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ARTICLE

Proline-functionalized chitosan-palladium (II) complex, a novel nanocatalyst for C-C bond formation in water

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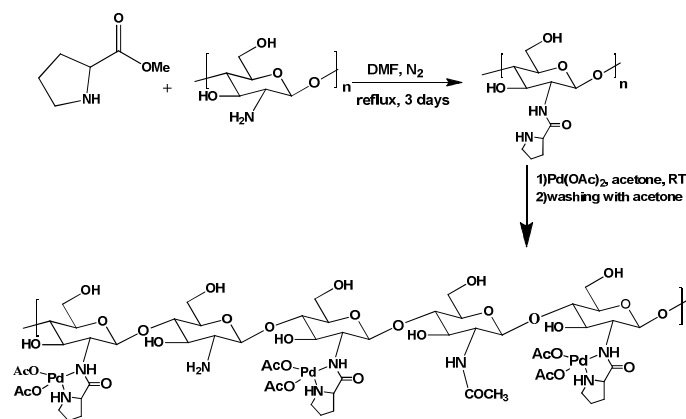
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An environmentally friendly palladium-based catalyst supported on proline-functionalized chitosan was successfully prepared and evaluated as heterogeneous nanocatalyst in Suzuki cross-coupling reaction of various aryl halides and phenylboronic acid. The resultant catalyst was characterized by FT-IR, FE-SEM, TEM, XRD, SEM-EDX, ICP and TGA techniques and exhibited reasonable catalytic activity in the reaction system and the substituted biaryls were produced in good to excellent yields. In addition, the catalyst could be recovered in a facile manner from the reaction mixture and recycled for the several times.

Introduction

In recent years, many efforts have been focused on development of green chemistry in the synthesis routes which minimize contamination and pollution in chemical synthesis. The goal is following usage of green reagents in producing materials. To reach these goals, greatly active immobilized metal catalysts^{1–3} were used to meaningfully facilitate these reactions. The heterogeneous catalyst is often readily removed by filtration and can be successfully recycled several times. Polysaccharides have been widely applied as a suitable architecture for solid catalysts. Chitosan (CS), the N-deacetylated derivative of chitin, is a sample of such polysaccharides that is widely spread in living organisms. Due to the presence of a free-amino group, CS and its Schiff-base derivatives are considered to be proper solid supports for the immobilization of a metal catalyst⁴. A limiting issue in the consuming of CS is poor chemical resistance and mechanical strength, which significantly reduces the recycle life of this biopolymer. Physical and chemical modifications have been used to modify fresh CS properties. In order to improve pore size, mechanical strength, chemical stability, hydrophilicity and biocompatibility, modifications using cross-linking agents such as glutaraldehyde, epichlorohydrin, diisocyanates or ethylene glycol glycidyl ether have been reported^{5–13}. Amino acids, pyridine, alkaloids, biguanidine and piperidine are one of the most supported on solid substrates nanocatalysts^{14–19}. Proline is a green and applicable amino acid in the catalytic systems²⁰ especially for modification of various supports. These days, there are widespread trend to the use of modern heterogeneous nanocatalysts based on using amino acids such as proline²¹ for modifications and also using CS as a green support for

preparation of a heterogeneous nanocatalyst. All of these procedures result in faster times and lower temperatures and greener media, in comparison with conventional investigations, and definitely cause to form a brilliant nanostructure^{22,23}. In continuation of our recent investigations on the synthesis and applications of palladium-based catalysts²⁴, we present a novel synthetic method for the preparation of CS–proline–Pd (II) complexes in the state of a recyclable solid catalyst. (Scheme 1)



Scheme 1 The nanocatalyst preparation

The NH₂ functional group in CS was reacted with esterified proline and therefore proline-functionalized chitosan is formed via an amid-bond formation. Then, the resultant proline-functionalized chitosan was treated with Pd(OAc)₂ to form the complex shown in scheme 1.

The synthesis of CS-supported Pd (II) has already been reported in the literature as well as CS-imine derivatives used in

C–C coupling reactions^{25,26}. A study on the structure of CS supported ligand-free Pd (II) has already been reported²⁷ and, as far as we searched, only a few reports refer to their application in coupling reactions especially by employing amino acids such as proline²⁸.

