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## Heck reactions catalyzed by Pd(0)-PVP nanoparticles under conventional and microwave heating

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This paper is dedicated to the memory of Professor Octavio A.C. Antunes (Universidade Federal do Rio de Janeiro).

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#### 1. Introduction

# Nanoscience is a new interdisciplinary scientific field which develops and advances rapidly nowadays [1,2]. Miniaturization to nanometric scale in the range of 1–100 nm gives rise to qualitative changes in the physicochemical properties of the systems under study [3]. Nanoparticles are believed to have properties which lie somewhere between those of single-particle species and bulk materials [4]. An important field of application for nanoparticles is that of catalysis due to their large surface area [5,6]. In this regard the unique properties of these systems can lead to interesting applications [7,8].

Palladium colloids can be used as catalysts with high reactivity in C–C bond formation [9–11] reactions as the Heck and Nolley [12–15], Kumada and co-workers [16], Negishi [17], Suzuki and coworkers [18,19], Hatanaka and Hiyama [20], Sonogashira et al. [21] and Stille [22] reaction. These methodologies constitute an important tool for organic synthesis and have become a natural way of

#### ABSTRACT

Pd(0) nanoparticles stabilized by polyvinylpyrrolidone (Pd-PVP) with a diameter of 3–6 nm in ethanol catalyzed Heck coupling of iodobenzene with different alkenes under microwave heating. Products were obtained in good yields (62–99%) and good selectivity to the *E*-isomers. Microwave heating proved to be superior to conventional heating, providing products in higher yields and selectivities in short times (12 min).

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assembling important pharmaceuticals, natural products and multifunctional derivatives.

The palladium(0)-catalyzed arylation and vinylation of alkenes with aryl or vinyl halides, known as the Heck reaction, is a methodology of increasing versatility for the formation of new C-C bonds [23-25]. Although homogeneous palladium catalysts are usually effective in this reaction, their uses often bring about the typical problems associated to all homogeneous catalysts, that is, separation of the catalyst from the reaction products and catalyst recovery. One of the major drawbacks of the early homogeneous systems was the precipitation of palladium black with limitation of the lifetime of the active species. Addition of phosphine-ligands improves the stability of catalytic systems but, from an economical or an environmental perspective, development of phosphine-free systems is desirable [13]. Palladium(0) nanoparticles have been found to be involved in many phosphine-free reactions [26]. Actually, metal nanoparticles hold promises as recoverable and recyclable catalysts [6].

Polymers as polyvinylpyrrolidone (PVP) are efficient stabilizers for metal nanoparticles [10,11,19,27]. PVP is a cheap linear polymer which potential to stabilize palladium(0) nanoparticles was already reported. Pd-PVP nanoparticles have proven their effectiveness to catalyze C–C coupling reactions and the results reported

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in the literature indicate that the method used for the preparation of nanoparticles play a pivotal role in their catalytic activity. Whether nanoparticles act as an inert reservoir of active, soluble molecular palladium or as surface-active catalysts is a point of continuous debate in the literature. Recently, Lee et al. reported an elegant operand XAS study which revealed nanoparticles are stable to metal leaching throughout the reaction, with surface density Pd defect sites directly implicated in the catalytic cycle [28].

The majority of the reports of the literature, however, consist in their application in the Suzuki reactions. Little attention has been given to their application in Heck couplings. Trzeciak and co-workers [29] employed a two step procedure (obtainment of H<sub>2</sub>PdCl<sub>4</sub> acidic solution followed by the reduction of this complex by pyrogallol in the presence of PVP) to obtain PVP-stabilized nanoparticles (medium diameter = 19.8 nm) and applied this catalytic system to the mono and di-arylation of *n*-butyl acrylate with bromobenzene. These authors employed the TBAB (tetrabutylammonium bromide) as additive at 130 °C under N<sub>2</sub> atmosphere and conventional heating.

