Carbon–carbon bond formation *via* homocoupling reaction of substrates with a broad diversity in water using Pd(OAc)$_2$ and agarose hydrogel as a bioorganic ligand, support and reductant

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ABSTRACT

In this study, we have presented a new catalytic system in which Pd(OAc)$_2$ has been used as a pre-catalyst and agarose as a degradable bioorganic ligand, support and reductant for carbon–carbon bond formation *via* homocoupling reaction of different aryl halides, β-bromo styrene, phenylboronic acid and phenylacetylene as the substrates. The reactions proceeded smoothly with high yields at temperature <100 °C in water without using any organic co-solvent, phosphorus ligand or reducing agents. The catalyst is recyclable and has been recycled for four times with a tiny amount of leaching of Pd into the reaction media. The amount of leaching has been determined by ICP analysis.

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1. Introduction

In recent years, palladium catalyzed reductive homocoupling reaction of aryl halides has been of great interest for the synthesis of agrochemicals and natural products [1–4]. This reaction was first reported by Ullmann over a century ago [5]. Most of the traditional methods suffer from both high temperatures >200 °C and using stoichiometric amounts of copper salts [6]. As time goes on, many procedures have been reported for avoiding the drastic reaction conditions [7–9]. In recent years for this purpose, utilizing other transition metals such as palladium [10–12], barium [13], indium [14], zinc [15], gold [16] and nickel [17] have been reported.

The increasing troubles of environmental pollution have become a serious subject of concern among scientists [18–20]. Along this line, an endless activity in chemical communities has been started in academia and industries. For this effort, over the past few years, green media such as water, PEG and ionic liquids [21,22] have been under much attention for the replacement of organic solvents.

Although, many methods are reported for palladium catalyzed reductive homocoupling reaction of aryl halides [23], the use of aqueous solvent for this function has received less attention. Since most of the phosphine ligands used for the reaction are expensive, water-insoluble and toxic, we made a decision to investigate the possibility of employing a naturally occurring, non-toxic and degradable bioorganic material to replace phosphine ligands suitable for the reaction to be conducted in water. First, we decided to investigate the capacity of agarose hydrogel for this endeavour. Agarose is a polysaccharide, which is consisting of 1,3-linked-D-galactopyranose and 1,4-linked-3,6-anhydro-α-L-galactopyranose. This basic agarobiose repeat unit forms long chains with an average molecular mass of 120,000 Da (Fig. 1) [24]. Agarose shows distinctive properties such as flexibility, non-toxicity, freely soluble in hot water and forms a gel network that contains double helices, which are formed by the presence of water molecules bound inside the double helical cavity. Moreover, agarose contains free hydroxyl groups on its backbone, which has the potential for the reduction and chelation with transition metals. Therefore, is able to reduce Pd(II) to Pd(0) species without using any extra reducing agent. It also acts as a highly functionalized support to catch up and stabilize the Pd(0) species formed in the mixture by their ligation with agarose hydrogel. Furthermore, its low costs also add to its many advantages, which make it a high potential candidate for such an important venture.

In this article, we have presented a useful environmentally friendly method for C–C bond formation *via* homocoupling reaction of various aryl iodides, bromides and chlorides as well as heteroaryl halides, β-bromo styrene and phenylboranic acid using agarose

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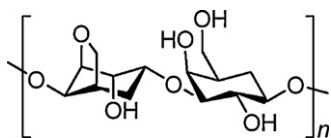iranpoor@chem.susc.ac.ir (N. Iranpoor).

Fig. 1. Agarose structure unit.

hydrogel as an effective bioorganic ligand, support and reducing agent for these reactions in water in the presence of Pd(OAc)$_2$ as the pre-catalyst.

Conjugated enzymes form building blocks of biologically active compounds, natural products, electronic and optical materials [25]. We have also presented that homocoupling of the terminal acetylenic groups in the presence of this catalytic system. For this purpose, the reaction of phenylacetylene as a model compound in water in the presence of Pd(OAc)$_2$ as the pre-catalyst and agarose hydrogel has been presented.

However, in recent years, water-soluble palladium catalysts have received significant attention from different sources due to their potential environmental and economic benefits [26].

