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### **ORIGINAL ARTICLE**

# Adsorption of Cu<sup>2+</sup> by modified chitosan microspheres and its application in homocoupling of arylboronic acid



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#### KEYWORDS

Chitosan; Microspheres; Arylboronic acids; Copper acetate-catalyzed; Homocoupling **Abstract** The C—C bond coupling reactions have a wide range of applications in the synthesis of natural substances and the synthesis of physiologically active compounds. We first prepared modified chitosan microspheres by emulsification and investigated the performance of the chitosan adsorbent for the adsorption of copper ions. We then evaluated the catalytic performance of chitosan-supported copper microspheres in the self-coupling of arylboronic acids using 4-methoxybenzene as the model substrate, while exploring a wide range of substrates including aryl boronic acid derivatives and heterocyclic arylboronic acids, including aldehyde, nitro, and aldehyde groups. The experimental results show that good to excellent yields (55%-95%) of the desired dimer products were obtained under mild conditions at room temperature and in air, and the catalytic material could be reused up to five times with no significant decrease in catalytic activity. © 2022 The Author(s). Published by Elsevier B.V. on behalf of King Saud University. This is an open

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#### 1. Introduction

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Many functional molecular materials and natural products often contain symmetrical diaryl structural units in their structure (Miyaura and Suzuki, 1995; Horton et al., 2003). Aryl-aryl coupling reaction is currently the most direct and efficient method for the synthesis of symmetrical aryl compounds (Alimardanov et al., 2004; Alberico et al., 2007). The main aryl-aryl couplings are the Suzuki-type reaction (Leadbeater and Marco, 2003; John et al., 2006; Kanchana et al., 2020) and the Ullmann-type reaction (Sun et al., 2018; Cai and Zhou, 2020).

Due to their stability and low toxicity, arylboronic acids have become the reagent of choice for aryl-aryl coupling in recent years and were widely used in the preparation of biphenyl compounds

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(Cravotto et al., 2005; Yang et al., 2008; Zhou et al., 2020; Osakada and Nishihara, 2022). Most studies on the self-coupling reactions of arylboronic acids have been catalyzed by noble metals, such as Pd (Adamo et al., 2006; Guo et al., 2015; Xu et al., 2018), Au (Zhang et al., 2010; Parida et al., 2011; Primo and Quignard, 2010; Sophiphun et al., 2012; Reddy et al., 2021), Rh (Vogler and Studer, 2008), and Ni (Percec et al., 1995; Guyu et al., 2006). Among these transition metals, the metal Pd has been the focus of research due to its low dosage, good reaction selectivity, and high product yields. Wong et al. (Wong and Zhang, 2001) have obtained arylboronic acid dimerization under alkaline conditions using Pd(OAc)<sub>2</sub> as a catalyst and phosphine or phosphite as a ligand. Mitsudo et al. (Mitsudo et al., 2009) have also found in the presence of Pd(OAc)<sub>2</sub>/TEMPO, several biaryls were obtained in good yields under mild conditions. Due to the disadvantages of organic solvents such as toxic, volatile, and flammable, more researchers have adopted green solvents to replace traditional organic solvents. Xu et al. (Xu et al., 2008) took the choice of acetone/water (v/v = 1:1) as the reaction solvent, symmetrical biaryl compounds were obtained at room temperature and without ligands. It was also observed that oxygen could increase the yield of the reactants. Zhou et al. (Zhou et al., 2007) have carried out homogeneous coupling experiments with arylboronic acids using supercritical carbon dioxide as a solvent in the presence of palladium chloride as a catalyst. Palladium-catalyzed systems require the use of organic ligands to facilitate the reaction, leading to higher catalyst costs and difficulties in subsequent processing, limiting their application in the preparation of biaryl compounds.