Evangelisti et al. [30] employed a metal vapor synthesis (MVS) technique to prepare PVP-stabilized palladium(0) nanoparticles (1.0–3.5 nm). These researchers employed this catalyst in the Heck couplings between aryl halides and *n*-butyl acrylate (acrylate/ArX=2) at 75–125 °C, under argon atmosphere, under conventional heating, with N(*n*-Pr)<sub>3</sub> as base in NMP.

Durap et al. [31] employed methanol and NaBH<sub>4</sub> as the palladium reducing agents with  $K_2PdCl_4$  as the Pd(II) source in the presence of PVP under refluxing conditions to obtain Pd-PVP nanoparticles (diameter = 4.5 nm). The catalyst thus prepared was employed in the Heck coupling between styrene (styrene/ArBr = 1.5) and bromobenzenes (bromobenzene, bromoanisole, 4-bromotoluene) (DMF,  $K_2CO_3$ , 120 °C, inert atmosphere). *E*-stilbenes were obtained in 45 min in yields ranging from 34% to 100%.

The use of microwave as alternative energy source to input chemical reactions has received considerable amount of attention in the last years [32,33]. Microwave irradiation has been applied successfully to different types of reactions and in many cases, increased yields, reduced reaction times and enhanced selectivity of the reaction compared to conventional heating.

In the previous reports where Pd-PVP nanoparticles were applied to the Heck couplings only the conventional heating was employed with styrene or *n*-butyl acrylate [29–31]. No considerations have been made about the occurrence of hydroarylation processes and the influence of the solvent in the selectivity of the coupling.

In this work we present results demonstrating the quite good efficiency and selectivity of Pd(0) nanoparticles stabilized by polyvinylpyrrolidone (Pd-PVP) as catalyst in the Heck reaction in the absence of phosphine ligands or phase transfer catalysts, Scheme 1. A straightforward approach was employed in the preparation of the palladium nanoparticles. Different alkenes (monosubstituted and disubstituted) were employed in the couplings with iodobenzene, under conventional heating. As far as we concern microwave irradiation was not employed to accelerate the Heck couplings catalyzed by Pd-PVP nanoparticles. Furthermore, in the present work, we present results concerning the selectivity

between arylation and hidroarylation in Heck couplings catalyzed by Pd-PVP nanoparticles.

#### 2. Experimental

#### 2.1. Materials

The reagents used in the Heck reactions were purchased from commercial sources and used without further purification. Polyvinylpyrrolidone (40,000 Da) was used as stabilizer for the palladium(0) nanoparticles.

#### 2.2. Preparation of the catalyst [34]

PVP (2.5 g) with an average molecular weight of 40,000 Da was added to methanol (150 mL) and stirred until the total solubilization of the polymer. To this solution, it was added  $Pd(OAc)_2$  (0.05 g) and the mixture was immersed in a pre-heated oil bath at 85 °C under constant magnetic stirring for 3.0 h. Temperature was controlled to be maintained between 85 and 90 °C. Next, methanol was removed in a rotary evaporator and the palladium(0)-PVP catalyst was transferred quantitatively to a 25 mL volumetric flask using ethanol as solvent. This solution of Pd(0)-PVP in ethanol was directly used as the catalyst for the Heck reactions.

#### 2.3. Heck reaction under microwave irradiation

Reactions were carried out with a single mode cavity Discover Microwave synthesizer (CEM Corporation, NC, USA) producing continuous irradiation at 2455 MHz and infrared temperature control system. Microwave experiments were carried out in sealed tubes with an efficient magnetic stirring (which avoids problems of non-homogeneity in temperature) and with simultaneous cooling. In a typical experiment, a tube equipped with a magnetic stirrer was charged with K<sub>2</sub>CO<sub>3</sub> (2.0 mmol), ethanol (2.0 mL), iodobenzene (1.0 mmol), ethyl acrylate (1.3 mmol) and 0.22 mL of Pd(0)-PVP solution (0.1% of Pd with respect to the iodobenzene mass). This tube was sealed and the content was subjected to focused microwave irradiation at 300W for 12 min, with 120 °C as the general final temperature. Then, the reaction mixture was cooled to room temperature and diluted with 8.0 mL of diethyl ether and stirred until the nanoparticles and the inorganics have precipitated. Organic phase was analyzed by GC-MS. Afterward the remaining precipitate was washed with diethyl ether. The combined organic phases were filtered through celite, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed by rotary evaporation to give the crude product. Products obtained were analyzed by GC-MS, <sup>1</sup>Hand <sup>13</sup>C-NMR spectroscopy.

