Pd Loaded Nanocellulose-Based Materials as Heterogeneous Catalysts for Suzuki-Miyaura Coupling Reactions

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1. Introduction

With the EU energy conservation, emission reduction and low carbon requirements, green chemistry and sustainable development of the chemical industry are becoming more and more important. As a bio-friendly natural material, cellulose is easy to functionalize, combining high reactivity and eco-compatibility [1]. In this study, TEMPO-oxidized cellulose nanofibers and cross-linking agents were combined to form networked cellulose nanosponges (CNS) [2] which can be used as innovative support for palladium, synthesizing an innovative heterogeneous catalyst for the Suzuki-Miyaura coupling reactions. The morphological structure and the metal loading of Pd-CNS were investigated by SEM-EDS and ICP-OES analytical methods.

With the aid of a microwave reactor, different reaction parameters were investigated: reaction time, temperature, Pd-catalyst and phase transfer catalyst amount. Reusability test were also conducted to verify the possibility to reuse this cellulose-based Pd-loaded catalyst several times, considering both the high costs of Pd and the sustainable development of new technologies.

2. Materials and Methods

2.1. CNS-Pd

For the synthesis of CNS-Pd, cotton linters was used as a cellulose source. According to the work of Isogai *et al.*, TEMPO/KBr/NaClO system was used for cellulose oxidation to obtain TEMPO-Oxidized Cellulose NanoFibers (TOCNF) with an oxidation degree of 1.304 $mmol_{COOH}$ /g_{TOCNF}. This
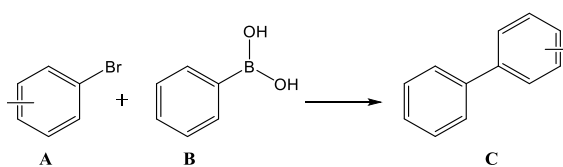
latter was calculated by means of a titration using phenolphthalein as colorimetric indicator. TOCNF were dispersed in water and cross-linked with 25 KDa branched polyethylenimine (bPEI) and citric acid (CA) to prepare cellulose nanosponges (CNS), using a weight ratio of 1 : 1 between TOCNF and bPEI. Citric acid was added as a co-crosslinking agent, with a percentage equal to the 18% of the amount of primary amino groups in bPEI.

In order to obtain the micro- and nano-porous architecture characteristic of CNS, the mixture of bPEI, TOCNF and CA was frozen-dried and then thermally treated in a laboratory oven, favoring the formation of amidic bonds between the carboxylic groups of TOCNF and amino groups of bPEI [4]. CNS were then grinded into a fine powder and put into a saturated solution of $PdCl_2$ in 0.1 M HCl. CNS were immersed in this solution until complete adsorption of Pd (10 minutes), repeating the adsorption cycle three times to obtain Pd-loaded CNS (CNS-Pd, Figure 1).
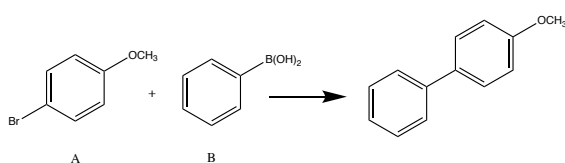

Figure 1.CNS (on the left) and CNS-Pd (on the right).

2.2. Suzuki-Miyaura coupling

Scheme 1. Suzuky-Miyaura reaction.

R= OCH_3, CH_3, Br, H, CN.

Scheme 2. Basic standard reaction for Suzuky-Miyaura reaction

In a 2-5 mL microwave vial, CNS-Pd (2-10% w/w compared to reagent A), KOH (2 eq), reagent B (1.5 eq) and 2.5 mL of water as solvent were added. Then, tetrabutylammonium bromide (TBAB) (0.15 – 0.6 eq) and reagent **A** (1 eq) were put in the vial. The reaction was performed under microwave irradiation in a temperature range of 40 - 130°C and for reaction times between 10 minutes and 1 hour [5].