Compared to the metal Pd, the metal Cu and its salts are of increasing interest due to their wide availability, low cost, and mild reaction conditions (Chemler, 2015; Allen et al., 2013). There have been many reports (Kirai and Yamamoto, 2009; Cheng and Luo, 2011; Kaboudin et al., 2011; Puthiaraj et al., 2014; Raul et al., 2015; Cao et al., 2017; Long et al., 2019; Yuan et al., 2019; Das et al., 2020) on the homologous coupling reactions of arylboronic acids by copper under mild conditions. And most studies have shown that the presence of oxygen is essential to the reaction. However, some issues such as catalyst residues, separation, and poor catalyst recovery have not been addressed in these reports. Chitosan (Mourya and Inamdar, 2008; Kou et al., 2021; Ambaye et al., 2022) is a natural macromolecule obtained by the removal of acetylation from chitin. Its molecular structure is rich in functional groups such as hydroxyl or amino groups, which can be effectively coordinated with metal ions, making it an excellent carrier for metal catalysts (Corma et al., 2007; Kayser et al., 2014; El Kadib, 2015). Chitosan can be easily modified by chemical or physical methods to prepare chitosan derivatives such as microspheres (Liao et al., 2021), membranes (Lou et al., 2022), gel beads (Zhao et al., 2007), hollow fibers (Zailani et al., 2021), etc. These physicochemical methods can increase the strength of chitosan and improve the affinity of the adsorbent for metals. Chitosan loaded with metals has the advantages of both homogeneous and multiphase catalysts: high stability, low corrosion, multiple recycling, and recovery of the metal can be solved by biodegradation or incineration. Up to date, several chitosan-supported copper catalysts with high catalytic performance have been developed and applied to different coupling reactions. The C-S coupling reaction of aryl halides with sodium sulfate has been catalyzed by Chao et al. (Shen et al., 2014) using a chitosan@Cu(OAc)<sub>2</sub> catalyst for the synthesis of aryl sulfones. Motahharifar et al. (Motahharifar et al., 2020) prepared tetrazolium compounds by the coupling reaction of cyanide with sodium azide using Cu NPs@Fe<sub>3</sub>O<sub>4</sub>-Chitosan as the catalyst. Chutimasakul et al. (Chutimasakul et al., 2020) have prepared a spherical copper/chitosan bead material with a narrow size distribution that can be efficiently synthesized as an imine by the oxidative self- and cross-coupling of amines. So far the use of chitosan-supported inexpensive copper catalysts for the self-coupling reaction of arylboronic acids has not been reported (Primo and Quignard, 2010; Sophiphun et al., 2012; Reddy et al., 2021).

The development of a simple, effective, and catalytic self-coupling of arylboronic acids is an interesting topic. Zhong et al. (Zhou et al., 2020) have reported the synthesis of a series of symmetrical diaryl compounds from arylboronic acids using palladium salts as catalysts and glucose-substituted imidazole as ligands (Scheme 1a), although in yields up to 98 %, the ligands were complex and expensive. Chun et al (Yuan et al., 2019) have improved the performance of coppercatalyzed (hetero)arylboronic acids with natural ligands (Scheme 1b), but the experimental procedure was more complicated. Cao et al (Guo et al., 2015) have achieved a ligand-free, rapid (15 min reaction time) synthesis of diarylboronic acids (Schemelc) using copper chloride, but the catalyst could not be recycled. Based on the reusability of chitosan-loaded copper catalysts, we tried to use them for the coupling reaction of arylboronic acids using the method of Scheme 1d. Firstly, we have prepared 2-pyridine carboxaldehyde modified chitosan microspheres using an emulsion dispersion method, then investigated the adsorption properties of chitosan microspheres on copper acetate. and finally investigated the catalytic and recovery properties of selfcoupling reactions on arylboronic acids using chitosan loaded with copper acetate as a catalyst.(See Scheme 2.).