The palladium-catalyzed Suzuki cross-coupling reaction is a considerable method for Carbon–Carbon bond formation, especially for the synthesis of biaryl derivatives compounds, which are used as the building blocks for most of the natural products, pharmaceuticals and advanced materials²⁹. Phosphine ligands are so toxic and sensitive to air and moisture^{30,31}, so phosphine free catalyst are so valuable.

Result and Discussion

In Fig. 1a, the XRD pattern shows that palladium (II) complexes spread on the amorphous modified-chitosan support. By the SEM-EDX analysis the presence of palladium in the catalyst was approved (Fig 1b).

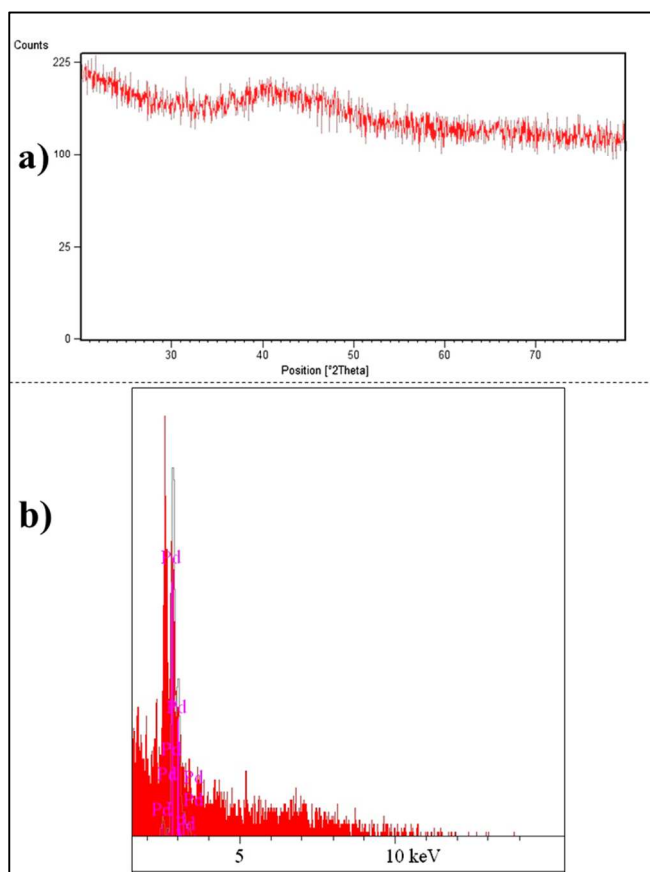


Fig.1 XRD pattern (a) and SEM-EDX spectrum (b) of the CS-proline-Pd (II) complex

Field emission scanning electron microscopy (FE-SEM) images in Fig. 2 demonstrate the phase morphology of CS-proline-Pd (II). Fig. 3 shows the TEM (Transmission Electron

Microscopy) images of catalyst. TEM micrographs show the distribution of particles and confirm that the nano-sized particles have been well distributed throughout the polymer matrix. The black spots and translucent parts show nanoparticles and polymer, respectively.

The palladium amount of the catalyst was 2 wt%, which was determined by ICP technique. We proposed that the complex is formed randomly on the support surface between CS-proline and Pd (II) ions and this helps the system to make a better nanostructure.

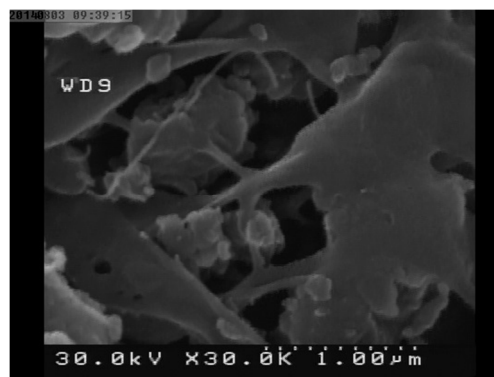


Fig.2 FE-SEM image of CS-proline-Pd (II) complex

The TGA thermograms of weight loss as a function of temperature for CS-proline-Pd (II) nanocatalyst is shown in Fig. 4. The TGA analysis results illustrate that the catalyst is stable over 200 °C and a total of 52.7% weight loss is due to the decomposition of polysaccharide chain.

