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Short Communication

Facile and efficient Suzuki–Miyaura coupling reaction of aryl halides catalyzed by $Pd_2(dba)_3$ in ionic liquid/supercritical carbon dioxide biphasic system

Hong Bo Wang [a], Yu-Lin Hu [a,b,*], De-Jiang Li [a]

[a] College of Materials and Chemical Engineering, China Three Gorges University, Yichang 443002, People's Republic of China
[b] Key Laboratory of Inorganic Nonmetallic Crystalline and Energy Conversion Materials, China Three Gorges University, Yichang 443002, People's Republic of China

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ABSTRACT

A general and efficient catalytic system for $Pd_2(dba)_3$-catalyzed ligand-free Suzuki cross-coupling reactions was developed. The cross-couplings of a wide range of aryl halides with various arylboronic acids were feasible under mild conditions in environmental friendly [hmim]NTf_2/supercritical CO_2 biphasic system employing K_2CO_3 as a base, which provided in good to high yields to the corresponding products. The catalytic system could be recycled and reused without significant loss of catalytic activity. Additionally, a possible mechanism of the Suzuki cross-coupling reaction is depicted in this paper.

1. Introduction

The carbon–carbon bond formation reaction is one of the most fundamental transformations due to the large number of applications of the resulting compounds in organic, pharmaceutical, and polymer chemistry [1]. Therefore, there has been tremendous interest in developing efficient methods for such a conversion, and a well known method constitutes the Suzuki–Miyaura cross-coupling reaction. The Suzuki–Miyaura cross-coupling reaction is a powerful tool for the formation of carbon–carbon bond, which is characteristic of mild conditions, high selectivity, and tolerance with a broad range of functional groups [2]. Traditionally, the most common way for performing such a transformation is palladium complexes-catalyzed cross-coupling reaction between organoboron compounds and organic halides or triflates [3,4]. However, the cost of reagents, removal of trace palladium from late stage synthetic intermediate, and the use of expensive, difficult to prepare and handle ligands are the major drawbacks of this method. Moreover, in many cases, ligands are air and moisture sensitive, which makes reaction setup too complex for straightforward scale-up and makes ligand-free palladium applications the alternative of choice from a green chemistry perspective. In addition to palladium catalysts, a variety of transition metal complexes catalysts, such as iron [5,6], manganese [7], cobalt [8,9], ruthenium [10], copper [11,12], gold [13], nickel [14], rhodium [15], and other complexes [16–18], have been developed for this conversion. However, these procedures still suffered from the use of expensive reagents, difficulties in work up, environmental hazards, and difficulties in recycling of the catalyst. Sometimes, complicated coordinating and expensive ligands are often required to stabilize the active metal intermediates during the reactions.

Supercritical carbon dioxide ($scCO_2$) is an abundant, inexpensive, nontoxic and non-flammable reagent, and it has received considerable attentions as a reaction medium for organic reactions due to the attractive physical and toxicological properties [19]. CO_2 could be a particularly advantageous reaction medium when it serves as both a reactant and a solvent. In fact, the Suzuki–Miyaura reaction is very suitable for proceeding under supercritical conditions, because $scCO_2$ possesses high solvating power towards various organoboron compounds and organic halides. A number of catalytic processes based upon the combination of transition metals and $scCO_2$ have been developed for such a conversion [20–22]. However, these methods suffered from environmental hazards, poor recovery of expensive metal catalysts and laborious work-up procedures. Ionic liquids (ILs) have received considerable attention as alternatives to the traditional organic solvents. Because of their interesting physical and chemical properties, such as negligible vapor pressure, unique permittivity, high thermal stability, good solvents for both organic and inorganic substances, high electrical conductivity and wide electrochemical window [23–25], ionic liquids have found an application in many chemical reactions [26] and processes including extraction and separation [27]. Up to now, examples of their application in the Suzuki–Miyaura cross-coupling reaction were also reported

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* Corresponding author at: College of Materials and Chemical Engineering, China Three Gorges University, Yichang 443002, People's Republic of China.
E-mail address: huyulin1982@163.com (Y.-L. Hu).