#### 2. Materials and methods

#### 2.1. Materials

Chitosan (viscosity, 200–400 mPa.s, deacetylation > 95 %), Span 60 (AR), Tween 60 (AR), n-Hexane (AR), MeOH (AR), EtOH (AR), THF (AR), Pyridine-2-carbaldehyde (AR), Acetic acid (AR), Cu (AR), Cu(OH)<sub>2</sub> (AR), CuCl (AR), CuCl<sub>2</sub> (AR), Cu(OAc)<sub>2</sub> (AR), CuSO<sub>4</sub> (AR), NaOH (ACS), Na<sub>2</sub>CO<sub>3</sub> (AR), K<sub>2</sub>CO<sub>3</sub> (AR), Cs<sub>2</sub>CO<sub>3</sub> (AR), (4methoxyphenyl)boronic acid (1a,98 %), (3-methoxyphenyl) boronic acid (1b,98 %), (2-methoxy)phenylboronic acid (1c,98 %), (2-ethoxyphenyl)boronic acid (1d,98 %), ptolylboronic acid (1e,98 %), (2-isopropylphenyl)boronic acid (1f,98 %), (4-(*tert*-butyl)phenyl)boronic acid (1 g,98 %), phenylboronic acid (1 h,98 %), (4-cyanophenyl)boronic acid (1i,98 %), (3-cyanophenyl)boronic acid (1j,98 %), (4formylphenyl)boronic acid (1 k,98 %), (3-acetylphenyl) boronic acid (1 1,98 %), (3-nitrophenyl)boronic acid (1 **m**,98 %), (4-(trifluoromethyl)phenyl)boronic acid (1n,98 %), (5-fluoro-2-methylphenyl)boronic acid (10,98 %), (2-chloro-5-methylphenyl)boronic acid (1p,98 %), (5-chloro-2 -methoxyphenyl)boronic acid (1q,98 %), (2-chlorophenyl) boronic acid (1r,98 %), naphthalen-1-ylboronic acid (1 s,98 %), (2-fluoropyridin-3-yl)boronic acid (1 t,98 %), (2chloropyridin-3-yl)boronic acid (1u, 98)%), (2methoxypyridin-3-yl)boronic %), (1v,98 (2acid methoxypyridin-4-yl)boronic acid (1w,98 %), thiophen-3ylboronic acid (1x,98 %). All of the above reagents were purchased from Energy Chemical. Copper standard solutions (NCS testing technology Co. ltd).

#### 2.2. Analytical methods

FTIR spectra of chitosan were obtained using a Nicolet iS5 spectrophotometer (Thermo, USA) to study the structure of the substance. Scanning electron microscopy (JEOL, JSM-6510, Japan) was used to test the morphology of the modified chitosan microspheres. X-ray photoelectron spectroscopy (XPS, ESCALAB 250xi, Thermo, USA) was used to obtain the interaction of the catalyst copper with chitosan. ICP-OES (IRIS Intrepid II, Thermo) was used to test the concen-

Report work: Pd or Cu catalyzed the homo-coupling reaction of arylboronic acids (ref. 12, 38, and 15) (a) cat. Pd<sub>2</sub>(dba)<sub>2</sub>, NaClO, Ligands,3h\_



This work: Chitosan Microspheres-supported copper catalyzed the homo-coupling of arylboronic acids



Scheme 1 Pd or Cu catalyzed the homo-coupling reaction of arylboronic acids.



Scheme 2 Self-coupling reaction of 4-Methoxyphenylboronic acid.

tration of copper in the solution. NMR (Bruker Avance III 400 Hz, Germany) was used to verify the structure of the products.

#### 2.3. Synthesis of chitosan microspheres

The process of preparing modified chitosan microspheres was referred to in literature (Leonhardt et al., 2010; Hussain et al., 2012). We first dissolved a certain amount of chitosan in 1 % acetic acid solution, then slowly added hexane solution containing Tween-60, and Span-60 under high-speed stirring to form a stable emulsion, and finally added 2-pyridine carboxaldehyde

solution and stirred at 40 °C for 8 h. After stopping the reaction, the chitosan was filtered, washed, and dried under a vacuum to obtain modified chitosan microspheres.

#### 2.4. Adsorption kinetics experiments

Standard Cu<sup>2+</sup> solutions of 20 mg/L-100 mg/L were prepared and the pH of the solution was adjusted with 0.1 mol/L dilute hydrochloric acid. 40 mg of chitosan microspheres (PCS) were accurately weighed and added to 20 mL of the solution. The solution was then shaken at 200 r/min at room temperature. After the adsorption was completed, the solution was left to stand for 1 h. The upper liquid layer was taken, and the residual Cu<sup>2+</sup> concentration in the solution was determined by ioncoupled mass spectrometry.