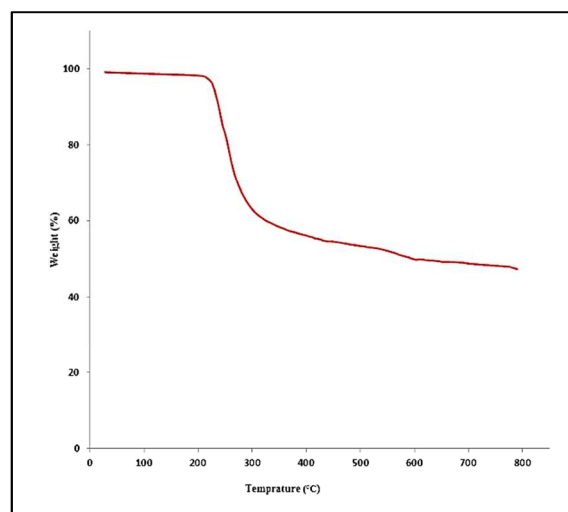
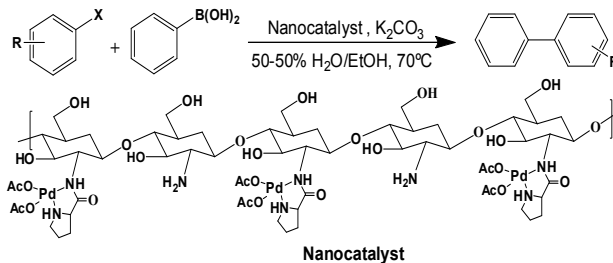


Fig.4 TGA thermogram

To explore the activity of the nanocatalyst, we use it in Suzuki cross-coupling reaction (Scheme 2). The reusability of

nanocatalyst was investigated, too. A model reaction with 4-bromonitrobenzene with phenylboronic acid was used to optimize reaction conditions. The catalytic activity of the catalyst with different amounts of catalyst was studied and comparable yields were obtained (Table 1).



Scheme 2 Suzuki cross-coupling reaction by CS-proline-Pd (II)

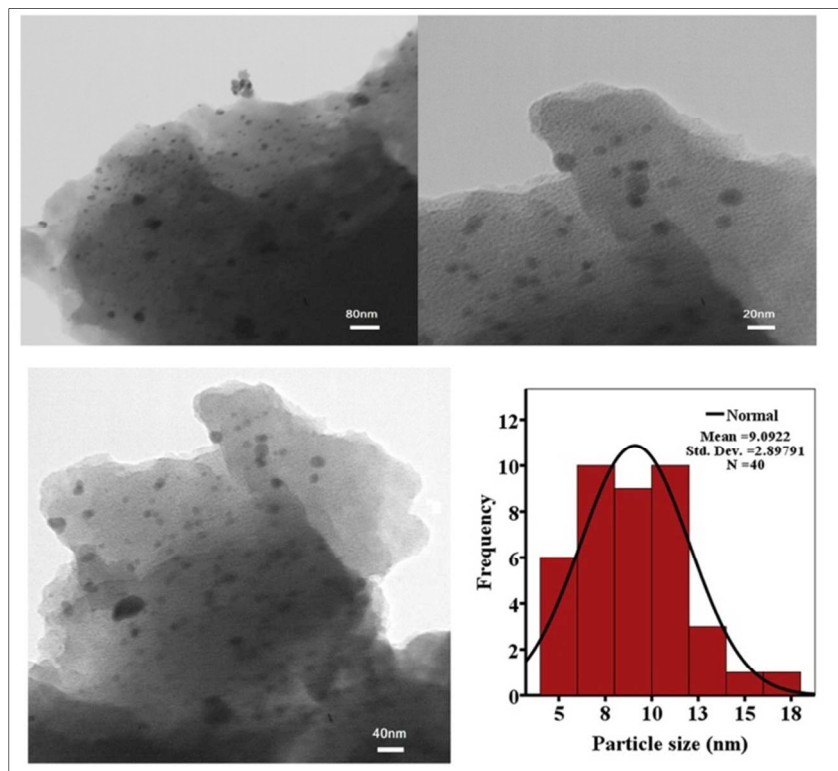


Fig.3 The TEM image of CS-proline-Pd (II) complex

Table 1 Optimization of main parameters in Suzuki cross-coupling reaction by CS-proline-Pd (II) nanocatalyst^a