#### 2.4. Heck reaction under conventional heating

A 10 mL round-bottomed flask equipped with a reflux condenser was filled with  $K_2CO_3$  (2.0 mmol), ethanol (2.0 mL), iodobenzene (1.0 mmol), ethyl acrylate (1.3 mmol) and 2.2 mL of Pd(0)-PVP solution (1.0% of Pd with respect to the iodobenzene mass). The flask was placed in an oil bath, and the mixture was stirred and heated at 80 °C. After a reaction time of 4 h, the flask was stirred until the precipitation of nanoparticles and inorganic. The organic phase was analyzed by GC-MS.

#### 2.5. Heck reaction with a pre-heated oil bath at 120 °C

A sealed tube equipped with a magnetic stirrer and charged with the reaction mixture (see Section 2.2) was immersed into a pre-heated oil bath at 120 °C for 12 min, after which this

mixture was treated the same manner described for the representative procedures under microwave heating.

#### 2.6. Methods for the catalyst analysis

Transmission electron microscopy (TEM) was performed with a JEOL-1210 microscope operating at 80 kV. Two drops of the Pd(0)-PVP solution was placed on a copper grid (300 mesh) coated by a piolophorm film and dried for 24 h at 60 °C. The nanoparticle size distribution for each sample was determined by counting the size of approximately 200 palladium nanoparticles from TEM images obtained from different places on the TEM grids.

### 2.7. Methods for identification and quantification of substrate and product

<sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded on a Brucker AMX-200 spectrometer operating at 200 MHz (<sup>1</sup>H) and 50 MHz (<sup>13</sup>C) in CDCl<sub>3</sub> with TMS as an internal standard. The analyses by GC-MS were performed on a Shimadzu GCMS-QP2010Plus. The separation of the compounds was achieved on RTx5MS ( $30 \text{ m} \times 0.25 \text{ mm} \times 0.25 \text{ µm}$ ). Helium was used as a carrier gas and the injection split ratio was 1:20. Separation was achieved using the following temperature program: 20 °C/min from 100 (hold time = 2 min) to 260 °C (hold time = 2 min). Injector and detector temperatures were 260 °C and ion source temperature was 200 °C. The ration of *E*- and *Z*-isomers of the coupling products were determined by <sup>1</sup>H-NMR analysis. Yields to the *E* products were based on the consumption of iodobenzene.

*E*-stilbene **3a** as a white solid – d<sub>H</sub> (200 MHz CDCl<sub>3</sub>); d<sub>C</sub> (50 MHz CDCl<sub>3</sub>) 7.54 (4H, d, *J* 7.1 Hz), 7.42–7.27 (6H, m), 7.23 (2H, s); d<sub>C</sub> (50 MHz CDCl<sub>3</sub>) 137.4, 128.8, 127.7, 126.6; *m/z* (EI) 180 (100%), 165 (53%), 152, 102, 89 (38%), 76, 63, 51

*E*-ethyl cinnamate **3c** as a colourless oil – d<sub>H</sub> (200 MHz CDCl<sub>3</sub>) 7.61 (1H, d, J 16 Hz), 7.50–7.41 (2H, m), 7.36–7.29 (3H, m), 6.36 (1H, d, *J* 16 Hz), 4.25–4.14 (2H, q), 1.30–1.16 (3H, t); d<sub>C</sub> (50 MHz CDCl<sub>3</sub>); *m/z* (EI) 176, 148, 147, 131 (100%), 103 (58%), 77, 51