The adsorption percentage and adsorption capacity are shown in equation (1) and equation (2), respectively.

Adsorption 
$$\% = \frac{(C_0 - C_l)}{C_0} \times 100\%$$
 (1)

Entry	pН	Original concentration ( $C_0$ , mg/L)	Adsorption Time (min)	Residual concentration (mg/L)	Absorption percentage (%)	Absorption capacity (q <sub>t</sub> , mg/g)
1	5	20.01	180	1.09	94.6 %	9.46
2	5	41.15	180	1.32	96.8 %	19.92
3	5	61.20	180	1.92	96.9 %	29.64
4	5	80.13	180	2.34	97.1 %	38.90
5	5	99.98	180	2.77	97.2 %	48.61
6	5	99.98	5	58.72	41.3 %	20.63
7	5	99.98	10	46.22	53.8 %	26.88
8	5	99.98	20	27.25	72.7 %	36.37
9	5	99.98	30	13.30	86.7 %	43.34
10	5	99.98	60	5.22	94.8 %	47.38
11	5	99.98	90	4.02	96.0 %	47.98
12	5	99.98	120	2.61	97.4 %	48.69
13	5	99.98	150	2.65	97.3 %	48.67
14	5	99.98	240	2.70	97.3 %	48.64
15	5	99.98	300	2.65	97.3 %	48.67
16	2	99.98	180	93.31	6.70 %	3.34
17	3	99.98	180	38.42	61.6 %	30.78
18	4	99.98	180	12.55	87.4 %	43.72

 Table 1
 The adsorption capacity and adsorption rate of modified chitosan microspheres for Cu<sup>2+</sup>



Fig. 1 Adsorption of  $Cu^{2+}$  by PCS is consistent with the pseudo-second-order kinetic model.



Fig. 2 Scanning electron micrograph of PCS.

$$q_t = \frac{(c_0 - c_t) \cdot V}{m} \tag{2}$$

 $C_0$  = Initial concentration of Cu<sup>2+</sup> solution, mg/L.

 $C_t$  = Concentration of Cu<sup>2+</sup> in the solution at time t, mg/L.

m = the mass of chitosan microsphere, g,

V = Volume of Cu<sup>2+</sup> solution, L.

 $q_t$  = the momentary adsorption capacity, mg/g.

The pseudo-first-order equation and the pseudo-secondorder equation are shown in Equations (3) and (4), respectively.

$$\lg (q_e - q_t) = \lg q_e - \frac{k}{2.303}t$$
(3)

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^2} + \frac{t}{q_e} \tag{4}$$



Fig. 3 Infrared spectra of CS, PCS, and PCS@Cu<sup>2+.</sup>



Fig. 4 The electron binding energy of the N element of PCS and  $PCS@Cu^{2+}$ .

 $q_e$  = the equilibrium adsorption capacity, mg/g,

 $q_t$  = the momentary adsorption capacity, mg/g,

 $k_I$  = the pseudo-first-order equation rate constant, min<sup>-1</sup>.

 $k_2$  = the pseudo-second-order equation rate constant, L/ (min mol),

#### 2.5. Arylboronic acid self-coupling reaction

0.2 mmol 4-methoxyphenylboronic acid, 0.1 mmol of Na<sub>2</sub>CO<sub>3</sub>, and 10 mg (3.8 mol%) catalytic material were added to the reaction tube with methanol as the reaction solvent, and the reaction was carried out at room temperature for 2 h. After stopping the reaction, the extraction partition was carried out. The mixture was separated by column chromatography using a mixture of ethyl acetate and petroleum ether as the eluent (v: v = 1:80-1:20). The structure of the product was verified by NMR. 
 Table 2
 Optimization of PCS@Cu<sup>2+</sup> catalyzed homocoupling of 4-methoxy benzene acid