Entry	Solvent	Temperature (°C)	Base	Catalyst mol %	Time (min)	Yield ^b
1.	PEG-200	70	K ₂ CO ₃ (1eq)	0.8	40	97
2.	CH ₃ OH	70	K ₂ CO ₃ (1eq)	0.8	30	80
3.	EtOH/H ₂ O (1:1)	70	K ₂ CO ₃ (1eq)	0.8	47	99

4.	H ₂ O	70	K ₂ CO ₃ (1eq)	0.8	45	99
5.	EtOH/H ₂ O (2:1)	70	K ₂ CO ₃ (1eq)	0.8	50	88
6.	EtOH/H ₂ O (1:2)	70	K ₂ CO ₃ (1eq)	0.8	56	73
7.	EtOH/H ₂ O (1:1)	70	KOH (1eq)	0.8	35	81
8.	EtOH/H ₂ O	70	Na ₂ CO ₃	0.8	55	87

	(1:1)	(1eq)				
9.	EtOH/H ₂ O	K ₂ CO ₃	0.8	60	45	
	(1:1)	(0.5eq)				
10.	EtOH/H ₂ O	K ₂ CO ₃ (2eq)	0.8	50	88	
	(1:1)					
11.	EtOH/H ₂ O	K ₂ CO ₃ (1eq)	0.8	50	40	
	(1:1)					
12.	EtOH/H ₂ O	K ₂ CO ₃ (1eq)	0.8	60	80	
	(1:1)					
13.	EtOH/H ₂ O	K ₂ CO ₃ (1eq)	0.4	47	100	
	(1:1)					
14.	EtOH/H ₂ O	K ₂ CO ₃ (1eq)	0.2	47	91	
	(1:1)					
15.	EtOH/H ₂ O	K ₂ CO ₃ (2eq)	0.4	47	97	
	(1:1)					

^a Reaction condition: 4-bromonitrobenzene (1mmol), phenylboronic acid (1.2mmol), CS-proline-Pd (II) catalyst, solvent (4 ml).

^b GC yield

We investigated efficiency of the different bases in Suzuki reaction (Table 1, entries 6-8). Among the selected bases, K₂CO₃ was found to be the most effective base. Several different solvents were examined, among the tested solvents 1:1 mixture of H₂O/EtOH gave the best result. We also optimized the catalyst concentration, employing various amounts of catalyst for this cross coupling reaction. The best result was obtained when the Suzuki coupling reaction was carried out with 0.4 mol % of catalyst (Table 1, entry 13). Temperature also was optimized for this catalytic system and 70 °C was selected for showing the best result in which the reaction time of the model reaction, was significantly reduced in comparison with other reports³².

The optimized parameters were applied to the reaction of various aryl halides with phenylboronic acid. the result is on table 2. The electronic effects on yields and conversion times of the reactions were examined. The nanocatalyst was compatible with a wide range of functional groups.

Aryl halides with electron donating group in comparison with aryl halides with electron withdrawing group have shown better conversions in shorter reaction time. As shown in Table 2, aryl halides with the leaving group of iodide react faster than aryl bromides (Table 2. entries 1, 2). Aryl bromides required longer reaction times and less yields were obtained.

The achievability of recycling the catalyst also examined. After the reaction the catalyst was simply recovered by filtration and washed with water and acetone, then dried at room temperature

and used in the next catalytic cycle according to the optimized conditions. However, no significant decrease of activity was observed until the fifth reuse.

