

Heck reaction using palladium-benzimidazole catalyst: synthesis, characterisation and catalytic activity

N R Said, M A Mustakim, N N Md Sani and S N A Baharin

School of Chemistry and Environment, Faculty of Applied Sciences, Universiti Teknologi MARA (UiTM) Cawangan Negeri Sembilan, Kampus Kuala Pilah, Pekan Parit Tinggi, 72000 Kuala Pilah, Negeri Sembilan, Malaysia.

Email: nurra1435@ns.uitm.edu.my

Abstract. Palladium is used as a catalyst for carbon-carbon couplings such as in the Heck, Stille, and Suzuki reactions. This research reports on two palladium catalysts for the Heck reaction, namely bi-1-3-bis(phenylmethyl) benzimidazolium bromo palladium(II) (Pd-NHC-H) and bi-1,3-bis[(4-chlorophenyl)methyl]-1-benzimidazolium bromo palladium(II) (Pd-NHC-Cl). The catalyst preparation involved two steps of synthesis. First was the synthesis of N-heterocyclic carbene (NHC) ligands by reacting benzimidazole with benzyl bromide and 4-chlorobenzylbromide. It was then followed by the reacting of both synthesized ligands with palladium chloride. The synthesized NHC ligands and catalysts were characterized using Fourier Transform Infrared (FT-IR), ^1H and ^{13}C Nuclear Magnetic Resonance (NMR), and UV-Vis spectroscopy. All results gave evidence of the successfulness of the synthesized compounds. A preliminary complexation study between the Pd^{2+} cation and N-heterocyclic carbene (NHC) ligand showed stoichiometric of 1 Pd^{2+} cation to 2 NHC ligand. The catalytic activity of the Pd-NHC-H and Pd-NHC-Cl was studied on a Heck carbon-carbon coupling reaction between 1-bromo-4-nitrobenzene and styrene at different catalyst loadings and reaction times. The catalytic performance was analysed using GC-FID. Results showed that excellent catalytic activity was achieved using Pd-NHC-Cl with a catalyst loading of 0.5 mmol% and 60 minutes of reaction time.

1. Introduction

Palladium catalysts are efficient and powerful tools for carbon-carbon bond formations as the reactions have a high reaction rate, good yield percentage and high turnover number. The Heck reaction, Suzuki reaction and Stille reaction are examples of reactions that use palladium as a catalyst. The reactions that are conducted via the insertion of alkenes and alkynes to the arylpalladium intermediates and alkenylpalladium are known as the Heck reactions [1]. In 2010, the Nobel Prize in Chemistry was awarded to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki for their work on palladium-catalysed cross couplings in organic synthesis.

The Heck reaction is the most powerful and widely used chemical reaction used to form substituted alkenes with organic moieties bearing a suitable leaving group such as halide, triflate or diazonium. Several intermediates in pharmaceutical and fine chemicals are synthesized using this method. For example, the synthesis of guaianolide-type sesquiterpene lactone derivatives as active compounds



inhibiting resistant acute leukemic cells, and the synthesis of cyclotene as an important material in wafer level chip packaging for smartphone screen manufacturing [2, 3].

Palladium (Pd) behaves as a catalyst in the Heck reaction and it can be present in several forms which are homogeneous and heterogeneous. Pd catalysts commonly form in these two types: Pd(0) bonded to phosphine ligand i.e., Pd(PPh₃), or as a palladium salt such as PdCl₂ or Pd(OAc)₂ [1]. Generally, the palladium catalyst contains a phosphine ligand, thus it can facilitate organic transformation efficiently. However, the phosphine ligand has a few disadvantages including high toxicity, costly and air sensitivity [4]. Some phosphine-free ligands such as Schiff base ligands, carbocyclic, thiols and N-heterocyclic carbene (NHC) have been tested and developed.

Among the phosphine-free ligands developed, NHC ligands show good quality for the palladium catalyst as it has stronger σ -donor properties and stability to air, moisture, and heat when compared to phosphine ligands [5]. This study, therefore, focuses on the synthesis and characterization of two palladium catalysts (Pd-NHC-H and Pd-NHC-Cl) and their catalytic activities in the Heck reaction.