2.3. Materials characterization

It can be seen from SEM analysis (Figure 2) that the obtained CNS are characterized by a layered and porous structure. This characteristic morphology provides a larger specific surface area, which can be exposed for the metal adsorption, also improving the catalytic performance effectiveness.
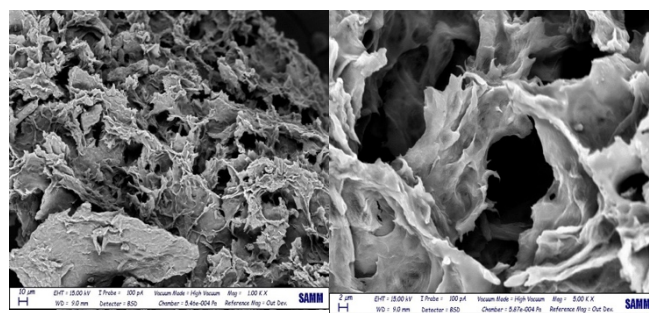

Figure 2. SEM images *of CNS-Pd: 10μm and 2μm*

From the EDS analysis (Figure 3 and 4), it can be noticed that after the complete Pd adsorption a high concentration of effective catalytic particles is uniformly distributed throughout the CNS structure.
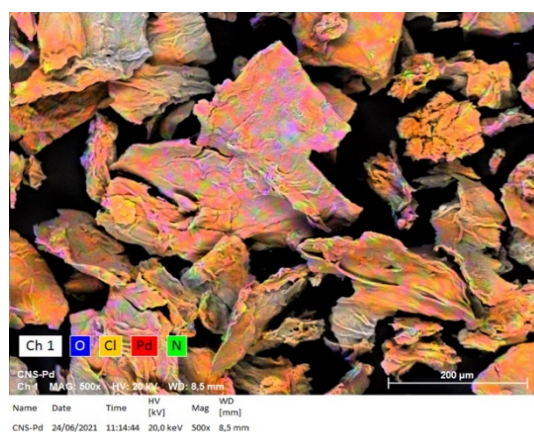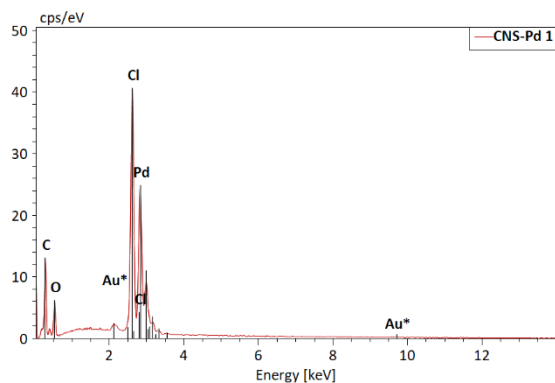

Figure 3. EDS image of CNS-Pd.

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Figure 4. EDS absorption spectrum of CNS-Pd.

CNS-Pd was characterized by ICP-OES measurements to further confirm the presence of palladium on the synthesized material, thus furnishing a quantitative value of the Pd-loading (Table 1).

Table 1. Pd % w/w on CNS-Pd calculated by ICP-OES.

Pd (w%)
22.7 ± 0.4

After performing leaching tests, it was observed that after one reaction cycle there is some leaching of Palladium, but in a not significant amount, thus confirming the possibility to reuse the catalyst several times without loss of efficiency, as observed in reusability tests described in Section 3.4.

3. Suzuki-Miyaura reaction optimization

The reference reaction, taken as model of study, was conducted using 4-bromoanisole and phenylboronic acid as reactants (Scheme 1 in Section 2.2.).
GC-MS and NMR with internal standard were used to obtain conversion rates and reaction yields.

3.1. Time and Temperature optimization

Thanks to the use of microwave reactors, the reaction can be optimized, varying reaction time and temperature and thus saving resource consumption, also maximizing the reaction yield.
The reaction conditions were investigated adhering to the principle of "time-temperature equivalence", shortening the reaction time under the condition of increasing temperature.

