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Synthesis of imine cyclopalladated compounds.

Síntesis de compostos ciclopal·ladats d'imina.

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Campus d'Excel·lència Internacional

Chemistry, unlike other sciences, sprang originally from delusions and superstitions, and was at its commencement exactly on a par with magic and astrology.

Thomas Thomson

En primer lloc, vull donar mil gràcies al Dr. Joan Albert per tantes hores de conversacions sobre els seus coneixements dels compostos ciclopal·ladats, i també, per la seva implicació i passió, que des de bon principi m'han ajudat a tirar endavant amb moltes ganes d'aprendre, tant en el treball al laboratori com en la redacció d'aquesta Memòria.

En segon lloc, agrair a la meva germana i a la meva parella per recolzar-me cada dia en qualsevol situació, i als meus pares per confiar en mi i donar-me forces per poder arribar fins al final d'aquesta etapa.

Per últim, però no menys important, dono gràcies als amics que han estat sempre al meu costat disposats a donar-me suport i a passar bones estones.

REPORT

CONTENTS

1. SUMMARY

Since cyclopalladated compounds were first described by the cyclopalladation reaction, these palladium complexes have important applications in a wide variety of fields, especially in organometallic catalysis. Besides, the usually thermodynamic stability and the low reactivity front air components allowed to develop mesogenic metallocycles, luminescent complexes, catalysts for different organic reactions or medicinal compounds based in palladium (II). Moreover, studies of cyclopalladation reaction about its mechanism, scope and optimization, and on the reactivity of its products are still very active areas of research.

The purpose of this Memory is dealing with the one-pot synthesis of cyclopalladated compounds. Particularly, we have studied the synthesis of imine cyclopalladated dimer with the formula $[Pd(C_6H_6\text{-}CH{=}N\text{-}CH_2\text{-}Ph]_2(\mu\text{-}OAc)_2$, by successive concatenation of condensation and cyclopalladation reactions (**System 1**), and likewise, the concatenation of oxidation, condensation and cyclopalladation reactions (**System 2**). The Memory focus on the research of the optimal reaction conditions for an easier obtention of this compound with high yields, however, it reviews splitting reactions of dinuclear compounds with Lewis bases, in particular deuterated pyridine, and secondary compounds obtained as well.

Keywords: Palladium (II), cyclometalation, condensation, oxidation, benzylamine.

2. RESUM

Des dels primers compostos ciclopal·ladats descrits mitjançant la reacció de ciclopal·ladació, aquests complexos de pal·ladi tenen aplicacions importants en una àmplia varietat de camps, especialment en la síntesi organometàl·lica. També, generalment, són estables termodinàmicament i presenten baixa reactivitat davant els components de l'aire, fent possible el desenvolupament de metal·locicles mesogènics, complexos luminescents, catalitzadors per diferents reaccions orgàniques o compostos medicinals basats en el pal·ladi (II). Amés, els estudis relacionats amb la reacció de ciclopal·ladació sobre el seu mecanisme, abast i optimització, i en la reactivitat dels seus productes són àrees molt actives d'investigació.

La finalitat d'aquesta Memòria és tractar amb la síntesi de compostos ciclopal·ladats en un únic reactor. Especialment, hem estudiat del dímer ciclopal·ladat d'imina amb la fórmula $[Pd(C_6H_6\text{-}CH{=}N\text{-}CH_2\text{-}Ph]_2(\mu\text{-}OAc)_2$, mitjançant el desencadenament successiu de reaccions de condensació i de ciclopal·ladació (**Sistema I**) i de la mateixa manera, el desencadenament de les reaccions d'oxidació, condensació i ciclopal·ladació (**Sistema II**). Aquesta Memòria se centra en la investigació de les condicions de reacció òptimes per a una obtenció més senzilla d'aquest compost amb rendiments elevats, tanmateix, també s'hi revisen les reaccions d'escissió dels compostos dinuclears amb bases de Lewis, particularment piridina deuterada, i els compostos secundaris obtinguts.

Paraules clau: Pal·ladi (II), ciclometal·lació, condensació, oxidació, benzilamina.

