A novel fluorous palladium catalyst for Heck reaction in a fluorous biphase system (FBS)

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Abstract

Palladium(II) perfluorooctanesulfonate [Pd(OSO$_2$R$_{f8}$)$_2$] catalyses the highly efficient Heck reaction in the presence of a catalytic amount of a perfluoroalkylated-pyridine as a ligand in a fluorous biphase system (FBS) composed of toluene and perfluorodecalin. 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

Since the technique of fluorous biphase system (FBS), as a phase-separation and catalyst immobilization technique, was first introduced by Horvath and Rabai [1], it has been used for many organic syntheses [2]. On the other hand, Heck reaction is one of the most important methods in synthetic organic chemistry for the formation of C–C bonds [3]. Traditionaly, palladium-catalyzed Heck reaction often requires relatively large amounts of catalysts, which have to be removed from the reaction product. Perfluoro-labelled Pd complexes offer a solution to this problem, since the perfluoro-labelled catalysts are soluble in fluorous solvents and can be separated from the organic product very easily by liquid–liquid extractions. There are several examples in the literature demonstrating the power of this methodology. Nakamura et al. [4,5], Pozzi and coworkers [6] and Grigg and York [7] research groups reported palladium-catalyzed Heck reaction in the presence of the fluorous phosphine ligands. However, recovery and reuse of the ligands were not efficient because of the instability of fluorous phosphines towards oxygen. Rocaboy and Gladysz prepared a fluorous Schiff base, which was convered into palladacycle for Heck reaction [8,9]. The results revealed a gradual loss of conversion and the yield of Heck products due to limited stability of the catalysts

in fluorous solvents. Pd nanoparticles stabilized by 1,5-bis[4-bis(perfluoroocty)phenyl]-1,4-pentadien-3-one were reported by Moreno-Mañas et al. for the reaction in a FBS [10,11]. Ryu and coworkers described Mizoroki–Heck reaction promoted by a fluorous Pd–carbene complex with no need of organic solvent using the fluorous solid–liquid extraction technique [12]. Curran et al. reported a perfluorinated silica gel pincer palladium complex for Heck reaction [13]. The complex can be recovered after reactions for reuse by fluorous solid phase extraction (F-SPE).
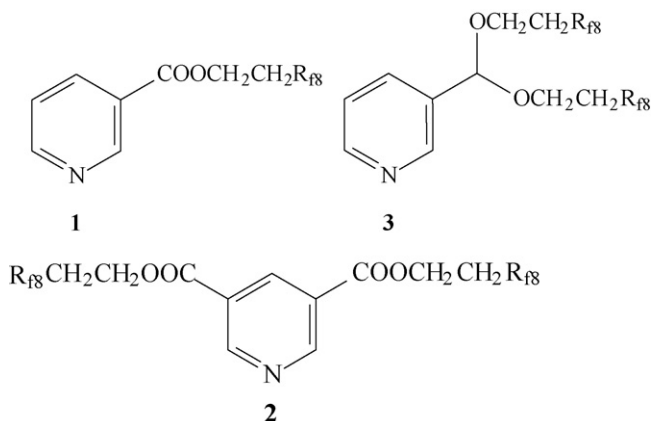
As a part of our studies to explore the utility of transition metal perflates catalyzed reactions in fluorous solvents [14–19], we decided to investigate the application of a novel fluorous palladium catalyst, palladium (II) perfluorooctanesulfonate (Pd(OSO$_2$R$_{f8}$)$_2$, Scheme 1) with various perfluoroalkylated-pyridine ligands (Scheme 2), to Heck reaction in FBS (Scheme 3). The coupling process can be performed in an air atmosphere. The fluorous palladium catalyst and perfluoroalkylated-pyridine are stable and easy to prepare. The fluorous phase containing the active palladium species is easily separated and can be reused several times without a significant loss of catalytic activity.

2. Experimental

2.1. General remarks

Mp was obtained with a Shimadzu DSC-50 thermal analyzer. IR spectra were recorded on a Bomem MB154S infrared

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$$R_{f8}SO_3H + PdCO_3 \longrightarrow Pd(OSO_2R_{f8})_2$$

$$R_{f8} = CF_3CF_2CF_2CF_2CF_2CF_2CF_2CF_2$$
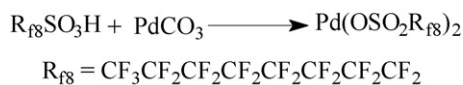
Scheme 1. Preparation of Pd(OPf)$_2$.

Scheme 2. Perfluoroalkylated-pyridine ligands.

analyzer. UV–vis spectra were obtained with a UV-1601 apparatus. ^{1}H NMR and ^{19}F NMR spectra were recorded with a Bruker Advance RX300 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. Perfluorodecalin was purchased from Aldrich Co. Heptadecafluorooctanesulfonic acid ($R_{f8}SO_3H$) was commercially obtained from ARCOS Co. Commercially available reagents were used without further purification.