2. Experimental

2.1. General

All chemicals were purchased from Merck, Fluka or Acros Chemical Companies and used without any further purification. NMR spectra were recorded with a BrukerAvance DPX-250 Spectrometer (^{1}H NMR 250 MHz and ^{13}C NMR 62.9 MHz) in CDCl$_3$ with TMS as the internal standard. UV–Vis spectra were recorded by PerkinElmer, Lambda 25, UV/Vis spectrometer to visualize the conversion of Pd(II) to Pd(0). Leaching of Pd into the mixture from agarose hydrogel was measured by ICP analysis using Varian, Vistapro. All products are known compounds and their spectral data along with their references are given in Section 2.

2.2. Homocoupling reaction of aryl halides (I, Br, Cl) catalyzed by Pd-supported agarose hydrogel catalyst in water

Agarose (0.05 g) and Pd(OAc)$_2$ (0.0044 g, 2 mol%)were dissolved in water (2 mL). The resulting solution was heated for 5 min at 90 °C. Then the aryl halide (1 mmol) and NaOH (0.6 g, 1.5 mmol) were added to the vessel containing the catalyst. The mixture was stirred for the specified time at 90 °C in the air (Table 3). After consumption of the starting material (TLC or GC), the reaction mixture was cooled to room temperature. A dark jelly like mass was appeared, which was extracted with Et$_2$O (2 × 3 mL). Evaporation of the solvent, gave the desired biaryl in an almost pure state. Further purification, if was necessary, was performed by silica gel column chromatography using n-hexane/Et(OAc)$_2$ as the eluent to give the pure product in high to excellent yields (Table 2).

2.3. Large-scale homocoupling reaction of 4-iodoanisole catalyzed by Pd-supported agarose hydrogel catalyst in water

To a flask containing water (20 mL), agarose (0.5 g) and Pd(OAC)$_2$ (0.022 g, 20 mol%) were added and the resulting mixture was heated at 90 °C for 10 min. To the obtained dark black-grayish mass, 4-iodoanisole (2.34 g, 10 mmol) and NaOH (6 g, 15 mmol) were added and the mixture was stirred at 90 °C for 2 h under the air. After completion of the reaction (TLC), the mixture was extracted with Et$_2$O (3 × 10 mL) and the ethereal solution was evaporated to give the desired biphenyl product in high purity>95% (GC). Further purification was accomplished by silica gel column chromatography eluted with an appropriate mixture of n-hexane/Et(OAc)$_2$.

Evaporation of the solvent gave the desired pure product as a crystalline compound.

2.4. Highly green procedure for homocoupling reaction of 4-iodoanisole catalyzed by Pd-supported agarose hydrogel catalyst in water

In a flask containing water (4 mL), agarose (0.1 g) and Pd(OAc)$_2$ (0.009, 4 mol%) were added and the resulting mixture was heated at 90° for 10 min. To the obtained black-grayish mass, 4-iodoanisole (0.468 g, 2 mmol) and NaOH (1.2 g, 3 mmol) were added, while the mixture was stirred at 90 °C under the air for 1.5 h. After completion of the reaction (TLC), the resulting hot mixture was filtered quickly through a thick cellulose paper under diminished pressure. The filter cake was washed with a portion of hot water (3 mL) and the combined hot aqueous filtrates were allowed to cool down to room temperature upon which the desired 4,4′-dimethoxybiphenyl was precipitated as white crystals which after drying under vacuum the desired product was isolated in 70–74% in a highly pure state.

2.5. Homocoupling reaction of β-bromo styrene catalyzed by Pd-supported agarose hydrogel catalyst in water

A mixture of agarose (0.05 g) and Pd(OAc)$_2$ (0.0044 g, 2 mol%) in a flask (5 mL) containing water (2 mL) was prepared and heated at 90 °C with stirring for 5 min. To the resulting mixture, β-bromo styrene (185 g, 1 mmol) and NaOH (0.6 g, 1.5 mmol) were added and stirred at 90 °C under the air for 12 h. The mixture was cooled to room temperature and the resulting jelly mass was extracted with diethyl ether (3 × 5 mL) and decanted. The ethereal solution was evaporated to give the desired crude homocoupled product. Purification of the crude was performed by silica gel column chromatography eluted with a mixture of n-hexane/ EtOAc. Evaporation of the solvent gave the pure product in 80–85% yield.