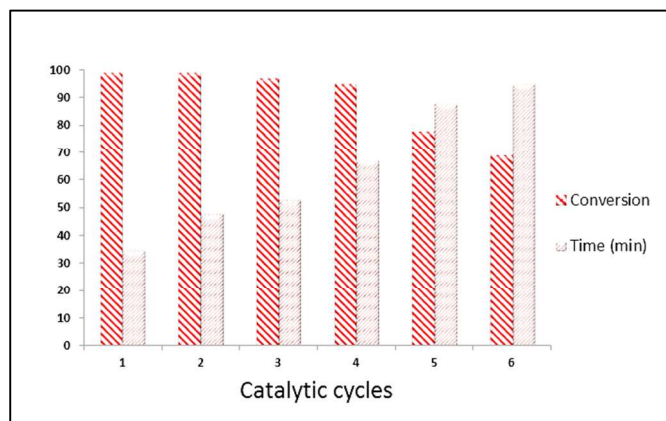


Fig.5 Reusability of CS-proline-Pd (II) catalyst

The supported-Pd nanocatalyst exhibited moderate activity in the Suzuki cross-coupling reactions in aqueous ethanol solvent. This catalyst displayed good activity at low Pd loading and in aqueous media. The chitosan modified by amino acid environment plays an essential stabilizing role for the supported catalysts in the coupling reactions. The heterogeneous catalyst could be easily separated and recovered from the reaction mixture (by filtration) and reused several times. The combination of advantages displayed by the supported catalysts such as: ease of preparation, reasonable catalytic activity, stability, reusability and versatility prove that this catalyst should be considered as a viable alternative in cross-coupling reactions on efficiency, environmental stewardship and economical grounds.

Only as a catalyst reservoir, the use of chitosan beads allowed loading of palladium because of the ability of metal ion sorption capacity of chitosan.

Experimental

All chemical reagents were purchased from Merck and were used without further purification. Chitosan was purchased from Acros Organics and its molecular weight was 100000-300000. ¹H-NMR spectra were recorded on a Bruker 400 spectrometer using tetramethylsilane as an internal standard in CDCl₃ and FT-IR spectra were obtained as KBr pellets on a JASCO 680-Plus spectrophotometer. Also we used gas chromatography (GC) (BEIFIN 3420 gas chromatograph equipped with a Varian CP SIL 5CB column: 30 m, 0.32 mm, 0.25 mm), field emission scanning electron microscopy [FE-SEM, HITACHI (S-4160)], Inductive coupled plasma Perkin Elmer Optima 7300 DV, for examination of reactions conversions.

General procedure for Suzuki cross-coupling reaction by CS-proline-Pd (II) nanocatalyst

The aryl halides (1 mmol) and the phenylboronic acid (1.1 mmol, 0.13 g) were dissolved in H₂O/EtOH 50:50 (4 ml). CS-proline-Pd (II) nanocatalyst and K₂CO₃ (1 mmol, 0.14 g) were added. The mixture was stirred at 70 °C (see Table 1) by conventional heating. The mixture was stirred continuously during the reaction and monitored by both TLC and GC. After the reaction was completed, the mixture was cooled to room temperature, 30 ml water was added and the product was extracted with n-hexane (3*10 ml). The organic phase was dried over CaCl₂, concentrated under vacuum and purified by column chromatography on silica gel (n-hexane:EtOAc, 9:1). The products were characterized by comparing their melting point, FT-IR spectra, ¹H-NMR spectra with those reported in the literature³³.

General Procedure for the synthesis of chitosan modified by methyl proline (CS-proline)

Methyl proline (5 mmol, 0.64 g) and chitosan (0.5 g) in DMF (20 ml) in a round-bottom flask refluxed for 3 days under N₂ atmosphere. The reaction mixture was cooled down to room temperature followed by filtration to produce the proline-functionalized chitosan. After that, the product was collected, washed with methanol several times to remove the impurities and dried.

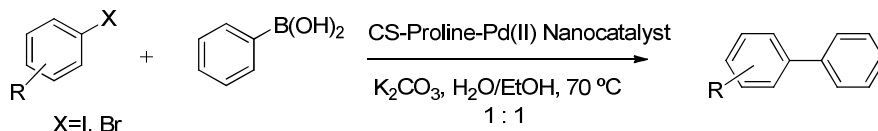
General procedure for synthesis of CS-proline-Pd nanocatalyst

The proline-functionalized chitosan (0.026 g) and Pd(OAc)₂ (0.02 g) in 10 ml acetone in a round-bottom flask, stirred for 3 days. Then, the powder was filtered and washed with acetone. The CS-proline-Pd (II) catalyst was obtained as a brown powder.