*E-t*-butylcinnamate **3d** as a colourless oil –  $d_H$  (200 MHz CDCl<sub>3</sub>) 7.52 (1H, d, J 16 Hz) 7.47–7.42 (2H, m), 7.32–7.19 (3H, m), 6.3(1H, d, J 16 Hz) 1.47 (9H, s);  $d_C$  (50 MHz CDCl<sub>3</sub>); *m/z* (EI) 204, 189, 147 (100%), 131 (65%), 103, 77, 57 (43%)

*E*-cinnamamide **3b** as a white solid –  $d_H$  (200 MHz CDCl<sub>3</sub>) 7.71 (1H, d, J 15.7 Hz), 6.47 (1H, d);  $d_C$  (50 MHz CDCl<sub>3</sub>); *m/z* (EI) 147, 146 (100%), 131 (50%), 103 (82%), 77, 51, 44

#### 3. Results and discussion

The procedure reported by Bradley et al. [34] was followed in preparing the palladium colloidal solution stabilized by PVP.  $Pd(OAc)_2$  was employed as the palladium source and methanol as the reducing agent in the presence of varying amounts of PVP as stabilizer. After refluxing for 2–3 h, methanol was removed using a rotary evaporator and the residue was dissolved in ethanol. The solution thus prepared had a dark brown colour and was stable for weeks at room temperature. Following this methodology we could obtain nanoparticles with a particle size between 3 and 6 nm as revealed by TEM analysis (Fig. 1).

Li et al. have also employed the Pd-PVP nanoparticles, prepared according to Bradley's methodology, in the Sonogashira couplings [35]. The optimized conditions employed by Li et al. (2.0 mmol  $K_2CO_3$ , 1% Pd-PVP, ethanol, 80 °C) were utilized in the present work as the initial conditions for the coupling between iodobenzene (1) and styrene (2a) (Scheme 2, Table 1: entry 2). Excellent result was obtained employing such conditions (93%, entry 2). Since the nature of the base is of great importance in the Heck couplings, other bases were also tested in the Heck coupling between iodobenzene and

#### Table 1

Heck reaction between iodobenzene (1) and styrene (2a) under conventional heating.

Entry	Conditions <sup>a</sup>	Yield% <sup>b</sup>
1	K <sub>2</sub> CO <sub>3</sub> , room temperature, 48 h	20
2	K <sub>2</sub> CO <sub>3</sub> , 80 °C, 4 h	93
3	KOAc, 80°C, 4 h	84
4	NaHCO3, 80°C, 4h	85
5	K <sub>3</sub> PO <sub>4</sub> , 80 °C, 4 h	84

<sup>a</sup> Conditions: 1% Pd-PVP,  $K_2CO_3$  (2.0 mmol), ethanol (2.0 mL), iodobenzene (1.0 mmol); **2a** (1.2 mmol), 80 °C, 4 h, round-bottomed flask equipped with a reflux condenser.

<sup>b</sup> GC-MS yield to *E*-stilbene related to iodobenzene, normalized areas.



Fig. 1. TEM image of the Pd(0)-PVP nanoparticles.



Scheme 2. Heck reaction between iodobenzene and styrene under conventional heating.

styrene (Table 1, entries 3–5), using the same temperature and catalyst loading with ethanol as solvent. Reactions under conventional heating (Tables 1 and 2) were performed in rounded-bottomed flask coupled to a reflux condenser.

Reactions with potassium carbonate (Table 1, entry 2) and sodium bicarbonate (entry 4) as bases were cleaner than the reactions carried out with potassium acetate (entry 3) and phosphate (entry 5). The use of  $K_2CO_3$  provided better yields to *E*-stilbene than NaHCO<sub>3</sub>; indeed in the later case a greater amount of stilbene isomers was obtained, indicating that double bond isomerization can occur (entry 4). The reaction was also performed at room temperature (entry 1) but, as it can be observed; poor yield was obtained



Scheme 3. Heck reaction between iodobenzene and alkenes under conventional heating.



Scheme 4. Heck reaction between acrylonitrile (2e) and iodobenzene (1) catalyzed by Pd-PVP under conventional heating.