2.6. Homocoupling reaction of phenylboronic acid catalyzed by Pd-supported agarose hydrogel catalyst in water

Agarose (0.05 g) and Pd(OAc)$_2$ (0.0044 g, 2 mol%) were dissolved in water (2 mL) and heated at 90 °C for 5 min in a flask. To the resulting solution, phenylboronic acid (0.12 g, 1 mmol) and NaOH (0.6 g, 1.5 mmol) were added while being stirred at 90 °C under the air atmosphere for 10 h. The mixture was cooled to room temperature in which a gelatinous mass was appeared. EtOAc or diethyl ether (3 × 5 mL) were used to extract the desired product from the hydrogel mass. Evaporation of the solvent gave the crude biphenyl product. Purification of the product was performed by column chromatography on silica gel eluted with an appropriate mixture of light petroleum ether/EtOAc to afford the pure biphenyl compound in 75–80% isolated yield.

2.7. Homocoupling reaction of phenylacetylene catalyzed by Pd-supported agarose hydrogel catalyst in water

Phenylacetylene (0.102 g, 1 mmol) and NaOH (0.6 g, 1.5 mmol) were added to a solution composed of a preheated (90 °C) mixture of agarose (0.05 g), Pd(OAc)$_2$ (0.0044 g, 2 mol%) and water (2 mL). The resulting mixture was stirred at 90 °C under the air atmosphere for 12 h. The mixture was cooled down to room temperature to result a hydrogel mass. Extraction of the gel by diethylether (2 × 10 mL) and evaporation of the solvent gave the desired crude dienyne product, which was purified by column chromatography on silica gel eluted with a mixture of n-hexane/EtOAc to give the pure product in 75% isolated yield.

2.8. Recycling of the catalyst

To a flask (5 mL) containing agarose hydrogel (0.05 g), Pd(OAc)$_2$ (0.0044 g, 2 mol%) and water (2 mL) while being stirred at 90 °C, 4-iodoanisole (1 mmol, 0.233 g) and NaOH (1.5 mmol, 0.6 g) were added and steering was continued for 1.5 h at 90 °C. The resulting mixture was cooled to room temperature upon which a gelatinous mass was formed. Addition of diethyl ether (5 × 10 mL) to the jelly mass produced two distinct phases. The ethereal solution was decanted and the dark gelatinous mass was reused for another batch of the similar reaction. This process was repeated for four repeated runs (Table 4).

2.9. Spectral data

2a: White crystals, m.p. 71–72 °C (lit. 69–70 °C) [27], ^{1}H NMR (250 MHz, CDCl$_3$): 7.64–7.32 (m, 10H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 145.5, 130.3, 127.4, 127.2.

2b: White crystals m.p. 119–120.5 °C (lit. 118–120 °C) [28], ^{1}H NMR (250 MHz, CDCl$_3$): 7.41–7.38 (m, 4H), 7.2–7.1 (m, 4H), 2.52 (s, 6H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 139.2, 137, 129.5, 126.8, 21.0.

2d: White crystals m.p. 176–177 °C (lit. 178–179 °C) [29], ^{1}H NMR (250 MHz, CDCl$_3$): 7.42–7.38 (m, 4H), 6.9–6.8 (m, 4H), 3.75 (s, 6H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 159, 133.4, 127.7, 114.7, 55.83.

2i: White crystals m.p. 142–143 °C (lit. 142–145 °C) [28], ^{1}H NMR (250 MHz, CDCl$_3$): 7.42–7.38 (m, 2H), 7.36–7.2 (m, 2H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 138.5, 133.7, 129.0, 128.2.

2h: White crystals m.p. 234–237 °C (lit. 236–240 °C) [30], ^{1}H NMR (250 MHz, CDCl$_3$): 7.7–7.6 (m, 4H), 7.4–7.2 (m, 4H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 109.2, 120.2, 126.5, 133.4, 148.6.

2c: Yellow solid, m.p. 237–239 °C (lit. 240 °C) [31], ^{1}H NMR (250 MHz, CDCl$_3$): 7.85–7.82 (m, 4H), 7.45–7.43 (m, 4H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 152.5, 147.5, 125.7, 124.5.

2j: Orange solid, m.p. 230–231 °C (lit. 232 °C) [32], ^{1}H NMR (250 MHz, CDCl$_3$): 8.8 (s, 2H), 8.4–8.6 (m, 6H), 7.8–7.9 (m, 4H), 7.42–7.45 (m, 5H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 150.4, 149.5, 136.8, 133.5, 123.3.