Entry	Catalyst	Solvent(2 mL)	Time(h)	Base	Yield (%)
1	Cu	MeOH	4	$Na_2CO_3$ (0.5 eq)	< 5 %
2	CuCl	MeOH	4	$Na_2CO_3$ (0.5 eq)	81
3	CuCl <sub>2</sub>	MeOH	4	$Na_2CO_3$ (0.5 eq)	93
4	$Cu(OAc)_2$	MeOH	4	$Na_2CO_3$ (0.5 eq)	90
5	CuSO <sub>4</sub>	MeOH	4	$Na_2CO_3$ (0.5 eq)	31
6	Cu(OH) <sub>2</sub>	MeOH	4	$Na_2CO_3$ (0.5 eq)	trace
7	_	MeOH	4	$Na_2CO_3$ (0.5 eq)	-
8	$PCS@ Cu^{2+}$	MeOH	4	$Na_2CO_3$ (0.5 eq)	91
9	$PCS@Cu^{2+}$	i-PrOH	4	$Na_2CO_3$ (0.5 eq)	17
10	$PCS@ Cu^{2+}$	H <sub>2</sub> O	4	$Na_2CO_3$ (0.5 eq)	trace
11	PCS@ Cu <sup>2+</sup>	THF	4	$Na_2CO_3$ (0.5 eq)	< 5 %
12	PCS@ Cu <sup>2+</sup>	EtOH	4	$Na_2CO_3$ (0.5 eq)	78
13	PCS@ Cu <sup>2+</sup>	MeCN	4	$Na_2CO_3$ (0.5 eq)	21
14	PCS@ Cu <sup>2+</sup>	MeOH	4	_	trace
15	PCS@ Cu <sup>2+</sup>	MeOH	4	$K_2CO_3$ (0.5 eq)	90
16	PCS@ Cu <sup>2+</sup>	MeOH	4	NaOH (0.5 eq)	trace
17	PCS@ Cu <sup>2+</sup>	MeOH	4	$CS_2CO_3$ (0.5 eq)	91
18	PCS@ Cu <sup>2+</sup>	MeOH	4	$Na_2CO_3$ (0.2 eq)	83
19	PCS@ Cu <sup>2+</sup>	MeOH	4	$Na_2CO_3$ (0.3 eq)	92
20	PCS@ Cu <sup>2+</sup>	MeOH	4	$Na_2CO_3$ (0.4 eq)	90
21	PCS@ Cu <sup>2+</sup>	MeOH	0.1	$Na_2CO_3$ (0.4 eq)	73
22	PCS@ Cu <sup>2+</sup>	MeOH	0.2	$Na_2CO_3$ (0.4 eq)	81
23	PCS@ Cu <sup>2+</sup>	MeOH	0.3	$Na_2CO_3$ (0.4 eq)	89
24	PCS@ Cu <sup>2+</sup>	MeOH	0.5	$Na_2CO_3$ (0.4 eq)	92
25	PCS@ Cu <sup>2+</sup>	MeOH	1.0	$Na_2CO_3$ (0.4 eq)	91

Reaction conditions: 1a (0.2 mmol), catalyst (3.8 mol%), base, solvent (2.0 mL), r.t., air.

#### 3. Results and discussion

#### 3.1. Dynamic adsorption of the modified chitosan microspheres

The effectiveness of the pyridine-2-carbaldehyde modified chitosan microspheres (PCS) in the adsorption of metal ions is shown in Table 1.  $Cu(OH)_2$  precipitation occurs at pH = 6 for 100 mg/L of  $Cu^{2+}$  and the carrier chitosan dissolves at high acidity. To eliminate the effect of precipitation and dissolution on adsorption, we have set the pH of the solution to take a range of values from 2 to 5.