3. INTRODUCTION

Organometallic compounds that contain in their structure metallocycles with a Y-M-C sequence of sigma bonds are named cyclometallated compounds. The C is a carbon atom with sp^3 or sp^2 hybridization, Y is a two-electron donor heteroatom such as N, P, O or S and M is a transition metal centre. Figure 1 presents some examples of these structures for this type of compounds with the Y-M-C sequence indicated in blue. [1]

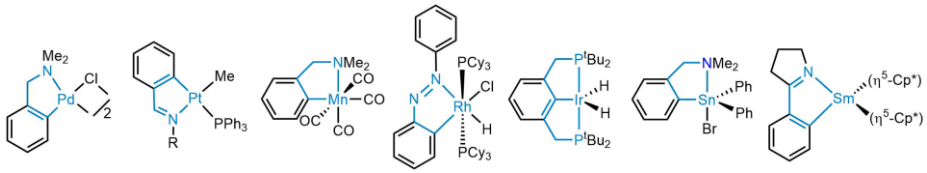


Figure 1: Examples of cyclometallated compounds

The most efficient method of preparing cyclometallated compounds is by the cyclometallation reaction (Figure 2). The reaction undergoes into two steps. The first move is the coordination of a heterosubstituted organic molecule with a donor atom to a metal centre, reorganizing its coordination sphere. Consequently, takes place the intramolecular C-H activation to produce an organometallic compound with a cycle containing the Y-M-C sequence of sigma bonds exemplified in the previous figure. Note in Figure 2 that the leaving hydrogen atom, designed as [H], does not reflect if it dissociates with the appropriate ligand or it remains bonded to the metal centre, so then it can be a proton (H^+), a hydride (H^-) or a radical ($H^\cdot$) depending on the mechanism of the C-H bond activation. [2] Nevertheless, sometimes the cyclometallation reaction fails or it is not efficient enough, for instance, to generate three- or four-membered metallocycles. Thus, cyclometallated compounds can be also prepared by oxidative addition, transmetallation or transcyclometallation or through an external nucleophilic attack to an unsaturated ligand coordinated to the metal centre in κ^1-η^2 coordination mode. [3]

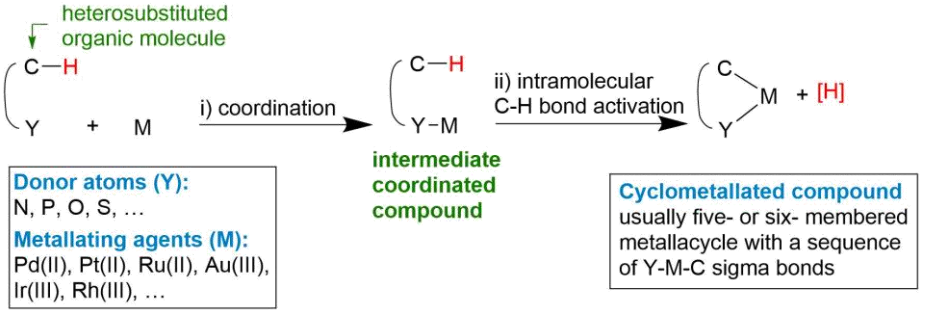


Figure 2: Steps of cyclometallation reaction.

Last decades, the development of studies related with Pd (II), Pt(II), Ru(II), Au(III), Ir(III) and Rh(III) cyclometallated compounds have increased due to their growth in different applications as organometallic catalysis, organic synthesis, bioimaging, medicinal and biological chemistry and components of electro-optical devices between other purposes. Thereby, these compounds can frequently be easy to handle because of their relatively high thermodynamic and kinetic stability (Figure 3). In most of the cases, the structure of these compounds contains a rather robust five or six-membered metallacycle owed to: i) the chelate effect induced by the κ^2-Y,C coordination mode of the cyclometallated ligand promoting the intramolecular process and ii) the relative strength of the bonds formed by metal centres and the coordinated atoms of the heterosubstituted cyclometallated ligand, one carbon atom sp^2 or sp^3 hybridization and one adequate sigma donor heteroatom Y (intermediate or soft) inducing to the resulting lower energetic stability of the compound. Moreover, other co-ligands attached to the metal centre in these compounds promote further their energetic stabilization, some common examples are as PPh_3 or chloride co-ligands. These properties allow high thermal stability either in solid-state or in solution and the unreactivity in contact with air components, comparing it with other organometallic compounds, favouring on the development of their applications commented before [3-7]. It should be remarked from Figure 3 that the coordinated carbon atoms of these complexes have a high *trans* influence because of their σ-donor and π-acceptors character that exhibit strong *trans effect* and this encourage kinetically the substitution of the ligands trans to them. [8]

