

Short communication

A novel fluorous palladium catalyst for Suzuki reaction in fluorous media

Ming-Gui Shen, Chun Cai^{*}, Wen-Bin Yi

Chemical Engineering College, Nanjing University of Science & Technology, Nanjing 210094, China

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Abstract

Palladium(II) perfluorooctanesulfonate [Pd(OSO₂R_{f8})₂] catalyses the highly efficient Suzuki reaction in the presence of a catalytic amount of perfluoroalkylated-pyridine as a ligand in a fluorous biphasic system (FBS). The fluorous phase containing the active palladium species is easily separated and can be reused several times without a significant loss of catalytic activity.

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1. Introduction

Horváth and Rábai introduced the concept of fluorous biphasic system (FBS) in 1994 [1]. As a new kind of phase-separation and catalyst immobilization technique, FBS has been used for many organic syntheses [2].

The Suzuki reaction has been regarded as one of the most important tools to create C–C bonds [3]. Many efficient and selective catalytic systems were developed for the reaction [4]. However, Suzuki reactions remain a tough challenge for chemists in designing recyclable systems because the catalytic cycle is unstable, responsive to various factors [5]. Schneider and Bannwarth applied fluorous bis(triphenylphosphine)palladium dichloride complexes as catalyst precursors to Suzuki reactions [6]. It could be shown in one example that the amount of catalyst could be reduced from 1.5 mol% to 0.1 mol% still resulting in a high yield (>86%) in first run. However, in repetitive cycles, considerable loss of activity of catalyst was found. Rocaboy and Gladysz used the soluble fluorous palladacycle complexes as the catalyst in Suzuki reactions [7]. Nevertheless, under fluorous recycling conditions decreased activities of the catalysts were observed. As a part of our studies to explore the utility of transition metal perfluorates catalyzed reactions in fluorous solvents [8], we decided to

investigate the application of a novel fluorous palladium catalyst, palladium(II) perfluorooctanesulfonate [Pd(OSO₂R_{f8})₂] with perfluoroalkylated-pyridine ligand (Scheme 1). We prepared a novel fluorous palladium catalyst with perfluoroalkylated-pyridine as ligand, for using in the Suzuki reaction. The perfluoroalkylated-pyridine ligand was prepared according to the method described by Uemura (Scheme 2) [9].

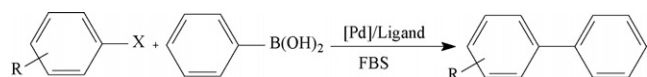
2. Results and discussion

First, we prepared Pd(OSO₂R_{f8})₂ from palladium carbonate (PdCO₃) by stirring it with heptadecafluorooctanesulfonic acid (R_{f8}SO₃H, PfoH) (Scheme 3). Then, the influences of bases and solvents on catalytic property of the Pd(OSO₂R_{f8})₂-ligand **1** were investigated by using coupling reaction of bromobenzene with phenylboronic acid. The results were shown in Table 1. It was found that among the bases tested (K₃PO₄, Na₂CO₃, and NEt₃), K₃PO₄ proved to be the most efficient. Among the solvents used (DMF, dioxane, and H₂O), DMF was the best choice. Taken together, excellent result was obtained when the coupling reaction was carried out using K₃PO₄ as the base and DMF as the solvent (Table 1, entry 1).

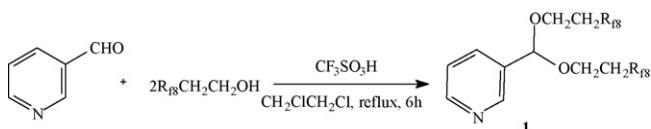
We next examined whether Pd(OSO₂R_{f8})₂ could be used directly, without any other ligand, to catalyze the Suzuki reactions. To begin our study, we performed the Suzuki reaction between bromobenzene and phenylboronic acid. It was found that the reaction using Pd(OSO₂R_{f8})₂ as catalyst alone could

^{*} Corresponding author. Fax: +86 25 84315030.