Firstly, the adsorption capacity of chitosan microspheres (PCS) for copper ions was investigated by setting a gradient of Cu2+ concentration at room temperature for 180 min and adjusting the pH of the solution to 5 (Table 1, Entry 1-5). At an initial  $Cu^{2+}$  concentration of 100 mg/L, the adsorption rate of copper ions by 40 mg chitosan microspheres was 97.2 %. As shown in entries 5-15, the chitosan adsorption rate increases with increasing adsorption time. From the beginning to 30 min the adsorption rate was faster, after 30 min the adsorption slowed down, at 60 min the adsorption approached equilibrium, and at 120 min the adsorption equilibrium was reached. The whole adsorption process could complete within 120 min. The adsorption performance of modified chitosan microspheres to the pH of the solution is shown in entries 16-18. The performance of chitosan microspheres in adsorbing copper ions was significantly affected by different pH conditions. At pH = 2, the adsorption of PCS was only 3.34 mg/g. When pH = 3, the adsorption of PCS could rapidly increase to 30.78 mg/g, and when the pH of the solution was increased to 5, the adsorption increased to 48.67 mg/g. This phenomenon may be due to the competitive adsorption between  $H^+$  and  $Cu^{2+}$  in the solution (Ngah et al., 2011).

A pseudo-first-order reaction model and a pseudosecondary reaction mode were adopted to linearly fit the experimental data in Table 1, and the model equations are shown in equations (3) and (4). As shown in Fig. 1 and S1, the experimental data are more consistent with the pseudo-secondary reaction mode fit. According to the fitted model, the maximum adsorption capacity of the chitosan microspheres can reach 48.61 mg/g, which was close to the experimentally measured equilibrium adsorption capacity. The fitted results indicate that the diffusion of copper ions has a great influence on the adsorption process.

### 3.2. Scanning electron microscopy analysis of chitosan microspheres

We have characterized the catalyst structure of modified chitosan microspheres adsorbed with copper (100 mg/L). The morphology of the prepared modified chitosan microspheres (PCS) is shown in Fig. 2. Most of the chitosan microspheres were spherical in shape and the size of the microspheres was not uniform, ranging from 10 to 80 um in diameter, and a small number of the microspheres were broken.







Scheme 3 Gram scale synthesis of 2a and 2x.

## 3.3. Infrared absorption spectroscopy analysis of chitosan microspheres

The IR spectra of chitosan, modified chitosan (PCS), and modified chitosan with loaded copper ions (PCS@ $Cu^{2+}$ ) are shown in Fig. 3. The basic characteristic peaks of chitosan were present in all three plots. In Fig. 3b, a new sharp and strong peak at 1647 cm<sup>-1</sup> appeared, which should be the characteristic peak from the C=N bond (Yusong and Yonghong, 2001), proving the Schiff base reaction of chitosan with 2pyridine carboxaldehyde. The broadening of the peak near  $3270 \text{ cm}^{-1}$  for modified chitosan compared to chitosan, and the sharp peak near 2890  $\text{cm}^{-1}$  may be a stretching vibration of the C-H group near the C=N (Pawlak and Mucha, 2003). The peaks at 1575  $\text{cm}^{-1}$  and 775  $\text{cm}^{-1}$  may be vibrational absorption peaks of the pyridine ring. These data suggest that C=N was introduced into chitosan. In Fig. 3c, the intensity of the peak at 1640 cm<sup>-1</sup> becomes weaker, presumably due to the complexation of the C=N bond with the copper ion.

### 3.4. Study of the complexation site of modified chitosan with $Cu^{2+}$

Cu<sup>2+</sup> has free electron orbitals, while the N atom has a pair of electrons. If the interaction between Cu<sup>2+</sup> and N atoms was chemisorption, the electron binding energy of element N would increase (Biesinger et al., 2010), which was shown in the XPS spectrum as the peak position of the N element shifted to the right. As shown in Fig. 4, the electron binding energy of element N in PCS was 398.76 eV, while the binding energy of element N in PCS@Cu<sup>2+</sup> was 399.98 eV. The electron binding energy of element N increases after solid loading of  $Cu^{2+}$ , which indicates that the adsorption between N atom and  $Cu^{2+}$  in chitosan was chemisorption. It can also be seen from Fig. 3, the wave number of the pyridine ring shifted from 1647 cm<sup>-1</sup> to 1640 cm<sup>-1</sup> after the adsorption of  $Cu^{2+}$  by PCS, and the C-H stretching vibration at 2890 cm<sup>-1</sup> became weaker. These data indicate the successful chelation of C=N with copper ions.