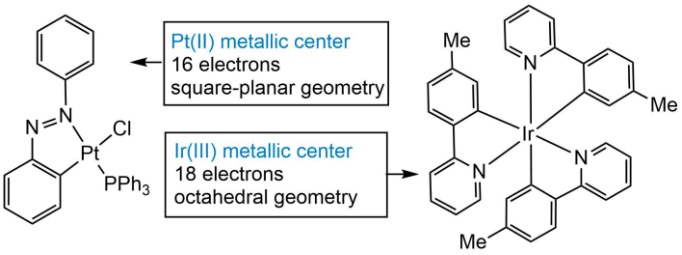


Figure 3: Examples of easily handle cyclometallated compounds with a metal centre from the second or third transition series with high thermodynamic and kinetic stability

3.1. CYCLOPALLADATED COMPOUNDS

Cyclopalladated compounds are cyclometallated compounds within palladium (II) as a metal centre. These compounds, and their structural analogues of platinum(II) as well, are being developed vigorously because of their growing use and new developments in organometallic catalysis and medicinal chemistry respectively, between other fields [3,4,9]. Furthermore, when the first cyclopalladated compounds derived from N,N-dimethylbenzylamine and azobenzene were obtained at the '60s by means of the cyclopalladation reaction, researchers established the preferent activation of C_{sp2}-H bonds over C_{sp3}-H bonds and the structural bent for five-membered metallocycles over the six-membered [10.11]. Since then, there has been much interest in the mechanism, in the extension of the reaction and the structure and reactivity of cyclopalladated compounds. [1-3,12-14]

Structurally, cyclopalladated compounds can be first classified according to the nature of the ligands as a four-electron donor (CY) or six-electron donor (YCY). YCY cyclopalladated compounds are symmetrical or asymmetrical and for CY-type can be mononuclear or dinuclear. In this last dinuclear structure, two geometrical isomers are possible: cis and trans, and can usually have planar or folded formations with halides or acetate bridges respectively. Y-donor heteroatoms in palladacycles are often N, O, P, S or As, however, the most common cyclopalladated compounds are the ones within N-donor heteroatom. They mainly derive from tertiary amines and imines, besides, from pyridines, azobenzenes and oxazolines and are frequently five or six-membered metallocycles. These N-donor cyclopalladated compounds frequently are quite thermally stable and unreactive in front of air components, both in solution and in solid-state (Figure 4). [3,12]

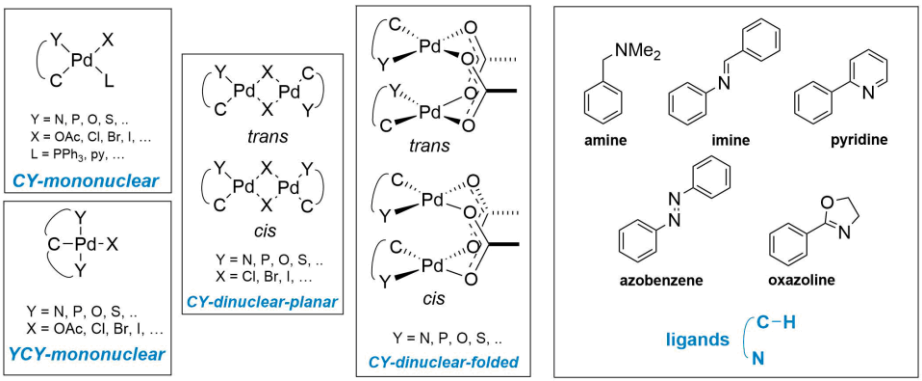


Figure 4: Structures of CY and CYC types and examples of κ^2-N,C chelating ligands.