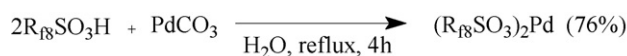
E-mail address: c.cai@mail.njust.edu.cn (C. Cai).



Scheme 1.



Scheme 2.



Scheme 3.

catalyze the Suzuki reaction in successful yield, however, great decrease of the catalytic activity was observed in the recycles (Table 2, entry 1).

Using the perfluoroalkylated-pyridine ligand, the Suzuki reaction of iodobenzene with phenylboronic acid was then examined. After a typical experiment, the course of the reaction was followed by GC. Thus, in the presence of $Pd(OSO_2R_{18})_2$ and ligand **1**, the coupling product was obtained in 99% GC yield after 4 h (Table 2, entry 2). Using the same reaction conditions, we next examined the application of $Pd(OSO_2R_{18})_2$ -ligand **1** to the cross coupling of a variety of aryl iodides. Both the electron-rich and electron-poor aryl iodides could be efficiently converted to the desirable products in high yields (entries 3–7). Besides aryl iodides, aryl bromides could also be successfully transformed to the desired Suzuki coupling products under a longer reaction times (entries 8–14). But, it was not active enough to handle an aryl chloride (entries 15–17) even under much longer reaction times. It provided a much lower yield between 45% and 53%. When the reaction was run in 10 mmol scale (halobenzene), the present catalyst precursor system was robust enough and the yield do not drop at larger scales (entry 18).

We next sought to probe whether the catalytically active species or a precursor could be recycled. Only a slight decrease of the catalytic activity was observed even after three recycles

Table 1

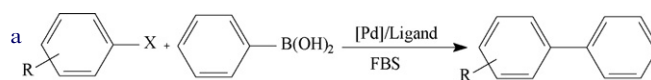
Coupling reaction of bromobenzene with phenylboronic acid in the presence of several bases and solvents

Entry	Base	Solvent	Yield (%) ^a
1	K ₃ PO ₄	DMF	98
2	K ₃ PO ₄	Dioxane	95
3	K ₃ PO ₄	H ₂ O	38
4	Na ₂ CO ₃	DMF	78
5	Na ₂ CO ₃	Dioxane	70
6	Na ₂ CO ₃	H ₂ O	35
7	NEt ₃	DMF	18
8	NEt ₃	Dioxane	20
9	NEt ₃	H ₂ O	26

^aGC yield based on bromobenzene.

Table 2

$Pd(OSO_2R_{18})_2$ -**1** catalyzed Suzuki reactions in FBS



Entry	Aryl halide	Time (h)	Yield (%) ^b
1 ^c	PhBr	6	92, 25, 9
2 ^d	PhI	4	99, 97, 96, 94
3	2-CH ₃ C ₆ H ₄ I	4	98
4	3-CH ₃ C ₆ H ₄ I	4	99
5	4-CH ₃ C ₆ H ₄ I	4	97
6	2-NO ₂ C ₆ H ₄ I	4	98
7	4-NO ₂ C ₆ H ₄ I	4	99
8 ^d	PhBr	6	98, 96, 94, 92
9	4-NO ₂ C ₆ H ₄ Br	6	97
10	4-CH ₃ C ₆ H ₄ Br	6	96
11	4-CH ₃ COC ₆ H ₄ Br	6	98
12	4-CH ₃ OC ₆ H ₄ Br	6	98
13	4-CHOC ₆ H ₄ Br	6	95
14	2-CH ₃ OC ₆ H ₄ Br	6	98
15	PhCl	8	53
16	4-CH ₃ C ₆ H ₄ Cl	8	45
17	4-CH ₃ COC ₆ H ₄ Cl	8	52
18 ^e	PhBr	6	97

^a Reaction conditions: Halobenzene (0.5 mmol), PhB(OH)₂ (0.75 mmol), $Pd(OSO_2R_{18})_2$ (0.001 mmol), Ligand (0.004 mmol), K₃PO₄ (1 mmol), Water (1.00 mL), DMF (1.5 mL).