As reported in Table 2, we can notice that under the conditions of 25 °C for a long reaction time (48 h) the reaction yield was very low.

Table 2. Result for different reaction time and temperature. [a]

T	t	Yield
80 °C	30 min	57.%
100°C	30 min	92%
100 °C	20 min	71.5%
RT	48 h	19.3*

[a] Reaction conducted using 0.6 eq of TBAB, KOH as base with a 2% w/w catalyst amount. Yields were calculated by ^{1}H NMR using acetonitrile as internal standard.

Increasing the temperature, reaching conditions of 80 °C and 100 °C, the reaction yields increased a lot, reaching values higher then 90%, in particular in the case of 100 °C temperature. Temperature higher than 100°C were also tested, reaching 130 °C, but the increase in yield achieved was not sufficient to support the use of such high reaction temperatures. The selected temperature under optimized conditions was therefore 100 °C.
According to the yield calculation results, we can see that at the same temperature, the longer the reaction time, the greater the product yield, and after 30 min, the basic yield can reach more than 95%, so we selected as optimized reaction condition 30 minutes of reaction time and 100 °C of reaction temperature.

3.2. Catalyst, Base and TBAB optimization

After temperature and time optimization, the amount of catalyst was investigated. Table 3 shows the results obtained.

Table 3. Result for different catalyst percentages. [a]

T	t	Cat. %	Yield
100 °C	30 min	2%	92%
100 °C	30 min	5%	95%
100 °C	30 min	10%	94%

[a] Reaction conducted using 0.6 eq of TBAB and KOH as base. Yields were calculated by ^{1}H NMR using acetonitrile as internal standard.

It can be clearly seen from the experiment that the reaction does not follow the principle of "the more catalyst is used, the higher reaction yield is". In fact,

it was observed that when the catalyst dosage was increased from 5% to 10% w/w, the yield slightly decreased slightly. The reason of this yield decreasing could be related to the conversion of the Pd (II) into Pd^0: as the amount of the base is fixed, the excess of Pd (II) added cannot be reduced to Pd^0, so it is not able to participate in the reaction. These unreduced Pd (II) particles hinder the contact between the catalyst and the reactants, which affecting the catalytic efficiency.

As the main reactant, the function of base is to provide the basic environment required for the coupling reaction. Different bases, in particular NaOAc, Na_2CO_3, K_2CO_3 and KOH were considered. The experimental results are reported in Table 4:

Table 4. Results under the influence of different bases.

Cat. %	Base	Yield
2	KOH	92%
2	NaOAc	54%
2	Na_2CO_3	25%
2	K_2CO_3	25%
10*	-	55%

[a] The reaction was carried out at room temperature for 48h while all other reactions were conducted in MW for 30 minutes at 100 °C. Yields were calculated by ^{1}H NMR using acetonitrile as internal standard.

The results obtained show that NaOAc, Na_2CO_3, K_2CO_3 and other salts cannot provide a sufficient alkaline environment in the reaction system, and the catalyst reduction is poor. If no base is added, the alkaline environment provided by the amonio groups of CNS is not enough to induce the reduction of Pd (II) to Pd^0 and the product conversion rate is low.

The use of microwave to promote the Suzuki reaction in aqueous phase has been successfully applied in industrial production and this is the reason why we chose water as reaction solvent. But using this reaction conditions, the addition of a phase transfer catalyst was needed. TBAB was used as a phase transfer agent to help the reactants, mainly organic, entering the water phase. But during the reaction work-up, due to the existence of hydrophilic groups and hydrophobic groups of

TBAB, this latter was not easy removed during the extraction process and this fact affected the purity of the product. So, an optimization process on the amount of TBAB used was performed. The amount of TBAB was reduced from 0.6 to 0.15 equivalents, obtaining results showed in Table 5.

Table 5. Reaction results for different amounts of TBAB. [a]

Base %	TBAB eq.	Yield
100	0.6	92%
100	0.3	96.5%
100	0.15	97%
100	0	90%
0	0	0%

[a] Reaction conducted using KOH as base, at 100 °C for 30 minutes, with a catalyst amount of 2% w/w. Yields were calculated by ^{1}H NMR using acetonitrile as internal standard.