Scheme 5. Heck reaction between iodobenzene (1) and *n*-butyl methacrylate (8) and  $\alpha$ -styrene under conventional heating (80° C, 4 h).

even after 48 h (monitored by GC/MS), indicating that higher temperatures are necessary for the oxidative addition to occur.

After reactions, diethyl ether was added to the reaction mixture in order to precipitate the palladium nanoparticles and all the inorganics. Crude coupling products were obtained from combined organic phases, after removing solvents under reduced pressure.

In an attempt to extend the application of our system under the optimized conditions for styrene (2.0 mmol K<sub>2</sub>CO<sub>3</sub>, 1% Pd-PVP, ethanol, 80 °C; Table 1, entry  $2 \rightarrow 3a$ , 93%), the coupling of iodobenzene (1) with other alkenes (**2b-e**) was also carried out (Scheme 3, Table 2).

#### Table 2

Heck reaction between iodobenzene (1) and alkenes (2a-e) under conventional heating.

Entry <sup>a</sup>	R	Yield % <sup>b</sup>	Product
1	Ph	93	3a
2	CONH <sub>2</sub>	>99 (70) <sup>c</sup>	3b
3	CO <sub>2</sub> Et	78	3c
4	CO <sub>2</sub> t-Bu	>99 (77) <sup>c</sup>	3d
5	CN	22 (30) <sup>d</sup>	3e

<sup>a</sup> Conditions: 1% Pd-PVP,  $K_2CO_3$  (2.0 mmol), ethanol (2.0 mL), iodobenzene (1.0 mmol); alkene (1.2 mmol), 80 °C, 4 h, round-bottomed flask equipped with a reflux condenser.

<sup>b</sup> GC-MS yield to the *E*-alkene related to iodobenzene, normalized areas.

<sup>c</sup> Product isolated yield.

<sup>d</sup> GC-MS Yield to 3-phenylpropionitrile.

As shown in Table 2, good yields to *E*-alkenes were achieved in 4 h of reaction, under conventional heating at 80  $^{\circ}$ C, for substrates **2a-d**.

The reaction of iodobenzene and acrylonitrile (**2e**) (entry 5), however, led to a mixture of products: Heck products (monoarylated **3e** and the diarylated alkene (**4e**), reduced products (**5e**, **6e**) and the Michael adduct (**7e**) derived from ethanol (Scheme 4).

The unusual selectivity towards reduced Heck products (hydroarylation) when acrylonitrile (**2e**) was employed in Heck coupling reactions was also observed by Antunes and co-workers. These authors employed 2-hydroxypropyl- $\alpha$ -cyclodextrins-capped palladium nanoparticles as catalysts.

Under thermal conditions, reaction of iodobenzene and *n*-butyl methacrylate (**8**) yielded a mixture 1:1 of the isomers *E* and *Z*-9 together with butyl 2-benzylacrylate (**9-gem**; Scheme 5). Employing  $\alpha$ -styrene as coupling partner also resulted in a mixture 1:1 of *E*/*Z* isomers.

Heck coupling reactions catalyzed by Pd-PVP nanoparticles also proceeded satisfactorily under microwave irradiation (Table 3, Scheme 6)



Scheme 6. Heck reaction between iodobenzene and alkenes under microwave irradiation.

Table 3	
Heck reaction between iodobenzene and alkenes under microwave irradiation.	

Entry <sup>a</sup>	R	$T(^{\circ}C)$	Yield ( <b>3a-e</b> ) % <sup>b</sup>	Yield ( <b>5a-e</b> ) (%) <sup>c</sup>
1	Ph	80	82	-
2	Ph	120	70 (1.0) <sup>c</sup>	1.0
3	CONH <sub>2</sub>	80	<1.0	-
4	CONH <sub>2</sub>	120	62 (<1.0) <sup>c</sup>	15
5	CO <sub>2</sub> Et	80	45	33
6	CO <sub>2</sub> Et	120	83 (12) <sup>c</sup>	7.0
7	CO <sub>2</sub> t-Bu	80	22	31
8	CO <sub>2</sub> t-Bu	120	72 (11) <sup>c</sup>	1.0
9	CN	120	38 (<1.0) <sup>c</sup>	44

 $^a$  Conditions: 0.1% Pd-PVP,  $K_2CO_3$  (2.0 mmol), ethanol (2.0 mL), iodobenzene (1.0 mmol); alkene (1.2 mmol), 120  $^\circ$ C, 300 W, sealed tube, 12 min.