2. Experimental

2.1. Reagents and Instruments

The chemicals and solvents used were palladium chloride, benzimidazole, benzyl bromide, 4-chlorobenzyl bromide, tetrahydrofuran (THF), methanol, dimethyl sulfoxide (DMSO), 1-bromo-4-nitrobenzene, styrene, N,N-dimethylacetamide (DMA), dimethyl sulfoxide (DMSO), dimethylformamide (DMF), ethyl acetate, ether, dichloromethane, sodium carbonate (Na₂CO₃), sodium hydroxide (NaOH) and magnesium sulphate (MgSO₄). All of the above were purchased at analytical grade and used without further purification.

The characterization of the synthesized complexes was conducted using instrumentation methods such as Fourier Transform Infrared (FT-IR), ¹H and ¹³C Nuclear Magnetic Resonance (NMR) and UV-Vis spectroscopy. The catalytic study for the Heck reaction performance was analyzed using GC-FID.

2.2. Synthesis of Palladium-Benzimidazole Catalyst

The synthesis routes used in the preparation of NHC ligands are shown in figure 1. Benzimidazole (1.1814 g; 10 mmol) was dissolved in 10 mL of THF in a beaker and stirred. Benzyl bromide (3.7629 g; 20 mmol) was then added into the beaker. The mixture was stirred for 24 hours. Then, the expected compound, 1,3-bis(phenylmethyl) benzimidazolium bromide (NHC-H) was separated using vacuum filtration and washed with THF and water. Then it was dried in a vacuum desiccator. The steps were repeated to produce 1,3-bis[(4-chlorophenyl)methyl]-1-benzimidazolium bromide (NHC-Cl) by reacting the Benzimidazole (1.1814 g; 10 mmol) with 4-chlorobenzyl bromide (4.1096 g; 20 mmol).

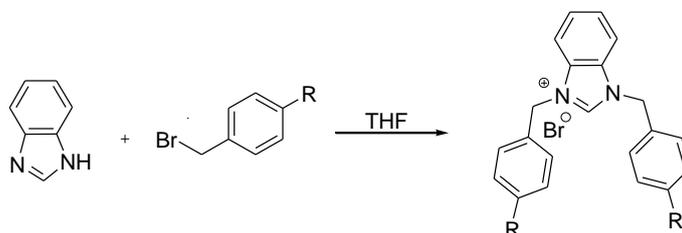


Figure 1. Synthesis route of NHC ligands, where R= H or Cl

The synthesis steps were continued with the stirring of NHC-H ligand (0.2 mmol) in 15 mL dry methanol, and then palladium chloride (0.1 mmol) was added slowly into the solution. The solution was refluxed for 2 hours. After refluxing, 37% NaOH (3.5 mL, 2.0 M) was added dropwise over 30 minutes. Then, it was further stirred for 24 hours at room temperature. The suspension obtained was filtered, washed with diethyl ether and dried in a desiccator. The product obtained was the Pd-NHC-H catalyst.

The steps were repeated using NHC-Cl ligand to obtain the Pd-NHC-Cl catalyst. The synthesis route is shown in figure 2.

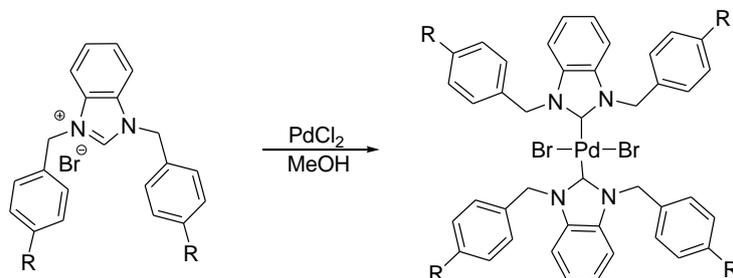


Figure 2. Synthesis route of palladium catalyst, where R= H or Cl

2.3. Preliminary Complexation Study

The UV-Vis titration experiments on both N-heterocyclic carbene ligands with palladium metal were conducted to understand the stoichiometry of the formed complexes of N-heterocyclic carbene ligands and Pd²⁺ cation. N-heterocyclic carbene ligand in DMSO (2.3×10^{-6} mmol) and palladium chloride in DMSO (1×10^{-4} mmol) were prepared. 3 ml of N-heterocyclic carbene ligand was put into a cuvette and the palladium metal was added bit by bit until the ratio of metal added to the N-heterocyclic carbene ligand was 2:1 [6].