3.2. SYNTHESIS OF CYCLOPALLADATED COMPOUNDS: ORTHOPALLADATION REACTION

The cyclopalladation reaction is the simplest and direct method for the synthesis of cyclopalladated compounds. The reaction consists in the direct palladation by the intramolecular activation of a C-H bond from the ligand, which was already coordinated via the heteroatom. When the intramolecular C-H bond activation involves the ortho position of the aromatic ring of the ligand is named as orthopalladation [12]. For instance, N,N-dimethylbenzylamine [14], azobenzene [15] and the imine (E)-N-benzyl-1-phenylmethanimine [16], prepared by the condensation of benzaldehyde and benzylamine, are some ligands which undergo quite simply the orthopalladation reaction with $Pd(OAc)_2$ obtaining their corresponding dinuclear CY-folded cyclopalladated compound with acetate bridges.

Furthermore, the regioselectivity of cyclopalladation is affected by the structure of the ligand. Some of the ligands are potentially polyfunctional. That means that they may have more than one C-H bond susceptible to their intramolecular activation. For instance, the imine (E)-N-benzyl-1-phenylmethanimine, represented below in Figure 5, presents two different ortho C-H bonds that can experience the activation so they can form two different isomers: *endo*- and *exo*-, depending on if the C=N bond is inside or outside the metallacycle respectively. There is a clear regioselectivity tendency on the cyclopalladation of imines and oxazolines to the formation of the *endo*--cyclopalladated compound, being probably the thermodynamic isomer.[2,3,16]

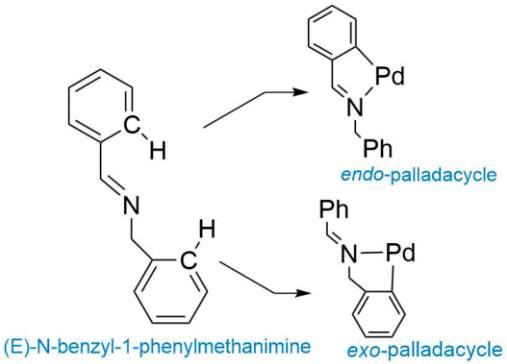


Figure 5: *endo*- and *exo*- isomers of the cyclopalladated (E)-N-benzyl-1-phenylmethanimine.

The proposed mechanism for the orthopalladation reaction, outlined below in Figure 6, is a computational study of the reaction mechanism of N,N-dimethylbenzylamine with $Pd(OAc)_2$. During the transition step, the C-H activation occurs when the ortho-H of the N,N-dimethylbenzylamine establish an agostic interaction with the Pd (II) centre, producing a three-centres and two-electron bond system, weakening the C-H bond as a result. The agostic H-transferring occurs through the agostic C-H intermediate when the *cis* acetate ligand displaces to the ortho C-H bond and interacts with the H forming a non-conventional hydrogen bond, a three-centres and four-electrons bond system. At the final step, the H-acceptor acetate round aside the agostic C-H bond and donates the hydrogen to the second acetate, which is located *trans* to the new Pd-C bond. [17-19]

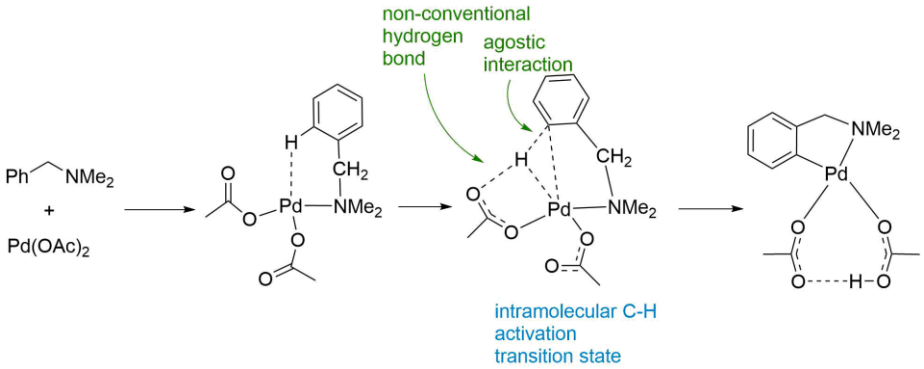


Figure 6: Proposed computational mechanism of orthopalladation reaction between N,N-dimethylbenzylamine and $Pd(OAc)_2$.