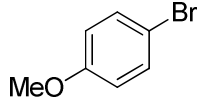
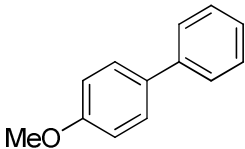
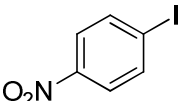
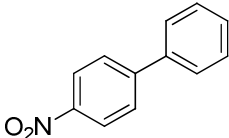
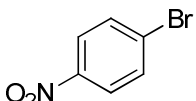
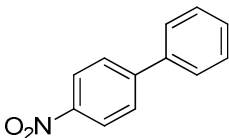
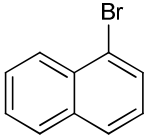
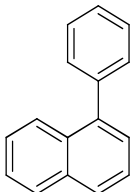
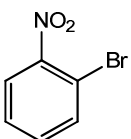
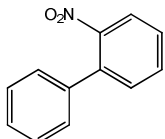
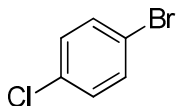
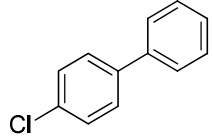
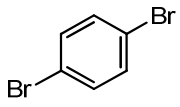
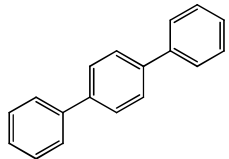
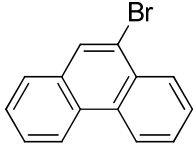
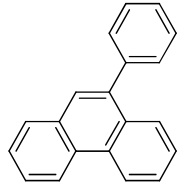
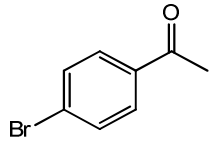
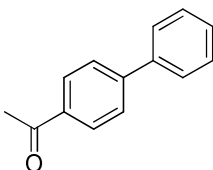
Conclusions

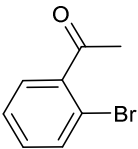
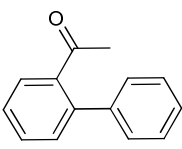
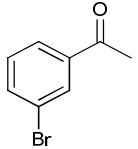
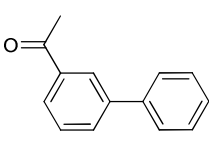
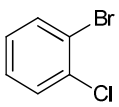
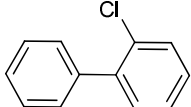
In this work we have reported the use of a chitosan-Proline-Pd(II) complex nanocatalyst for the Suzuki coupling carried out in aqueous media. Excellent yields have been achieved in relatively short reaction times on a wide array of iodo- and bromo-arenes bearing both electron-donating and electron-withdrawing groups. The gradation of the aryl bromide conversion slightly depended on the electronic effect of substituent in para position to the bromine. Remarkably advantageous condition like the low catalyst loading, the use of eco-friendly support (chitosan) and green solvent provide to the method great benefits in terms of safety, economy and sustainability. In addition, the use of water as an additive proved to be particularly advantageous for its ability to dissolve boron side-products coating the catalyst surface. Consequently, we believe that it can compete with the most efficient known protocols, and due to its simple operating procedure we can anticipate that it will find wide applicability. Further application of this new catalytic system is under investigation in our laboratory.

Table 2. Suzuki cross-coupling reaction of various aryl halides with phenylboronic acid by Cs-proline-Pd (II) nanocatalyst



Entry	Aryl halide	Product	Time (min)	Yield ^b
1			8	100
2			30	100
3			36	99

4			60	81
5			10	100
6			30	100
7			39	100
8			3h	89
9			40	99
10			60	89
11			60	93
12			53	95

13			69	68
14			60	87
15			69	85

^a Reaction condition: aryl halide (1mmol), phenylboronic acid (1.2mmol), K₂CO₃ (1mmol), 1:1 EtOH/H₂O (4 ml), CS-proline-Pd (II) catalyst 0.4 mol%, 70 °C.
^b GC yield

Acknowledgements

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References and Notes

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Characterization data of products. See DOI: 10.1039/b000000x/

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