2.4. Catalytic Study

Both synthesized palladium catalysts, Pd-NHC-H and Pd-NHC-Cl, were tested for their catalytic activity in a Heck reaction by reacting 1-bromo-4-nitrobenzene with styrene monomer to produce 3-(4-nitrophenyl)-benzene, respectively (figure 3). 1-bromo-4-nitrobenzene (0.2083 g; 1 mmol), styrene monomer (0.2083 g; 2 mmol), Na₂CO₃ (0.25 g, 2.4 mmol), palladium(II) catalyst (1.0 mmol%) and DMA (10 mL) as solvents were mixed together in a three-neck round bottom flask and refluxed in the presence of nitrogen gas for 1 hour. The mixture was poured into separating funnels with the addition of water (30 mL) and dichloromethane (3×10 mL). The mixture was let to sit for 30 minutes, and organic material was extracted and removed. Then, it was dried over MgSO₄ and the mixture was filtered in vacuo, leaving the crude product. Finally, the product was evaporated using a rotary evaporator and dried in an oven [7]. The FT-IR spectroscopy was used to characterize the final product. The procedure was repeated with 0.50 mmol% catalyst loading. All reactions were monitored every 15 minutes. The sampling was taken at 15, 30, 45 and 60 minutes and the crude product was analyzed using GC-FID.

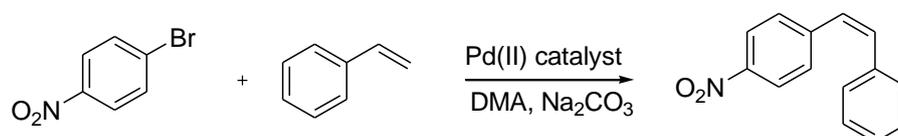


Figure 3. Catalytic reaction of 1-bromo-4-nitrobenzene and styrene, where Pd(II) catalyst = Pd-NHC-H or Pd-NHC-Cl

3. Results and discussion

3.1. Characterisation

NHC ligands and their Palladium complexes (catalyst) were synthesized by the method shown in figure 1 and figure 2. The physical properties of the compounds are listed in table 1. After complexation, the product changed in color and increased in melting temperature when compared with its ligand. This is

due to the presence of the palladium metal attached to the structure of the ligand as proof of the successfulness of the complexation reaction.

Table 1. Physical properties of synthesized compounds

Compound	Colour	Melting point (°C)	% Yield
NHC-H	White	153	78.4
NHC-Cl	Orange	178	90.1
Pd-NHC-H	Brown	167	70.4
Pd-NHC-Cl	Grey	224	82.8

The structure of synthesized compounds was confirmed using FT-IR, $^1\text{H-NMR}$, and $^{13}\text{C-NMR}$. The FT-IR spectra in figure 4 show the transformation from benzimidazole to palladium catalyst. Observe that in the spectrum of benzimidazole, C=N peaks appeared at 1589 cm^{-1} . However, after introducing benzyl substituent to the benzimidazole nitrogen atom, the C=N peak of NHC ligand (NHC-H) shifted to a lower frequency of 1558 cm^{-1} due to the conjugation of unshared pair electrons on the nitrogen atom that had increased the single bond character [1]. After complexation, the FT-IR spectrum of the synthesized palladium catalyst (Pd-NHC-H) showed a peak of C-N bond at 1658 cm^{-1} to replace the C=N bond. However, the C-N absorption peaks appeared at an unusually high value due to the electronegativity of palladium which developed a polarised Pd-Br bond and led to a relative strengthening of Pd-C and C-N bonds [8]. A similar observation can also be seen in the spectra for the transformation of NHC-Cl to Pd-NHC-Cl where the C=N peak at 1601 cm^{-1} disappeared after the complexation process, followed by the appearance of new C-N peaks at 1672 cm^{-1} .