<sup>b</sup> GC-MS yield to *E*-alkene product.

<sup>c</sup> GC-MS yield to *E*-alkene using a sealed tube equipped with magnetic stirring immersed in a pre-heated oil bath for 12 min.

Gratifyingly, upon decreasing the catalyst loading from 1% to 0.1%, an excellent level of conversion could still be achieved at 80 °C (entry 1) in 12 min. We have also observed in a general manner, that better yields to *E*-alkenes were obtained when the temperature of the reaction was increased from 80 to 120 °C. No appreciable yield was achieved for the coupling of iodobenzene with acrylamide when reaction temperature was 80 °C (Entry 3, Table 3). At this temperature, almost only biphenyl was formed (23% yield) as the product of the homocoupling reaction of iodobenzene. Increasing reaction temperature to 120 °C resulted in a dramatic increase of the yield of *E*-cinnamanide – 62% (entry 4). The corresponding hydroarylated product (**5b**: 15%) was also observed for the reaction with acrylamide at this temperature.

Yields to the corresponding coupling products apparently follow the alkene (2a-e) reactivities. It can be observed from the data shown in Table 3 that ethyl acrylate (entry 5) is more reactive than t-butyl acrylate (entry 7) for steric reasons and acrylamide (entry 3) is a less electron deficient alkene than acrylates. Acrylonitrile (entry 9) is a very reactive alkene from the electronic viewpoint, as well as from the stereo reason. Heck reaction between iodobenzene and acrylates (entries 5 and 7, Table 3) and acrylonitrile (entry 9) also furnished greater amounts of the reduced product compared with the coupling with acrylamide (entry 3) and styrene (entry 1). In the case of the acrylates, yields to the reduced products decrease with increasing temperature (entries 5 versus 6 an 7 versus 8). Heck reaction between iodobenzene and ethyl acrylate was carried out under microwave irradiation with simultaneous coupling and without cooling. No appreciable change in reaction yields or selectivities were observed comparing these two reaction conditions.

Kappe and co-workers [33] applied microwave heating to the Heck reaction between iodobenzene and butyl acrylate, in the presence of Pd/C as catalyst. Under the employed conditions [5% Pd/C, Et<sub>3</sub>N, MeCN, 180 °C], moderate (62%, 10 min of irradiation) and excellent (>99%, 20 min of irradiation) were obtained. Compared to the use of Pd/C as a heterogeneous catalyst (5% Pd, 10 min), the palladium nanoparticles developed in the present work (0.1% Pd, 12 min) allow not only the use of the catalyst in lower loading, but also better conversions to the coupling products (62–83%).

Michael adducts of ethanol and olefins were formed when acrylates and acrylamide were used as coupling partners, under microwave irradiation. Control experiments were carried out in order to investigate if palladium was acting as a Lewis acid catalyst (Scheme 7). It was found that Michael products were formed even in the absence of the palladium nanoparticles, as well as in the absence of added  $K_2CO_3$ .

In Fig. 2, we can observe the difference between the heating profiles of the test reactions performed with the aim of knowing if the nanoparticles were acting as Lewis catalysts in Michael reactions between the ethyl acrylate and ethanol. Dashed lines represent



Scheme 7. Michael reaction between ethyl acrylate and ethanol under microwave heating.