**Fig. 5** Recovery and reuse of PCS@  $Cu^{2+}$ .

# 3.5. $PCS@Cu^{2+}$ catalyst in homocoupling reaction of arylboronic acid

We have used modified chitosan microspheres with adsorbed copper (100 mg/L) as a catalytic material. In such coppercatalyzed couplings as having been reported, the addition of base was generally required to enhance the activity of the phenylboronic acid and the reaction needs to be carried out under aerobic conditions or in air, so we have optimised the reaction conditions using 4-methoxyphenylboronic acid as the raw material and sodium carbonate as the base.

For a thorough reaction, we set the reaction conditions as follows: 4-methoxy phenylboronic acid (**1a**, 0.2 mmol), base (0.1 mmol), PCS@Cu<sup>2+</sup> (3.8 mol%), methanol (2 mL) was chosen as a solvent, and the reaction was carried out for 4 h in air and at room temperature. The different catalysts were first screened (Table 2, Entry 1–8). The results showed that when no catalyst, or when copper metal or Cu(OH)<sub>2</sub> was added, and very little coupling product was obtained. When CuSO<sub>4</sub> was used as a catalyst,

a yield of 31 % was obtained. When CuCl, Cu(OAc)<sub>2</sub>, and CuCl<sub>2</sub> were used as catalysts, higher product yields were obtained, all in the range of 81 % to 93 %. A yield of 91 % was obtained using PCS@Cu(OAc)<sub>2</sub> as a catalyst, indicating that the reactivity of the catalyst did not decrease when Cu (OAc)<sub>2</sub> was loaded onto the chitosan. The effect of solvent on the reaction was further investigated using sodium carbonate as the base (Table 2, Entry 9-13). The yields of 4,4'-dime thoxy-1,1'-biphenyl (2a) were in the order: i-PrOH (17 %), MeCN (21 %), EtOH (78 %), THF (<5%) and H<sub>2</sub>O (trace) (Table 2, Entry 9–13). Protonic solvents may be more conducive to the reaction, with MeOH probably being the best solvent. We then chose the common carbonates and sodium hydroxide as bases for the reactions and the results showed that the catalytic effect with carbonates  $(M_2CO_3)$  was good, except for sodium hydroxide (Table 2, Entry 15-17). When no base was added, the reaction cannot proceed (Table 2, Entry 14). Comparative experiments (Table 2, Entry 8, 18-19) were carried out by adjusting the amount of base (0.2 eq - 0.5 eq). The results showed that the best results were obtained when the amount of base was 0.3 times that of 4-methoxy phenylboronic acid. When the reaction time was 0.5 h, the yield can reach 92 %, longer reaction time yields no change. Therefore, the following optimal conditions were chosen: catalyst (3.8 mol%), Na<sub>2</sub>CO<sub>3</sub> as a base (0.3 eq), MeOH as a solvent, reaction time 0.5 h, and room temperature.

We have investigated the applicability of this catalytic approach to different arylboronic acids using optimized reaction conditions (Table 3). Firstly, we obtained dimeric products in high yields (81 %-95 %) using aromatic phenylboronic acids containing electron-donating groups such as methoxy (1a-c), ethoxy (1d), methyl (1e), and tertbutyl (1 g) as reactants. We found that it was easier to obtain coupling products using para- and meta- substituted aryl boronic acids than using *ortho*-substituted phenylboronic acids. When the osubstituted groups have a large spatial structure, such as isopropyl (1f) and Naphthalenyl (1 s), relatively low yields of the coupling products were obtained. This may be due to the steric effect of the substituents.

We have also used phenylboronic acids containing electronwithdrawing groups such as nitro (1 m), formyl (1 k), cyano (1i,1j), and trifluoromethyl (1n) as reactants to obtain dimeric products in high yields (65–82 %). Heterocyclic compounds have been poor reactants in various coupling reactions. As a result of our attempts, we have also obtained the coupling product (2 t-2x) of heterocyclic boronic acids in high yields (71–93 %). We have found that pyridine boronic acids with electron-withdrawing groups are more active than those with electron-donating groups.