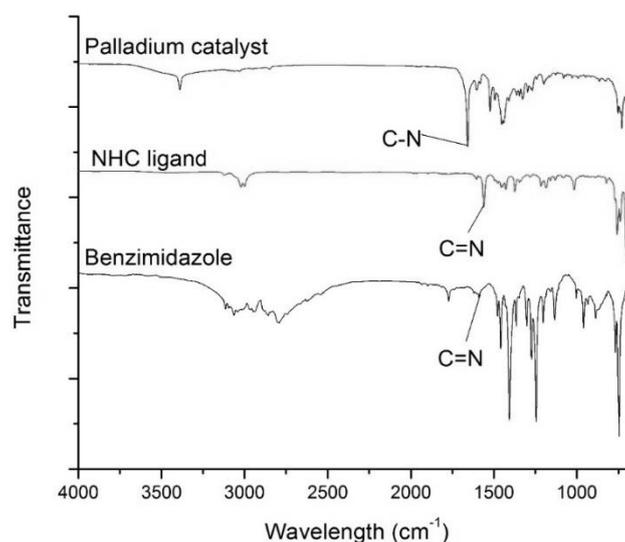


Figure 4. FT-IR spectra of synthesis compounds

In the $^1\text{H-NMR}$ spectra (figure 5), a notable change was observed by the disappearance of the chemical shift of the carbene proton in the spectra of Pd-NHC-H and Pd-NHC-Cl at δ 10.32 ppm and 10.20 ppm, which were present in the spectra of the NHC-H and NHC-Cl ligands, respectively. This is upon the deprotonation and coordination of Pd(II) metal cation with the carbene carbon position. The results from the $^1\text{H NMR}$ spectra data for synthesized ligands and palladium catalysts are listed in table 2.

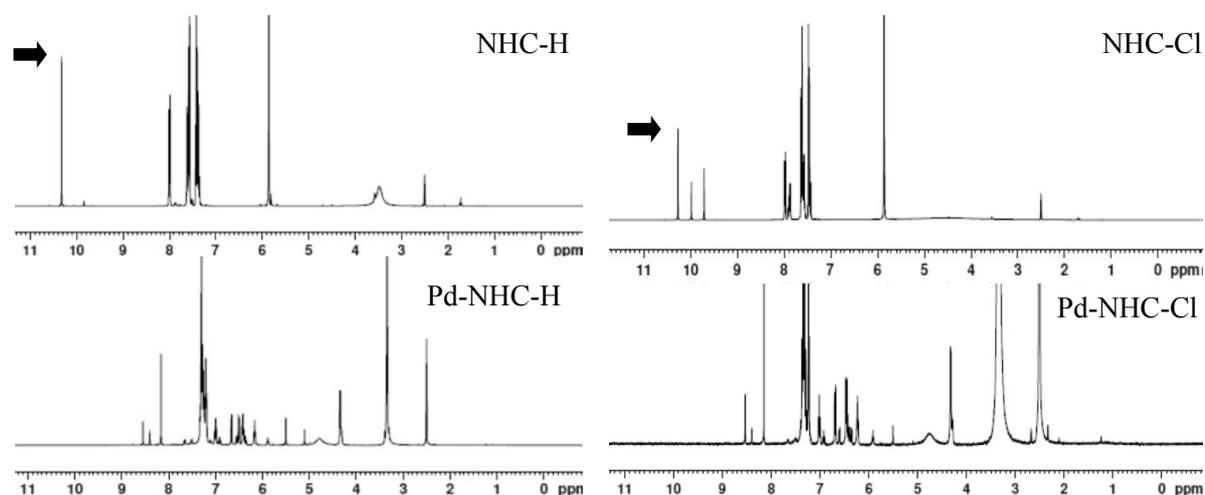


Figure 5. ^1H -NMR spectra of synthesis compounds

Table 2. Significant attributions ^1H NMR data of synthesis compounds

Attributions	Chemicals Shift, δ (ppm); [multiplicity]			
	NHC-H	NHC-Cl	Pd-NHC-H	Pd-NHC-Cl
N-CH-N (H carbene)	10.32 [s]	10.20 [s]	-	-
CH-Ar	7.99 [m]	8.00 [m]	8.16 [m]	8.10 [m]
CH-Ar	7.61 [m]	7.80 [m]	7.25 [m]	7.20 [m]
CH-Ar	7.39 [m]	7.60 [m]	7.02 [m]	7.00 [m]
Ar-CH ₂ -N	5.86 [s]	5.90 [s]	5.50 [s]	5.60 [s]

The ^{13}C -NMR spectra in figure 6 show that most of the resonance of the palladium catalyst is almost the same as the resonance of the NHC ligand. Only the carbene carbon chemical shift showed a significant change after the complexation reaction with Pd(II) metal cation. In the Pd-NHC-H spectrum, it was observed that the carbene carbon was resonated at δ 163.72 ppm, while in NHC-H ligand, it resonated at δ 143.19 ppm. Comparable results can also be seen in the NHC-Cl and Pd-NHC-Cl spectra. After complexation, the chemical shift representing the carbene carbon was resonated at a higher chemical shift from δ 143.3 ppm to 163.76 ppm. The corresponding signal is due to the attachment of palladium metal at the carbene carbon positions. Other significant chemical shifts of the ^{13}C NMR spectra are summarised in table 3.