2k: White crystals m.p. 131–132 °C (lit. 131–133 °C) [33], ^{1}H NMR (250 MHz, CDCl$_3$): 7.27 (s, 1H), 7.20–7.18 (m, 2H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 118.9, 118.2, 115.7, 93.3.

3i: White crystals m.p. 85–87 °C (lit. 86–87 °C) [34], ^{1}H NMR (250 MHz, CDCl$_3$): 7.38–7.34 (m, 4H), 7.29–7.23 (m, 4H), 7.19–7.15 (M, 2H), 6.9–6.86 (d of d, J = 15.8 Hz, J = 2.7 Hz), 6.65–6.61 (d of d, J = 15.8 Hz, J = 2.7), ^{13}C NMR (62.5 MHz, CDCl$_3$): 136.7, 133.8, 129.7, 128.5, 126.9, 126.1.

5j: White crystals m.p. 84–85 °C (lit. 85–86 °C) [35], ^{1}H NMR (250 MHz, CDCl$_3$): 7.5–7.45 (m, 4H), 7.32–7.2 (m, 6H), ^{13}C NMR (62.5 MHz, CDCl$_3$): 133.6, 129.2, 128.5, 121.7, 80.7, 73.1.

3. Results and discussion

First of all, for preparation of the catalyst, agarose (0.05 g) and Pd(OAc)$_2$ (0.0044 g, 2 mol%) were dissolved in water (2 mL) to produce a homogenous solution in slight brownish colour (Fig. 2A). The resulting solution was stirred for 5 min at 90 °C. In this operation, the colour of the solution turned black (Fig. 2B). The resulting mixture on cooling to room temperature produced a gelatinous mass in the reaction vessel. Our preliminary investigations were focused on the characterization of the resulting composite. UV–Vis spectrum of the produced hydrogel reveals the disappearance of the peak at 420, which shows the reduction of Pd(II) to Pd(0) is occurred by agarose hydrogel in the reaction mixture (Fig. 3) [36].

Pd-catalyzed organic reactions are sensitive towards the nature of the base and the solvent used for the reaction. Therefore, optimization of the reaction condition with respect to bases and the
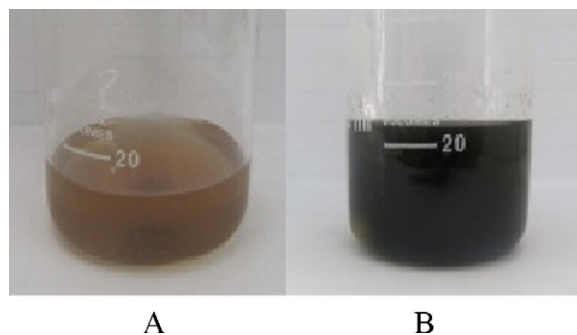
Fig. 2. (A) Slight brownish colour homogenous solution of the mixture of agarose hydrogel and Pd(OAc)$_2$ in water. (B) Black homogenous solution of Pd(OAc)$_2$ in water after heating in the presence of agarose hydrogel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)
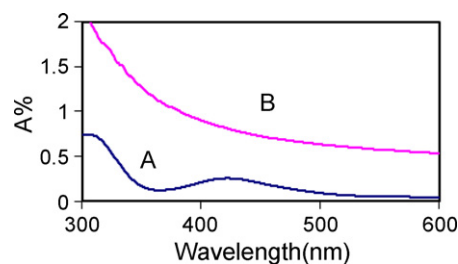

Fig. 3. (A) UV–Vis spectra of Pd(II) before reduction with agarose hydrogel before heating. (B) UV–Vis spectra for the formation of Pd(0) species after reduction with agarose hydrogel after heating.

solvents was investigated for the reaction of 4-iodoanisole (0.234 g, 1 mmol) as a model compound employing a variety of bases and solvents in the presence of agarose (0.05 g) using Pd(OAc)$_2$ (0.0044 g, 2 mol%) as the pre-catalyst. For this purpose, PEG, NMP, DMSO, TBAB, PEG/H$_2$O, DMSO/H$_2$O, dioxane, toluene and H$_2$O were examined as the solvents in the presence of NaOH, KOAc, DBU, K$_3$PO$_4$, Pr$_3$N and K$_2$CO$_3$ as bases (Table 1).