2.2. Preparation of Pd(OSO$_2$R$_{f8}$)$_2$

A mixture of a solution of $R_{f8}SO_3H$ (1.23 g, 1.5 mmol) in water (5 ml) and palladium carbonate (0.17 g, 1.0 mmol) was refluxed with stirring for 4 h. The resulting gelatin-like solid was collected, washed 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) υ 1230 (CF$_3$), 1148 (CF$_2$), 1080 (SO$_2$), 1061 (SO$_2$), 752 (S–O) and 640 (C–S) cm^{-1}. Anal. calcd for C$_{16}$O$_6$F$_{34}$S$_2$Pd: Pd, 9.63; C, 17.38. Found: Pd, 9.61; C, 17.29. ^{19}F NMR: δ −126.2, −121.2, −114.2, −81.4.

Scheme 3. Heck reactions in FBS.

2.3. Typical procedure for Heck reaction in a FBS

To a mixture of Pd(OSO$_2$R$_{f8}$)$_2$ (55 mg, 0.05 mmol) and toluene (2 ml) in a glass tube was added ligand **3** (204 mg, 0.2 mmol) under vigorous stirring. After 10 min, perfluorodecalin (4 ml), iodobenzene (10 mmol) and NEt$_3$ (2.1 ml, 15 mmol) were introduced into a glass tube, and then styrene (12 mmol) in toluene (2 ml) was added. After stirring at 80 °C for 6 h, the mixture was cooled to 0 °C. Then, the fluorous layer on the bottom was separated for the next reaction. The reaction mixture (organic phase) was diluted with water (5 ml) and extracted with ether (2 × 10 ml). The combined organic extracts were dried over Na$_2$SO$_4$ for GC analysis. GC showed that conversion and selectivity in **4** were 100% and 97% respectively. After GC analyses, the solvents and volatiles were removed under vacuum, and then the residue was subjected to column chromatography on silica gel with hexane and EtOAc (9:1, v/v) as eluent to give *trans*-stilbene product (1.69 g, 94%). The product was characterized by GC/MS and ^{1}H NMR.

2.4. 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 toluene phase was separated using a pipette. The resulting fluorous phase was ready for further runs: that is, iodobenzene (10 mmol), NEt$_3$ (2.1 ml, 15 mmol) and styrene (12 mmol) in toluene (4 ml) was added to the fluorous phase and the mixture was stirred at 80 °C.

3. Results and discussion

We first examined the palladium-catalyzed Heck coupling of iodobenzene with styrene in the presence of palladium complexes in a FBS composed of toluene and perfluorodecalin at 80 °C (Scheme 3), using the perfluorinated pyridine **1**–**3**, whose synthesis was previously described by Uemura and coworkers [20], as ligands. The results are summarized in Table 1. The reaction using Pd(OSO$_2$R$_{f8}$)$_2$ as catalyst alone failed to produce the Heck product in a yield. Use of ligand **1** resulted in 100% conversion of iodobenzene with 94% selectivity in **4**; however, the recovered fluorous phase showed a lower catalytic activity, which could be ascribed to the loss of perfluorinated ligand in the toluene phase. Ligand **2** gave a poor result because of formation of palladium black due to the weaker coordinative ability of ligand **2**, which has two electron-withdrawing substituents on an aromatic nucleus. Although the reaction became slower in the reaction of ligand **3**, in this case the toluene (upper) phase was colourless after the reaction, suggesting that the palladium-**3** complex could dissolve in the fluorous phase. The separated fluorous phase could be reused for the next reaction without any specific treatment and the work-up procedure of recycling was accomplished by simple phase-separation (Scheme 4). There were no significant differences between the UV–vis spectra of the initial and recovered fluorous phase which may indicate that the fluorous palladium catalyst was recovered unaltered after the coupling process had taken place. Although a slight decrease

Table 1
Heck reaction of iodobenzene with styrene in FBS[a]

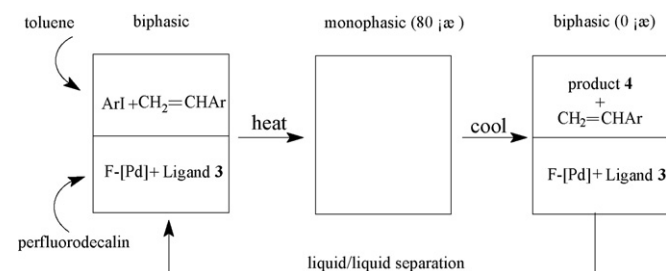| Entry[b]	[Pd]	Ligand	Time (h)	Conversion (%)	Selectivity in 4 (%)
1	Pd(OSO$_2$R$_{f8}$)$_2$	–	4	10	94
2	Pd(OSO$_2$R$_{f8}$)$_2$	1	4	100	92
2a	Pd(OSO$_2$R$_{f8}$)$_2$	1	4	83	88
2b	Pd(OSO$_2$R$_{f8}$)$_2$	1	4	70	90
3	Pd(OSO$_2$R$_{f8}$)$_2$	2	4	21	95
4	Pd(OSO$_2$R$_{f8}$)$_2$	3	6	100	97
4a	Pd(OSO$_2$R$_{f8}$)$_2$	3	6	100	96
4b	Pd(OSO$_2$R$_{f8}$)$_2$	3	6	99	96
4c	Pd(OSO$_2$R$_{f8}$)$_2$	3	6	99	95
5	Pd(OAc)$_2$	3	4	98	90
5a	Pd(OAc)$_2$	3	4	81	88
5b	Pd(OAc)$_2$	3	4	69	87
6	PdCl$_2$	3	8	43	82