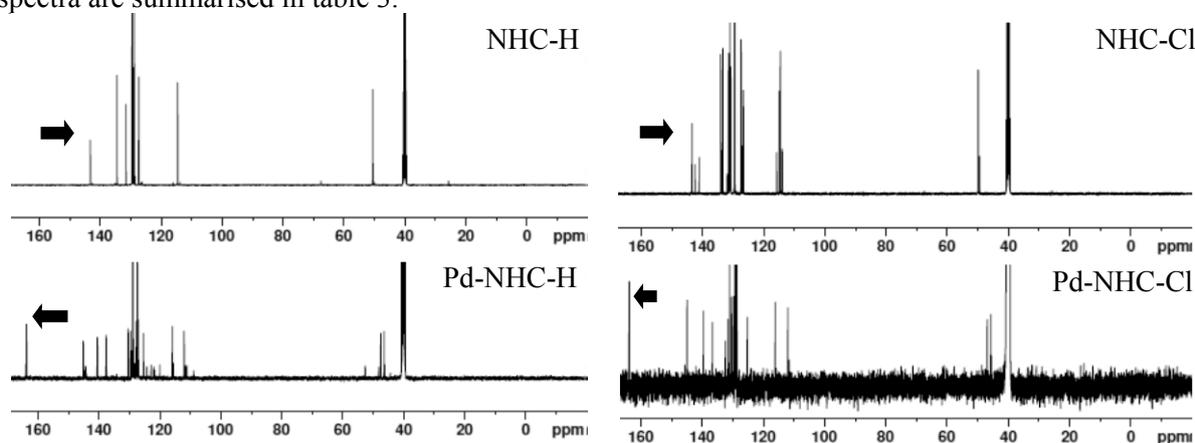


Figure 6. ^{13}C -NMR spectra of synthesis compound

Table 3. Significant attributions ^{13}C NMR data of synthesis compounds

Attributions	Chemicals Shift, δ (ppm)			
	NHC-H	NHC-Cl	Pd-NHC-H	Pd-NHC-Cl
N-CH-N (C carbene)	143.19	143.30	163.72	163.76
C-Cl	-	140.90	-	139.50
CH-Ar	131.51-114.59	130.90-113.80	130.35-115.85	132.30-111.90
Ar-C-N	51.10	49.30	49.8	46.85

3.2. Preliminary Complexation Study

The UV-Vis titration method was used to determine the stoichiometry between the Pd^{2+} metal cation and NHCL (NHC-H or NHC-Cl) in the formation of complexes. The graph plotted in figure 7 is assigned for the absorbance vs. $[\text{Pd}^{2+}]/[\text{NHCL}]$. This graph indicates that as the molar fraction of Pd^{2+} metal cation was added into the NHC-H and NHC-Cl, the absorption spectra produced gradually increased as the concentration of Pd^{2+} metal cation increased. However, it is notable that there is a breaking point at 0.5 $[\text{Pd}^{2+}]/[\text{NHCL}]$ ratio for both graphs which indicates the 1:2 stoichiometry in the formation of complexes [6]. Thus, the suggested general chemical reaction of the complexation is as follows:

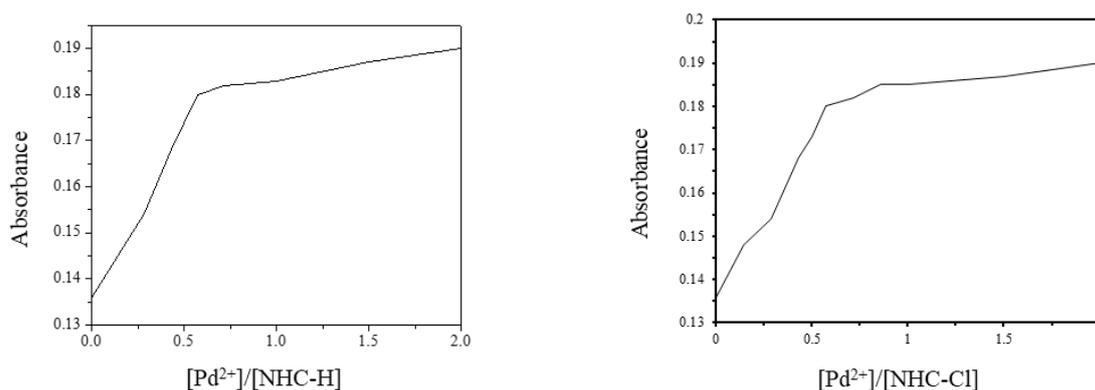


Figure 7. The graph plotted based on absorbance versus $[\text{Pd}^{2+}]/[\text{NHC-H}]$ and absorbance versus $[\text{Pd}^{2+}]/[\text{NHC-Cl}]$