The results show that using NaOH at 90 °C in H$_2$O (as indicated in Table 1 in bold letters) was the most suitable condition for this

Table 1
Optimization studies for the homocoupling reaction of 4-iodoanisole (0.234 g, 1 mmol) with respect to different bases (1.5 mmol) and the solvents using Pd(OAc)$_2$ (0.0044 g, 2 mol%) as a pre-catalyst in the presence of agarose hydrogel (0.05 g) in different solvents
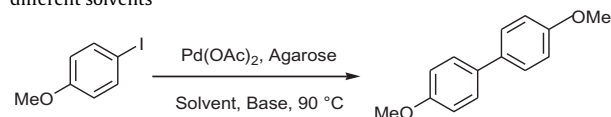
Entry	Base	Solvent	Temperature (°C)	Time (h)	Conversion % (GC)
1	**NaOH**	**H$_2$O**	**90**	**1.5**	**100**
2	NaOH	PEG	90	5	45
3	NaOH	NMP	100	5	35
4	NaOH	DMSO	90	7	45
5	KOAC	TABA	100	7	77
6	NaOH	PEG/H$_2$O	100	5	64
7	NaOH	DMSO/H$_2$O	100	5	55
8	KOAC	Dioxane	100	5	44
9	NaOH	Toluene	90	5	55
10	DBU	H$_2$O	90	5	70
11	K$_3$PO$_4$	H$_2$O	90	3	81
12	KOAC	H$_2$O	90	3	84
13	Pr$_3$N	H$_2$O	90	5	75
14	K$_2$CO$_3$	H$_2$O	90	2	78

Table 2
Optimization condition with respect to the amounts of Pd(OAc)$_2$ in the presence of agarose hydrogel (0.05 g) using NaOH (0.6 g, 1.5 mmol) and 4-iodoanisole (0.234 g, 1 mmol) in water
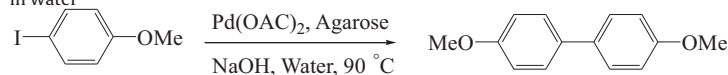
Entry	Pd(OAc)$_2$ (mol%)	Agarose (g)	Time (h)	Conversion % (GC)
1	1	None	48	0
2	2	None	48	0
3	5	None	48	0
4	10	None	48	0
5	1	0.05	48	70
6	2	0.05	1.5	100
7	5	0.05	1.5	100
8	10	0.05	1.25	100

homocoupling reaction producing the desired biphenyl compound in a quantitative yield within 1.5 h (Table 1, entry 1).

In order to show the importance of using agarose hydrogel as the ligand, reductant and support in the reaction, we studied the reaction of 4-iodoanisole (0.234 g, 1 mmol) as a model compound in the presence of NaOH (0.6 g, 1.5 mmol) using Pd(OAc)$_2$ (0.022 g, 10 mol%) in water at 90 °C in the absence of agarose hydrogel. Under these conditions, the reaction failed even after a long reaction time (24 h).

For optimization of the reaction conditions with respect to the amounts of Pd(OAc)$_2$, we have studied the reaction of 4-iodoanisole under the reaction conditions mentioned above by using 1, 2, 5 and 10 mol% of Pd(OAc)$_2$. First, we tried to conduct the reaction in the presence of 1 mol% of Pd(OAc)$_2$ in the absence of agarose hydrogel. The reaction was failed after 48 h reaction time (Table 2, entry 1). Increasing the amounts of Pd(OAc)$_2$ was not also successful for the reaction to proceed (Table 2, entries 2–4). Surprisingly, addition of agarose hydrogel to the reaction mixture put an excellent impact on the reaction. The homocoupling reaction of 4-iodoanisole in the presence of 1 mol% of Pd(OAc)$_2$ and agarose hydrogel (0.05 g) proceeded within 48 h to give 70% (GC) of the product (Table 2, entry 5). Increasing the amount of the catalyst to 2 mol% was accompanied with a quantitative conversion 4-iodoanisole (GC) to the homocoupled product in 1.5 h (Table 2, entry 6). Increasing the amounts of Pd(OAc)$_2$ did not affect noticeably the yields and the rates of the reaction. The results are summarized in Table 2.