Fig. 2. Potency and heating profiles for microwave-assisted Michael reactions.

the heating profile in the presence of the catalyst while the heavy ones represent the heating profile in the absence of the Pd/PVP nanoparticles. It can be observed, when the catalyst is present, the reaction mixture reaches rapidly the temperature limit ( $120^{\circ}$  C) which is maintained by irradiating the mixture at 200 W. When the nanoparticles are absent, however, even at 300 W the limit temperature ( $120^{\circ}$  C) is not reached. This result indicates that the mixture which contains the nanoparticles has a great capacity of transforming radiation in heat because the nanoparticles are good microwave absorbers.

When coupling reactions were carried out in sealed tubes in preheated oil baths at 120 °C for 12 min, in order to compare the results with reactions under microwave irradiation at this same temperature (entries 2, 4, 6, 8 and 9), poor yields to the coupling products were obtained. These results demonstrated the beneficial effect of the microwave irradiation over Pd-PVP catalyzed Heck reactions. It is important to emphasize that careful must be taken when comparing microwave heating experiments with the oil bath ones, since heating profiles under microwave heating could not be reproduced in the oil bath experiments. For example, heterogeneous palladium catalysts are great microwave absorbers leading to higher superficial temperatures that are not reproduced under conventional heating. It can be the case, in the present work if, as evidenced by Lee et al. [28], Pd-PVP catalyzed C-C bond forming reactions are heterogeneous in nature, since there are higher superficial temperatures due to preferential heating of the supported-catalyst in comparison with the solvent. As it could be observed by the heating profiles presented in Fig. 2, Pd-PVP nanoparticles are good microwave absorbers. Besides that, ionic bases, not soluble in ethanol, are strong microwave absorbers as well, leading to superior temperatures on their surfaces. Both effects could have contributed to the better results found in coupling reactions under microwave irradiation. Suzuki couplings reactions catalyzed by Pd-PVP nanoparticles are also accelerated under microwave heating [19].

As mentioned before, reduced products were also found in the Heck coupling reactions catalyzed by Pd(0)-PVP nanoparticles. Antunes and co-workers disclosed their results concerning the influence of the solvent and the type of palladium catalyst on the selectivity Sonogashira versus hydroarylation in the coupling

#### Table 4

Heck reaction between 2-iodotoluene and ethyl acrylate with different palladium nanoparticles and solvents.

Entry	Conditions of preparing the Pd(0)-PVP	Solvent	Yield ( <b>3a-e</b> ) % <sup>b</sup>	Yield <i>E-</i> alkene (%)	Reduced product (%)
1	2.5 g PVP, 30 min	EtOH	63	74	12
2	2.5 g PVP, 120 min	EtOH	63	74	21
3	2.5 g PVP, 180 min	EtOH	55	83	8
4	1.2 PVP, 120 min	EtOH	47	80	19
5	0.6 PVP, 120 min	EtOH	37	66	31
6	2.5 g PVP, 120 min	t-BuOH	23	>99	-
7	2.5 g PVP, 120 min	MECN	59	92	-

 $^aConditions:~0.1\%$  Pd-PVP,  $K_2CO_3~(2.0\,mmol),$  ethanol (2.0 mL), 2-iodotoluene (1.0 mmol); alkene (1.2 mmol), 120  $^\circ$ C, 300 W, sealed tube, 5 min.

<sup>b</sup> GC-MS yield to *E*-alkene product.

<sup>c</sup>GC-MS yield to *E*-alkene using a sealed tube equipped with magnetic stirring immersed in a pre-heated oil bath for 12 min.



Scheme 8. Catalytic cycle for hydroarylation in Sonogashira couplings.

reaction between iodobenzene and phenylacetylene [36]. These authors reported that the selectivity Sonogashira versus hydroarylation is influenced by the nature of the catalyst and that hydroarylation decreases when supported catalysts such as Pd/C are employed. In the same work [36], Antunes and co-workers also proposed, in agreement with other reports in the literature as that of Wu et al. [37] and Hierso et al. [38], that the palladium catalyst may act as hydrogen transfer catalyst. In this case, the solvent can be of great importance as a hydride source (Scheme 8). Based on these previous works, we decided to prepare the Pd(0)-PVP nanoparticles under different reaction conditions in order to investigate if catalysts with different activity and selectivity could be produced and how the selectivity hydroarylation versus Heck reactions could be influenced (Table 4). Different amounts of the stabilizing agent PVP and different reaction times were applied to the synthesis of the palladium nanoparticles (Table 4, entries 1–5). Methanol was employed as the reducing agent for the Pd(II) precursor in all the cases. In order to investigate the influence of the solvent on the selectivity of the coupling reactions, we performed the Heck reactions between 2-iodotoluene and ethyl acrylate (Scheme 9) under