3.3. Catalytic Activity Study

The reaction between 1-bromo-4-nitrobenzene and styrene (figure 3) was successfully synthesized in the presence of the Pd(II) catalyst to obtain a brown solid 1-nitro-4-styrylbenzene with a melting point of $155\text{ }^{\circ}\text{C}$. The structure of the synthesized compound can be confirmed by the presence of $\text{C}=\text{C}$ peaks in the FT-IR spectrum at 1641 cm^{-1} which is higher than $\text{C}=\text{C}$ peaks in the FT-IR spectrum of styrene at 1629 cm^{-1} . It shows the successful bonding between styrene and 1-bromo-4-nitrobenzene. This consequence is due to the transformation of alkene functionality from monosubstituted double bond to disubstituted double bond where the stability of the structure increased, thus increasing the FT-IR stretching vibration [1].

The catalytic performance of Pd-NHC-H and Pd-NHC-Cl were studied at different amounts of catalysts used which are 1.0 and 0.5 mmol%, respectively. The reaction was then monitored at a 15-minute interval until 60 minutes reaction time. Table 4 shows the results obtained from the GC-FID chromatogram analysis. Results show that the conversion rate of the product increased as the catalyst loading and reaction time increases.

From the data, the best catalyst activity condition for the Heck reaction based on TONs is using the palladium catalyst of Pd-NHC-Cl with a catalyst loading of 0.5 mmol% and reaction time of 60 minutes.

The presence of the Cl electronegativity group increases the stability of the Pd catalyst structure, thus leading to higher TONs [8].

Table 4. Catalytic activity at different catalyst loading and reaction time

Entry	Catalyst Loading (mmol %)	Reaction time (minutes)	Conversion of 1-bromo-4-nitrobenzene (%), (TON)	
			Pd-NHC-H	Pd-NHC-Cl
1	0.0	15	4.97 (0)	17 (0)
2		30	-10.38 (0)	3 (0)
3		45	9.16 (0)	20 (0)
4		60	-1.76 (0)	11(0)
5	0.5	15	18.18 (36.36)	9 (19)
6		30	39.00 (78.00)	16 (32)
7		45	41.22 (82.44)	40 (81)
8		60	44.82 (89.64)	62 (124)
9	1.0	15	14.52 (14.52)	26 (26)
10		30	40.14 (40.14)	49 (49)
11		45	44.16 (44.16)	68 (68)
12		60	46.10 (46.10)	78 (78)

4. Conclusions

This study revealed that the synthesized palladium catalysts, Pd-NHC-H and Pd-NHC-Cl, can be used as catalysts in Heck reactions. Pd-NHC-Cl shows good catalytic activity with a catalyst loading of 0.5 mmol% within 60 minutes reaction time in DMA as a solvent and Na₂CO₃ as a base.

Acknowledgments

The authors gratefully acknowledge to the Universiti Teknologi Mara (UiTM), Cawangan Negeri Sembilan, Kampus Kuala Pilah for the facilities and financial support.

References

- [1] Tsuji J 2006 *Palladium Reagents and Catalysts: New Perspectives for the 21st Century* (Great Britain-John Wiley & Sons) p 110-112
- [2] Ding Y H, Fan H X, Long J, Zhang Q and Chen Y 2013 *Bioorganic & Medicinal Chemistry Letters* **23(22)** 6087
- [3] Oberholzer M and Frech C M 2014 *Journal of Visualized Experiments: JoVE* **85** 51444
- [4] Yuan D, Chen L, Yuan L, Liao S, Yang M and Zhang Q 2016 *Chemical Engineering Journal* **287** 241
- [5] Yılmaz U, Küçükbay H, Deniz S and Şireci N 2013 *Molecules* **18(3)** 2501
- [6] Said N R, Rezayi M, Narimani L, Al-Mohammed N N, Abdul Manan N S and Alias Y 2016 *Electrochimica Acta* **197** 10
- [7] Arvela R K, Leadbeater N E, Sangi M S, Williams V A, Granados P and Singer R D 2005 *The Journal of Organic Chemistry* **70(1)** 161
- [8] Jagtap S 2017 *Catalysts* **7(9)** 267