In order to indicate the general application and the merit of this catalytic system for C–C bond formation, first we have applied it for reductive homocoupling reaction of a wide variety of aryl halides including the chlorides with success.

Substrates with electron-donating or electron-withdrawing functional groups afforded good yields of the desired products. The nature of the halides substituted on the aromatic rings affects the rates of the reaction and the sequence of the reactivity follows; I > Br > Cl (Table 3). However, the reductive homocoupling of aryl halides (I and Br) substituted with a nitro group was a rather difficult task and proceeded in longer reaction times. The reaction of an aryl chloride substituted with nitro group under similar reaction condition was failed completely (GC).

We have also scaled up the reaction of 4-iodoanisole (2.34 g, 10 mmol) in the presence of Pd(OAc)$_2$ (0.044 g, 20 mol%), NaOH (6 g, 15 mmol), agarose (0.5 g) at 90 °C. The reaction proceeded well within 2 h producing the desired biphenyl compound in 75–78% isolated yield.

However, we have also shown that by using this catalytic system, isolation of the pure product can be performed under highly green process. For this purpose, the reaction of 4-iodoanisole as a model compound was performed to completion under the optimized reaction conditions as discussed in the preceeding paragraphs. The hot reaction mixture was immediately filtered through

a thick cellulose paper which adsorbs the Pd–agarose mass. The resulting filter cake was washed with hot water. Combination of the filtrates followed by cooling gave the pure white crystals of 4,4′-dimethoxybiphenyl in a high yield.

In order to show the more application of this catalytic system in water, the homocoupling reaction of β-bromo styrene and phenylboronic acid under similar reaction conditions have been also presented. The reactions were performed well as shown in Schemes 1 and 2 and the desired coupled products were isolated in 80–85% and 75–80%, respectively.

By applying this catalytic system, we have also investigated the homocoupling reaction of phenylacetylene as a model compound for the coupling of terminal acetylenes in water at 90 °C. The reaction was performed well with a high isolated yield (75%) within 12 h as shown in Scheme 3.

In order to show that the catalyst acts heterogeneously in the reaction mixture, we have used the hot filtration test [37]. For this aim, we have studied the homocoupling reaction of iodobenzene under the above mentioned optimized conditions. The hot reaction mixture was filtered after 20% conversion of iodobenzene (GC)
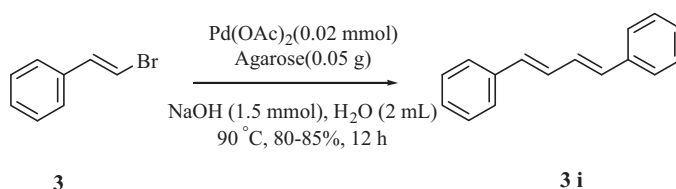

Scheme 1. Homocoupling reaction of β-bromo styrene in the presence of agarose hydrogel containing Pd(OAc)$_2$ in water using NaOH as a base.
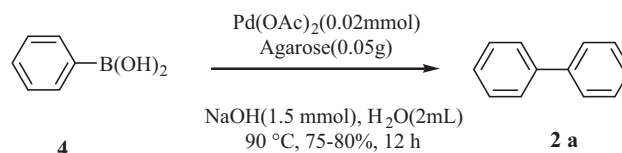
Scheme 2. Homocoupling reaction of phenylboranic acid by agarose hydrogel containing Pd(OAc)$_2$ in water using NaOH as base.
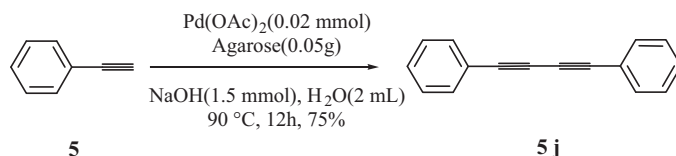
Scheme 3. Dimerization of phenylacetylene catalyzed by agarose hydrogel and Pd(OAc)$_2$ using NaOH in water.

