the surface of catalyst, which could be easily seen, as well as the phenomena of leaching (0.9% of initial amount of palladium on the magnetite surface was detected in the reaction solution by ICP-MS analysis). In order to exclude that the heterogeneous catalyst was only an initial source for the homogeneous palladium, a new reaction was carried out with the remaining solution obtained after performing the standard reaction between compounds **1a** and **2a** and isolation of magnetic catalyst. Phenylboronic acid (**2a**), 1-iodonaphthalene, and Na_2CO_3 were added to the above solution and the reaction was run for 4 days, with the expected compound **3f** being not detected.

Other impregnated metals on magnetite were also tested to evaluate their activity in comparison with palladium (entry 12 in Table 1). The reaction with only the magnetite support gave the expected product **3a** in modest 20% yield after 3 h (Table 2, entry 1).

Table 2
Optimization of the reaction catalyst[a]



Entry	Catalyst (mol %)	Yield (%)
1	Fe_3O_4 (22.0)	20
2	$Co(OH)_2/Fe_3O_4$ (1.4)	5
3	$Ni(OH)_2/Fe_3O_4$ (1.2)	65[b]
4	$Cu(OH)_2/Fe_3O_4$ (1.3)	12
5	$Ru(OH)_3/Fe_3O_4$ (1.3)	30

[a] Reaction carried out using compounds **1a** (1 mmol) and **2a** (3 mmol) in 2 mL of toluene.
[b] Reaction performed during 15 min.

Other impregnated catalysts, such as cobalt, copper or ruthenium derivatives did not improve the obtained results with the support. However, the impregnated nickel on magnetite showed a higher activity compared to the related catalysts (compare entries 2–5 in Table 2), but lower than the aforementioned palladium derivative.

Once the best conditions were found for this Suzuki–Miyaura process (entry 12 in Table 1), the same protocol was applied to other substrates in order to study the scope of the reaction (Table 3). The reaction gave excellent results for electron-rich four-substituted iodobenzenes independently of the electronic nature of boronic acid, with the yield being lower only in the case of thienyl derivative (compare entries 1–5 in Table 3).

The results were excellent in the case of using unsubstituted aromatic iodides, independently of the aromatic size (compare entries 6–8 in Table 3), with the reaction being a little slower for electron-withdrawing substituted aromatic boronic acids. The reaction could be performed with similar trends in the case of using electron-withdrawing substituted aromatic iodides (Table 3, entries 13–13), even in the case of using an iodopyridine derivative (Table 3, entry 14).