The results showed that the reaction yield was higher when using small amounts of TBAB (0.15 eq) in the optimized reaction and from Table 5 it can be also noticed that without using TBAB high yields can be obtained. Although, in view of the scale-up of the reaction, a small percentage of TBAB is certainly necessary to increase the efficiency of the reaction in the presence of large quantities of polar solvent. Using these small amounts of TBAB, the reaction treatment allowed to completely remove the residual phase transfer catalyst, obtaining a pure product.

3.4. Recycling and Reuse

The CNS-Pd catalyst prepared in this study, as a micro- and nano-porous stable structure, directly avoids the structural change caused by the excessive number of cycles of conventional palladium-catalyzed ligands. In order to verify the stability of the catalyst and its reusability, recycling tests were carried out. We repeated the reaction five times, recovering the catalyst powder after the reaction, rinsing it with ethyl acetate and water, and then drying it for the next cycles.

Observing experiment results, reported in Table 6, we noticed that the CNS-Pd catalyst prepared in this study had good recovery and reuse

Table 6. Yield rate obtained during recycling tests.[a]

Remark	Result
I	97%
II	83%
III	65%
IV	63%

[a] Reaction conducted in the optimized conditions, using KOH as base, at 100 °C for 30 minutes, with a catalyst amount of 2% w/w and a TBAB amount of 0.15 eq. Yields were calculated by ^{1}H NMR using acetonitrile as internal standard.

characteristics. After four cycles, more than 60% conversion was still achieved, demonstrating the long catalyst life. At the same time, it can still maintain an average recovery rate (almost 70%) after recycling, which reflects good environmental protection and economic value.

4. Conclusion and Outlooks

In this work, cellulose-based nanosponges (CNS) were prepared. TEMPO-oxidized cellulose nanofibers and branched polyethyleneimine were cross-linked together in presence of citric acid to obtain a micro- and nano.porous structure and this latter was then loaded with Pd (II) to obtain a potential heterogeneous catalyst for Suzuki-Miyaura coupling reactions. The morphology and structure of the material were characterized by various SEM-EDS and ICP-OES. An optimization study on the heterogeneous reaction was conducted, reaching optimal condition for the obtainment of high-rate yields. The catalytic recycling ability of the material and the catalytic effect for different substituents were also examined, confirming the possibility to reuse this sustainable catalyst several times.

Although the study of the Suzuki reaction has been completed, the catalytic role of CNS-Pd remains to be expanded. At present, the application in the Heck reaction has achieved preliminary results,

and also Sonogashira cross-coupling reaction is going to be explored.

5.   Bibliography

[1]. Isogai, A.; Saito, T.; Fukuzumi, H. TEMPO-oxidized cellulose nanofibers. nanoscale 2011, 3, 71-85.

[2]. Fiorati, A.; Pastori, N.; Punta, C.; Melone, L. Sponge-like functional materials from TEMPO-oxidized cellulose nanofibers. Nanosponges: From Fundamentals to Applications; Mele, A., Trotta, F., Eds 2019.

[3]. Riva, L.; Pastori, N.; Panozzo, A.; Antonelli, M.; Punta, C. Nanostructured cellulose-based sorbent materials for water decontamination from organic dyes. Nanomaterials 2020, 10, 1570.

[4]. Melone, L.; Rossi, B.; Pastori, N.; Panzeri, W.; Mele, A.; Punta, C. TEMPO-oxidized cellulose cross-linked with branched polyethyleneimine: Nanostructured adsorbent sponges for water remediation. ChemPlusChem 2015, 80, 1408-1415.

[5]. Kamal M. Dawood, Mohamed R. Shaaban, Manahil B. Elamin, Ahmad M. Farag, Catalytic activity of some oxime-based Pd(II)-complexes in Suzuki 10-4, 2017,473-479