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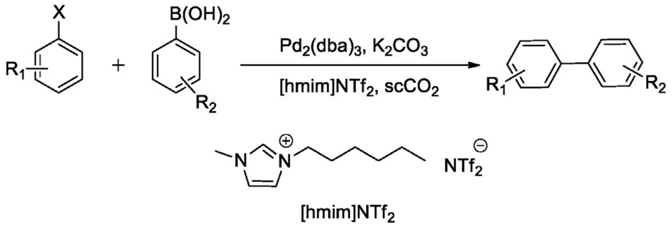

Scheme 1. The Suzuki cross-coupling reaction.

[28–32]. However, these reported protocols are still associated with one or more disadvantages, such as low catalyst activity, water or air sensitivity, and the requirement for expensive transition metal additives. Consequently, the search for new and environmentally benign synthetic methodologies for Suzuki–Miyaura cross-coupling reaction that address these drawbacks remains to be of value and interest.

In view of the above-mentioned advantages of $scCO_2$ and ILs, the combination of $scCO_2$ and ILs may provide a clean synthesis process in which reaction and separation occur consecutively. Due to the strong electrostatic forces between cations and anions, $scCO_2$ dissolves well in ILs, but ILs actually do not dissolve in $scCO_2$. The organic products from a reaction in the IL-phase can, therefore, be extracted by supercritical CO_2, allowing only a small amount of cross-contamination between the IL and $scCO_2$ phases [33,34]. Considering the good physical and toxicological properties of $scCO_2$ and ILs, the main aim of this work is to establish a new and efficient protocol for the Suzuki–Miyaura cross-coupling reaction in the presence of ionic liquid. Herein, we report an efficient, ligand-free and environmentally friendly protocol for the Suzuki–Miyaura coupling between aryl halides and aryl boronic acid catalyzed by tris(dibenzylideneacetone)dipalladium ($Pd_2(dba)_3$) with K_2CO_3 as the base in the presence of $scCO_2$ and 1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonyl) imide ($[hmim]NTf_2$) biphasic system (Scheme 1). In addition, recyclability of the catalytic system can be easily carried out up to six cycles.

2. Experimental

2.1. General remarks

All the chemicals were from commercial sources without any pretreatment. All reagents were of analytical grade. The ionic liquids were synthesized according to the literature procedure [25]. ^1H NMR spectra was recorded on a Bruker 500-MHz spectrometer using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard. High performance liquid chromatography (HPLC) experiments were performed on a liquid chromatograph (Dionex Softron GmbH, America), consisting of a pump (P680) and ultraviolet–visible light detector (UVD) system (170 U). Elemental analysis was performed on a Vario EL III instrument (Elmentar Anlalysensy Teme GmbH, Germany).

2.2. General procedure for the Suzuki reactions

The Suzuki reaction was carried out in a stainless-steel reactor equipped with a magnetic stirrer and automatic temperature control system. Aryl halide (1 mmol), arylboronic acid (1.1 mmol), $Pd_2(dba)_3$ (0.1 mol%), $[hmim]NTf_2$ (5 mL) and K_2CO_3 (1 mmol) were charged into the reactor. CO_2 was charged in the reactor and the pressure was adjusted to 10 MPa. The reactor was heated at 80 °C for an appropriate time (Table 3), and the pressure was kept constant during the reaction. At the end of the reaction, the reactor was cooled and the carbon dioxide was vented slowly. The products were analyzed by HPLC. The residue was purified by preparative thin-layer chromatography on silica gel (200–300 mesh) to afford the desired pure product. The rest of the ionic liquid and catalyst were recovered and reused directly without further treatment. Fresh substrates and CO_2 were then recharged to the recovered catalyst and then recycled under identical reaction conditions. The target substrates were characterized by Elemental analysis, ^1H NMR spectra or compared with their authentic samples. Spectral characteristics of the products in Table 3 were provided as follows.

2.2.1. 4-Methyl-1,1'-biphenyl (Table 3, entry 2)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 2.24 (s, CH_3, 3H), 7.25–7.36 (m, Ar–H, 4H), 7.39–7.52 (m, Ar–H, 5H). Anal. Calcd. for $C_{13}H_{12}$: C, 92.79; H, 7.17. Found: C, 92.81; H, 7.19.