3.3. METATHESIS AND SPLITTING REACTIONS OF DINUCLEAR N-CYCLOPALLADATED ACETATE OR CHLORIDE BRIDGED COMPOUNDS

Dinuclear cyclopalladated compounds with acetate bridges can undergo the metathesis reaction quite easily, switching the folded structure to a planar chloride bridged with LiCl. Besides, dinuclear palladacycles can be converted easily into mononuclear compounds by splitting reactions with phosphines or pyridines, where these ligands are preferentially located *cis* to the Pd-C bond rather than *trans*, called the antisymbiotic effect. [8] As a matter of example, an N-donor ligand in the bridged palladacycle increase the rate of the splitting reaction with PPh_3 when the N-donor atom is in *trans* position to the departing ligand. Therefore, the isolated mononuclear compounds present, almost invariably, the *trans*-***N,P***-[Pd(C,N)XPPh_3] isomer, known as the thermodynamic control product, rather than the kinetic one with formula *trans*-***C,P***-[Pd(C,N)XPPh_3], (X = OAc or Cl). [3,12,20]

Figure 7 exemplifies the products obtained for the specific dinuclear bridged *endo*-palladacycle of (E)-N-benzyl-1-phenylmethanimine: the splitting reaction from acetate to its chloride bridged derivative and the metathesis reaction of the dinuclear bridged *endo*-palladacycle with PPh_3 solutions in $CDCl_3$. [16]

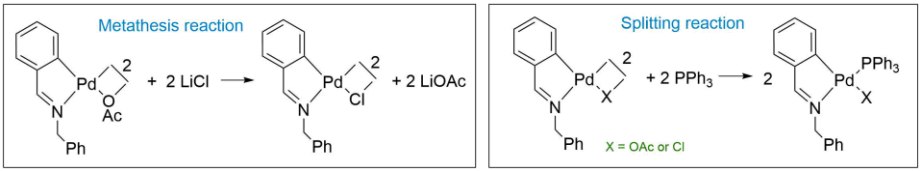


Figure 7: Splitting and metathesis reactions of dinuclear bridged *endo*-palladacycle of (E)-N-benzyl-1-phenylmethanimine.

The tendency to obtain these stereoisomers from the reactions above in Figure 7 is explained by Pearson's theory of hard and soft acids and bases. Palladium (II) is a soft Lewis acid, hence, the exchange in the metathesis reaction of Lewis hard base acetate for the intermediate Lewis hard/soft base chloride or the substitution in the splitting reaction of acetate or chloride ligands by the soft Lewis base PPh_3 occur as a result of the symbiotic effect. This effect establishes the affinity of hard Lewis bases to form stable adducts with hard Lewis acids and vice-versa with the soft Lewis acids and bases. In brief, substitution reactions of the soft Lewis acid Pd (II) with acetate for chloride or either both ligands for phosphines are favoured thermodynamically. [21,22]

Furthermore, in a few cases, compounds of formula [Pd(C-N)(X)(L)] have been reported as the *cis*-***N,L*** stereoisomer. As said before, when L is PPh_3 and X are independently OAc, Cl, Br or I, the splitting reaction favours the *trans*-***N,P*** isomer, however, when L is pyridine and X are Br or I, it favours the *cis*-***N,N*** isomer (Figure 8). The phenomenon is called the antisymbiotic effect, which establishes that the presence of two soft basic ligands attached in a mutual *trans* position to a square-planar soft acid metal, such as Pd (II) or Pt(II), have an energetic destabilizing effect on each other. Thus, for this type of compounds, the hardest X or L ligand tends to be *trans* to the soft carbon atom and the softest X or L ligand tends to be *trans* to the intermediate hard/soft nitrogen atom. [20-23]