Fig. 3. Particle size distribution for Pd(0)-PVP produced when 2.5 g of PVP was employed.



Fig. 4. Particle size distribution for Pd(0)-PVP produced when 0.6 g of PVP was employed.

microwave heating with ethanol, *t*-butanol and acetonitrile (entries 2, 6 and 7).

As it can be observed from the data presented in Table 4, the time of reaction employed to prepare the nanoparticles seems not to influence the conversions to products (entries 1-3). However, the amount of PVP employed as the capping agent influenced the conversion to the products as well as the selectivity Heck versus hydroarylation (entries 2, 4 and 5). Decreasing amounts of PVP in the catalysts resulted in decreasing conversions and slower reactions. Superior selectivity in favour of hydroarylated products were observed as decreasing amounts of PVP were employed. When 2.5 g of PVP was employed (entry 2), around 70% of the particles were in the range of 3–4 nm of diameter (Fig. 3) and when 0.6 g of PVP was employed, around 90% of the particles were in this range (Fig. 4). Smaller particles have a greater amount of palladium atoms on the surface able to coordinate with the solvent to form palladium hydride species, thus favouring the hydroarylated products when minor amounts of PVP are employed to synthesize the catalysts.



Scheme 9. Heck coupling between 2-iodotoluene and ethyl acrylate under microwave heating.

In order to highlight the influence of the solvent on the selectivity of the couplings, we performed the coupling reactions with different solvents. As it was envisaged that the hydrogen donated from the solvent was not the most acidic one, but the  $\beta$ -hydrogen, we employed *t*-butanol as solvent for the Heck coupling between 2-iodotoluene and ethyl acrylate (entry 6). Reaction was slower in t-butanol (entry 6) than in ethanol (entry 2), but more selective as the *E*-cinnamate was the unique product obtained. It was not detected the formation of cinnmate isomers or of reduced products. As expected, *t*-butanol could not transfer  $\beta$ -hydrogen to palladium and no reduced products were formed. These result prompted us to perform the reaction in acetonitrile which does not have  $\beta$ hydrogens, so no reduced products could be expected (entry 7). Reaction in acetonitrile was faster than in *t*-butanol, very good selectivity to the Heck product could be observed but lower than that observed for t-butanol since it was detected some presence of cinnamate isomers.

#### 4. Conclusions

In this work, we presented the results obtained with Pd-PVP nanoparticles under conventional and microwave heating. It was found that Pd-PVP nanoparticles are effective phosphine-free catalysts for Heck coupling. Good conversions to the coupling products were obtained with both heating sources but microwave heating was found to strongly accelerate the reactions. Higher turnover frequencies were achieved under microwave irradiation since a lower loading of the catalyst (0.1% compared with 1.0% employed in the conventional heated experiments) as well as shorter reaction times were need to obtain good conversions (62-99%). Phase-transfer catalysts were not necessary to be used and cheap inorganic bases like sodium and potassium carbonates and phosphates could be successfully utilized. Hydroarylated products were observed when electron-poor alkenes were employed as coupling partners. Hydroarylation was favoured with the decreasing of the capping agent PVP in the synthesis of the catalysts. Hydroarylation process was suppressed when solvents which cannot act as hydrogen donor to palladium were employed such as t-butanol and acetonitrile. In a general manner *E*-alkenes were found to be the principal products with the monossubstituted alkenes. Good conversions to the coupling products could be obtained with disubstituted alkenes but a mixture of isomers was observed.

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