[a] The reaction condition: iodobenzene, 0.01 mol; styrene, 0.012 mol; ligand, 0.2 mmol; [Pd], 0.05 mmol; fluorous solvent, 4 ml; toluene, 2 ml; NEt$_3$, 0.015 mol; 60 °C. The conversions and selectivities were calculated from GC of the mixture by incorporating an internal standard.

[b] Entries a, b and c correspond to the first, second and third recycling of the fluorous phase, respectively.

in the catalytic activity was observed, the Heck product was obtained in a 95% yield even after three recycles. It is important to study the leaching problem in these catalyst recyling systems. Based on ^{19}F NMR and UV–vis and GC–MS data, no loss of Pd(OSO$_2$R$_{f8}$)$_2$, ligand 3 or perfluorodecalin (C$_{10}$F$_{18}$) to the organic phases can be detected. In fact, we also investigated the exact amount of Pd(OSO$_2$R$_{f8}$)$_2$ and ligand 3 in the recovered fluorous phase by ICP, ^{19}F NMR and UV–vis, finding that 99.9% of Pd(OSO$_2$R$_{f8}$)$_2$ and ligand 3 retained in perfluorodecalin (C$_{10}$F$_{18}$). This result suggests the robustness of the catalytic system in recycled use.

We then screened other phosphine-free palladium catalysts for the reaction of iodobenzene with styrene in the presence of ligand 3. It was found that Pd(OAc)$_2$-3 complex had similarly high activity for the reaction with a quantitative conversion to the Heck product at 80 °C over 8 h. However, a obvious decrease in conversion was observed in the recycle of catalyst solution. In the case of PdCl$_2$, reaction only afforded the moderate conversion. From these observations it was revealed that Pd(OSO$_2$R$_{f8}$)$_2$-3 complex was the best choice as fluorous catalyst for our purpose to construct a recyclable catalytic system for the Heck reaction.

The coupling reaction catalyzed by Pd(OSO$_2$R$_{f8}$)$_2$-3 complex was extended to other aryl halids and olefins (Scheme 3, Table 2). Reaction of iodotoluene with styrene provided a high

Table 2
Pd(OSO$_2$R$_{f8}$)$_2$-3 catalyzed Heck reactions in FBS[a]

ArX	R	Time (h)	Conversion (%)	Selectivity in 4 (%)
2-CH$_3$PhI	Ph	4	100	92
3-CH$_3$PhI	Ph	4	100	94
4-CH$_3$PhI	Ph	4	100	94
4-NO$_2$PhI	Ph	4	100	45
PhBr	Ph	5	96	88
2-MeOPhBr	Ph	5	100	90
4-MeOPhBr	Ph	5	98	90
4-NO$_2$PhCl	Ph	12	42	88
PhI	CO$_2$CH$_3$	6	100	77
PhI	CN	6	100	74

[a] The reaction conditions: halobenzene, 0.01 mol; olefins, 0.012 mol; ligand 3, 0.2 mmol; Pd(OSO$_2$R$_{f8}$)$_2$, 0.05 mmol; fluorous solvent, 4 ml; toluene, 2 ml; NEt$_3$, 0.015 mol; 60 °C. The conversions and selectivities were calculated from GC of the mixture by incorporating an internal standard.

yield. However, 4-nitroiodobenzene had the yield of 45%, the side reaction was dehalogenation. Notably, yields in the reaction of bromobenzenes were higher than 85%. In the case of 4-nitrocholrobenzene, reaction only gave 42% conversion with 88% selectivity in 4 due to dehalogenation and high activation energy of C–Cl bond. Methyl acrylate and propenyl cyanide afforded required conversion and selectivity in 4.

In conclusion, the novel fluorous biphase system of a combination of Pd(OSO$_2$R$_{f8}$)$_2$ and perfluoroalkylated-pyridine 3 showed a high catalytic activity for Heck reaction. The fluorous phase containing the active palladium species is easily separated and can be reused several times without a significant loss of catalytic activity.

Acknowledgement

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Scheme 4. Illustration of reaction of iodobenzene with styene in FBS.

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