Table 3
Homocoupling reaction of different aryl halides (I, Br, Cl) by $Pd(OAc)_2$ in the presence of agarose hydrogel using NaOH in water
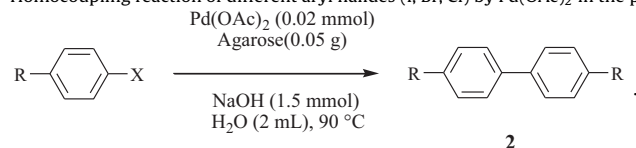
Entry	Aryl halide	Product	Time (h)	Isolated yield (%)[a]
1	1a	2a	1.5	96
2	1b	2b	3	85
3	1c	2c	18	68
4	1d	2d	1.5	85
5	1e	2a	3	91
6	1f	2b	6	87
7	1g	2c	18	62
8	1h	2h	3	89
9	1i	2i	4	91
10	1j	2j	16	56
11	1k	2k	2	91
12	1l	2a	24	83
13	1m	2b	24	80
14	1n	2h	24	86

[a] *Reaction conditions*: substrate (1.0 mmol), agarose (0.05 g), NaOH (0.6 g, 1.5 mmol) and $Pd(OAc)_2$ (0.0044 g, 0.02 mmol) at 90 °C.

to remove the Pd catalyst. Continuation of the reaction upon the resulting filtrate under the same conditions showed 35% conversion (GC) of iodobenzene after 4 h. This result shows that the amount of leaching of the catalyst into the reaction mixture should be low and confirms that the catalyst acts heterogeneously in the reaction. Quantitative measurement of the amount of Pd leached into the homocoupling reaction mixture of iodobenzene was determined by ICP analysis to be <3.5% after completion of the reaction.

Recycling of the catalyst is an important process from different aspects such as environmental concerns, costs of the catalyst and its toxicity. However, Pd salts are expensive, some of them are toxic, which makes the amounts of their leaching into the reaction

mixture a serious worry. Therefore, we studied the recycling of the Pd-supported agarose hydrogel for the homocoupling reaction of 4-iodoanisole. The reaction was allowed to proceed under optimized conditions as described in the preceeding section. After completion of the reaction and cooling the mixture to room temperature, a dark gelatinous mass was accumulated at the bottom of the reaction vessel. Upon addition of diethyl ether to the resulting jelly accumulation, two distinct phases were produced. The organic phase was decanted and the amount of the leached Pd form the agarose hydrogel core into the decanted ethereal solution was measured by ICP and atomic absorption analysis to be <3.5%. This amount of leaching makes this catalytic system suitable for the reactions conducted

Table 4

Recycling of the Pd-supported agarose hydrogel catalyst for homocoupling reaction of 4-iodoanisole in water at 90 °C using NaOH as base
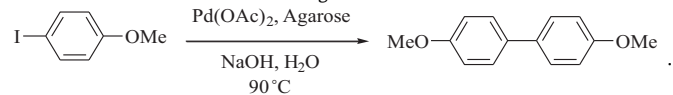
Run	Time (h)	Conversion % (GC)
1	1.5	100
2	2	100
3	2	100
4	3.5	100

in water. The leaching amounts of Pd also show that the agarose hydrogel has a high ability to entrap palladium in a good quantity without remarkable amounts of discharge of the Pd species into the reaction media. The resulting dark agarose hydrogel mass obtained after washing with diethyl ether was reused for another batch of the reaction. This process was repeated for four runs. As shown in Table 4, the catalytic activity of Pd-supported agarose hydrogel catalyst has been preserved to some extent during the recycling process.

4. Conclusion

In this study, a new protocol for carbon–carbon bond formation *via* homocoupling reaction of using different aryl halides including aryl chlorides in the presence of Pd(OAc)$_2$ as the pre-catalyst and agarose hydrogel as a reductant, support and bioorganic ligand in water at the temperatures <100 °C is discussed. Agarose is a naturally occurring polysaccharide, which is cheap, soluble in hot water, nontoxic and degradable in nature. All these make agarose hydrogel an attractive and a highly green material for conducting useful carbon–carbon bond formation using versatile substrates as reported in this article. In addition to the homocoupling reactions of aryl halides, important high yielding homocoupling reactions of β-bromo styrene, phenylboronic acid and phenylacetylene using this catalytic system have been conducted in the presence of this catalyst. The protocol has been also applied for a large-scale operation in which a high yield of the product was obtained. This catalyst is also a recyclable system. The leaching of Pd species into the reaction mixture was found to be rather small amounts <3.5%.

Acknowledgments

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2011.08.010.

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