2.2.2. 2-Methoxy-1,1'-biphenyl (Table 3, entry 3)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 3.84 (s, CH_3, 3H), 7.01–7.03 (m, Ar–H, 2H), 7.35–7.43 (m, Ar–H, 2H), 7.53–7.58 (m, Ar–H, 5H). Anal. Calcd. for $C_{13}H_{12}O$: C, 84.72; H, 6.54; O, 8.65. Found: C, 84.75; H, 6.57; O, 8.68.

2.2.3. 4-Methoxy-1,1'-biphenyl (Table 3, entry 4)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 3.86 (s, CH_3, 3H), 6.98–7.01 (m, Ar–H, 2H), 7.23–7.26 (m, Ar–H, 1H), 7.39–7.42 (m, Ar–H, 2H), 7.51–7.55 (m, Ar–H, 4H). Anal. Calcd. for $C_{13}H_{12}O$: C, 84.74; H, 6.52; O, 8.64. Found: C, 84.75; H, 6.57; O, 8.68.

2.2.4. 1,1'-Biphenyl-4-ol (Table 3, entry 5)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 4.75 (s, OH, 1H), 6.88–6.92 (m, Ar–H, 2H), 7.26–7.29 (m, Ar–H, 1H), 7.37–7.53 (m, Ar–H, 6H). Anal. Calcd. for $C_{12}H_{10}O$: C, 84.65; H, 5.91; O, 9.38. Found: C, 84.68; H, 5.92; O, 9.40.

2.2.5. 1,1'-Biphenyl-2-amine (Table 3, entry 6)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 3.74 (s, NH_2, 2H), 6.73–6.81 (m, Ar–H, 2H), 7.11–7.15 (m, Ar–H, 2H), 7.32–7.43 (m, Ar–H, 5H). Anal. Calcd. for $C_{12}H_{11}N$: C, 85.15; H, 6.54; N, 8.26. Found: C, 85.17; H, 6.55; N, 8.28.

2.2.6. 4-Nitro-1,1'-biphenyl (Table 3, entry 7)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.44–7.51 (m, Ar–H, 3H), 7.63–7.66 (m, Ar–H, 2H), 7.71–7.75 (m, Ar–H, 2H), 8.28–8.31 (m, Ar–H, 2H). Anal. Calcd. for $C_{12}H_9NO_2$: C, 72.32; H, 4.54; N, 7.01; O, 16.03. Found: C, 72.35; H, 4.55; N, 7.03; O, 16.06.

2.2.7. 1,1'-Biphenyl-4-carbaldehyde (Table 3, entry 8)

^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.43–7.52 (m, Ar–H, 3H), 7.62–7.65 (m, Ar–H, 2H), 7.73–7.76 (m, Ar–H, 2H), 7.94–7.96 (m, Ar–H, 2H), 10.03 (s, CHO, 1H). Anal. Calcd. for $C_{13}H_{10}O$: C, 85.68; H, 5.51; O, 8.75. Found: C, 85.69; H, 5.53; O, 8.78.

Table 1
Optimization studies for the Suzuki reaction of bromobenzene and phenylboronic acid.[a]

Entry	Ionic liquid	Base	Time (h)	Yield (%)[b]
1	–	–	12	<20
2	$[hmim]PF_6$	K_2CO_3	8	58
3	[hmim]OTf	K_2CO_3	8	42
4	$[hmim]BF_4$	K_2CO_3	2	78
5	$[hmim]NTf_2$	K_2CO_3	2	92
6	[hmim]Cl	K_2CO_3	2	65
7	$[bmim]NTf_2$	K_2CO_3	2	87
8	$[bpy]NTf_2$	K_2CO_3	2	72
9	–	K_2CO_3	8	48
10	$[hmim]NTf_2$	–	8	59
11	$[hmim]NTf_2$	Na_2CO_3	2	84
12	$[hmim]NTf_2$	Et_3N	2	75
13	$[hmim]NTf_2$	KOAc	2	68
14	$[hmim]NTf_2$	K_3PO_4	2	80
15	$[hmim]NTf_2$	KOH	2	72

[a] The reactions were carried out with bromobenzene (1 mmol), phenylboronic acid (1.1 mmol), $Pd_2(dba)_3$ (0.1 mol%), base (1 mmol), ionic liquid (5 mL), and CO_2 (10 MPa) at 80 °C.
[b] Isolated yield.