^b GC yield based on halobenzene.

^c The coupling reaction performed with no ligand, the fluoruous phase was run for three consecutive cycle.

^d The fluoruous phase was run for four consecutive cycle.

^e The reaction was run under 10 mmol scale (halobenzene).

(entries 2 and 8). It may be caused by the lost of the perfluoroalkylated-pyridine ligand in the recycle procedure. The amount of palladium which had leached into the product phase (DMF-H₂O) after the reaction was determined by ICP. Notably, the Pd-content was not detectable (<1 ppm). This result suggests the robustness of the catalytic system for recycle use.

In conclusion, the novel fluoruous biphasic system consist of $Pd(OSO_2R_{18})_2$ and perfluoroalkylated-pyridine **1** showed a high catalytic activity for Suzuki reaction. The fluoruous phase containing the active palladium species was easily separated and could be reused several times without a significant loss of catalytic activity when the perfluoroalkylated-pyridine ligand was used.

3. Experimental

3.1. General

Chemicals used were obtained from commercial suppliers and used without further purifications. Melting points were determined on a Shimadzu DSC-50 thermal analyzer. IR spectra were recorded on a Bomem MB154S infrared analyzer. UV-vis spectra were obtained with a UV-1601 apparatus. ¹H NMR and ¹⁹F NMR spectra were recorded with a Bruker Advance RX500 spectrometer. Mass spectra were recorded on a Saturn 2000GC/MS instrument. Inductively coupled plasma

(ICP) spectra were measured on an Ultima2C apparatus. Elemental analyses were performed on a Yanagimoto MT3CHN recorder.

3.2. Preparation of Pd(OSO₂R₁₈)₂

Palladium carbonate (0.17 g, 1.0 mmol) and a solution of R₁₈SO₃H (1.23 g, 1.5 mmol) in water (5 mL) was stirred at refluxing temperature for 4 h. The resulting gelatin-like solid was collected, washed with H₂O and dried at 160 °C for 24 h in vacuum to give a brown solid (0.84 g, 76%), which does not have a clear melting point up to 500 °C, but shrinks around 330 °C and 410 °C. IR (KBr) ν 1230 (CF₃), 1148 (CF₂), 1080 (SO₂), 1061 (SO₂), 752 (S–O) and 640 (C–S) cm⁻¹. ICP: calculated for C₁₆O₆F₃₄S₂Pd: Pd, 9.63; found: Pd, 9.61. Anal. calculated for C₁₆O₆F₃₄S₂Pd: C, 17.38; found: C, 17.29. ¹⁹F NMR (500 MHz, CF₃C₆H₅): δ -126.2, -121.2, -114.2, -81.4.

3.3. Typical procedure for Suzuki reaction in a FBS

To a mixture of Pd(OSO₂R₁₈)₂ (1.06 mg, 0.001 mmol) and DMF (1.5 mL) in a flask, ligand **1** (2.3 mg, 0.004 mmol) was added under vigorous stirring. After 10 min, perfluorodecalin (2 mL), iodobenzene (0.102 g, 0.5 mmol), PhB(OH)₂ (0.092 g, 0.75 mmol), and a solution of K₃PO₄ (0.266 g, 1 mmol) in water (1.00 mL) were added. The samples were vigorously stirred at 80 °C for 4 h. The resulting mixture was cooled with ice bath. Then, the fluoros layer on the bottom was separated for the next reaction. The reaction mixture (organic phase) was diluted with an aqueous KOH (10 mL, 1 M) and extracted with ether (2 × 10 mL). The combined organic extracts were dried over Na₂SO₄ for GC analysis. After GC analysis, the solvent was removed under reduced pressure and the residue was purified by a silica gel column chromatograph (eluent: petroleum ether/EtOAc = 25/1) to give a white solid. The product was characterized by GC/MS and ¹H NMR.