Next, we assessed the scalability of the reaction by selecting **1a** and **1x** as substrates and increasing the size of the reaction.

As shown in Scheme 3, the corresponding products 2a and 2x both achieve yields of 80 % at the gram scale.

#### 3.6. Catalyst reuse

The recovery and reuse of catalysts can be used to assess the effectiveness of catalytic systems in practice. When the reaction was complete, we separated the catalyst by filtration. The recovered catalyst was first treated with a 0.1 % acetic acid solution, then washed with water and methanol, and finally



Scheme 4 (a) By-products in the self-coupling reaction of 1 k, 1 l and 1 s.(b) Plausible mechanism for the PCS@  $Cu^{2+}$ - Catalyzed the self-coupling reaction, "L" represents "OAc" or "HCO<sub>3</sub>".

vacuum dried before being put back into the next cycle for reuse. Good product yields were obtained in each of the five reused cycles (Fig. 5).

#### 3.7. Proposed mechanism

Several teams (Kirai and Yamamoto, 2009; Cheng and Luo, 2011; Kaboudin et al., 2011; Puthiaraj et al., 2014; Raul et al., 2015; Cao et al., 2017; Long et al., 2019; Yuan et al., 2019; Das et al., 2020) have reported the possible reaction mechanism of copper-catalyzed self-coupling of arylboronic acid compounds. They found that the catalytic process is similar to that of the Chan-Lam coupling reaction (Chen et al., 2020), mainly involving the reduction and oxidation changes of copper between different valence states. However, the actual mechanism of copper-catalyzed self-coupling of arylboronic acid compounds needs to be further confirmed. Under the experimental conditions herein, the color of the reaction mixture changed as the reaction progressed. Chitosan microspheres started as green and turned yellow as the reaction progressed, which was consistent with the experimental observation of Kaboudin (Allen et al., 2013), and we speculated that oxygen was involved in the reaction in the catalytic system. We also found that some reactants in lower yields (1 k, 1 l, and 1 s) gave coupled products as well as by-products (3 k, 3 l, and 3 s, Scheme 4a), suggesting that the coupling reaction of arylboronic acids may be stepwise react.

By taking into account Gao's report (Cao et al., 2017) and the experimental phenomena, we hypothesized a mechanism for copper-catalyzed self-coupling, as shown in Scheme 4b. In the first step, the base combines with the arylboronic acid to form the activated arylboronic acid anion  $[ArB^{-}(OH)_{3}]$ . In the second step, arylboronic acid anion undergoes metal transfer under the action of PCS@Cu<sup>2+</sup> to obtain **intermediate I** (Ar-Cu<sup>II</sup>-L), and then **intermediate I** and another arylboronic acid molecule undergo further metal transfer to obtain **intermediate II** (Ar<sub>2</sub>Cu<sup>III</sup>-L). In the third step, the product Ar-Ar and **intermediate III** (Cu<sup>I</sup>-L) were obtained by reductive elimination and finally, PCS@Cu<sup>2+</sup> was formed by **intermediate III** to complete the catalyst cycle.

#### 4. Conclusion

We have investigated the adsorption of  $Cu(OAc)_2$  by modified chitosan adsorbents and developed an efficient catalytic method for the coupling of arylboronic acids. The catalytic system showed good tolerance to the administration of different arylboronic acids. The catalyst is easily separated and recovered and can be reused up to five times without significant loss of catalytic activity. The chitosan microspheres provide a sustainable route for the synthesis of arylaryl compounds the importance of heterocycles in medicinal chemistry.

We would like to submit the enclosed manuscript entitled "Adsorption of  $Cu(OAc)_2$  by Modified Chitosan Microspheres and Its Application in homocoupling of Arylboronic Acid", which we wish to be considered for publication in "Arabian Journal of Chemistry". No conflict of interest exits in the submission of this manuscript, and the manuscript was approved by all authors for publication. I would like to declare on behalf of my co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.arabjc.2022.104170.

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