3.4. Typical procedure for catalyst recycling

After the reaction as described above, the mixture was allowed to stand for *ca.* 5 min without stirring, and then the organic phase was separated using a pipette. The resulting fluoros phase was ready for further runs: that is, iodobenzene (0.5 mmol), DMF (1.5 mL), PhB(OH)₂ (0.75 mmol) and a solution of K₃PO₄ (0.266 g, 1 mmol) in water (1.00 mL) were added to the fluoros phase and the mixture was stirred at 80 °C.

Biphenyl (Lit. [10]) A white solid; mp 69–70 °C. ¹H NMR (500 MHz, CDCl₃) δ = 7.35 (tt, *J* = 7.4 Hz, *J* = 1.4 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 4H), 7.59 (dd, *J* = 8.5 Hz, *J* = 1.2 Hz, 4H). MS (EI) *m/z* 154 (*M*⁺).

2-Methylbiphenyl (Lit. [11]) A yellow liquid; ¹H NMR (500 MHz, CDCl₃) δ = 2.25 (s, 3H), 7.21–7.24 (m, 4H), 7.28–7.33 (m, 3H), 7.36–7.39 (m, 2H). MS (EI) *m/z* 168 (*M*⁺).

3-Methylbiphenyl (Lit. [12]) A yellow liquid; ¹H NMR (500 MHz, CDCl₃) δ = 2.37 (s, 3H), 7.12 (m, 1H), 7.29 (m, 2H), 7.36–7.38 (m, 4H), 7.55 (m, 2H). MS (EI) *m/z* 168 (*M*⁺).

4-Methylbiphenyl (Lit. [11]) A white solid; mp 45–48 °C. ¹H NMR (500 MHz, CDCl₃) δ = 2.36 (s, 3H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.30 (m, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 7.5 Hz, 2H). MS (EI) *m/z* 168 (*M*⁺).

2-Nitrobiphenyl (Lit. [13]) A yellow solid; mp 36–38 °C. ¹H NMR (500 MHz, CDCl₃) δ = 7.32–7.36 (m, 2H), 7.40–7.50 (m, 5H), 7.59–7.62 (m, 1H), 7.84–7.88 (m, 1H). MS (EI) *m/z* 199 (*M*⁺).

4-Nitrobiphenyl (Lit. [11]) A yellow solid; mp 113–114 °C. ¹H NMR (500 MHz, CDCl₃) δ = 7.42–7.50 (m, 3H), 7.59 (m, 2H), 7.73 (d, *J* = 8.9 Hz, 2H), 8.28 (d, *J* = 8.9 Hz, 2H). MS (EI) *m/z* 199 (*M*⁺).

4-Acetylbiphenyl (Lit. [10]) A white solid; mp 121–122 °C. ¹H NMR (500 MHz, CDCl₃) δ = 2.67 (s, 3H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 8.06 (d, *J* = 8.2 Hz, 2H). MS (EI) *m/z* 196 (*M*⁺).

4-Methoxybiphenyl (Lit. [11]) A white solid; mp 90–91 °C. ¹H NMR (500 MHz, CDCl₃) δ = 3.82 (s, 3H), 6.97 (m, 2H), 7.30 (d, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.52 (m, 4H). MS (EI) *m/z* 184 (*M*⁺).

4-Phenylbenzaldehyde (Lit. [14]) A yellow solid; mp 57–59 °C. ¹H NMR (500 MHz, CDCl₃) δ = 7.71–7.34 (m, 5H), 7.73 (m, 2H), 7.92 (m, 2H), 10.04 (m, 1H). MS (EI) *m/z* 182 (*M*⁺).

2-Methoxybiphenyl (Lit. [11]) A white solid; mp 30–31 °C. ¹H NMR (500 MHz, CDCl₃) δ = 3.80 (s, 3H), 7.97–8.02 (m, 2H), 7.29–7.34 (m, 3H), 7.39 (m, 2H), 7.50 (d, *J* = 6.9 Hz, 2H). MS (EI) *m/z* 184 (*M*⁺).

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