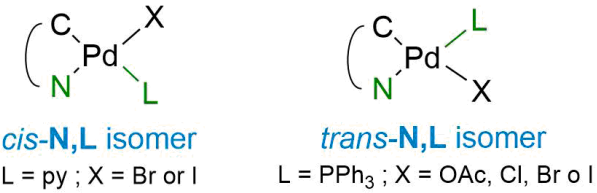


Figure 8: General stereoisomers *cis*- and *trans*-***N,L*** of compounds of formula [Pd(C-N)(X)(L)].

4. OBJECTIVES

The aim of this project is the synthesis of the endo-ortho-cyclopalladated dimer with acetate bridge of formula $[Pd(C_6H_4\text{-}CH{=}N\text{-}CH_2\text{-}Ph]_2(\mu\text{-}OAc)_2$, named as compound **1a,** with the (E)-N-benzyl-1-phenylmethanimine of formula $Ph\text{-}CH{=}N\text{-}CH_2\text{-}Ph$, as imine ligand **a**, already described in the literature [16], through a more practical one-pot method of synthesis. The principal strategy is to find more efficient designs of preparation for compound **1a** or, as well, new sequences of reactions in where this cyclopalladated compound generates at the same reactor.

This procedure could give a more efficient and simple method of preparing compound **1a** or extrapolate it for other similar imine systems. Furthermore, this procedure could make accessible new imine cyclopalladated compounds, which are difficult to obtain due to overly complicated chemical synthetic pathways or economic issues.

So far, the best method of preparation is reviewed in reference [16]. The treatment of imine **a** and $Pd(OAc)_2$ in a two-to-one molar ratio in acetic acid at reflux for 45 minutes and the appropriate procedure toward the reaction allows the isolation of compound **1a** in 87% yield. However, the synthesis is a two-step process: it starts with the preparation of imine **a** via the condensation between benzaldehyde and benzylamine in refluxing ethanol. Secondly, the cyclopalladation reaction of imine **a** with $Pd(OAc)_2$ as the metalating agent lets the obtention of the cyclopalladated imine **1a**. Both reaction products (**a** and **1a**) were isolated purely by vacuum distillation and column chromatography, respectively. The reaction pathway followed in reference [16] to obtain imine **a** and imine is pictured schematically in Figure 9. [16]

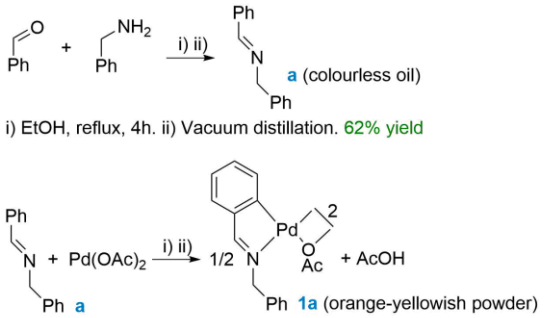


Figure 9: Scheme of the two-step preparation method[16] of the cyclopalladated imine **1a**

This Memory explores two synthesis methods of imine cyclopalladated compound **1a** in one-pot and three components system. Herein, it includes a discussion for optimization of the yield in the synthesis of compound **1a** in future experimental studies of these systems. On the one hand, a blend of benzylamine, benzaldehyde and $Pd(OAc)_2$ composes **System I**, in where the reactions presented before are concatenated: i) the condensation reaction to obtain in-situ the (E)-N-benzyl-1-phenylmethanimine and with the subsequent, ii) cyclometallation reaction to produce its acetate bridged *endo*-cyclopalladated dimer **1a**. On the second hand, a blend of benzylamine, $Pd(OAc)_2$ and $Cu(OAc)_2 \cdot H_2O$ composes **System II**, is where the attempted concatenation of reactions are: i) the catalytic oxidation of benzylamine with Pd (II), via an oxidant system constituted by Cu(II) and Pd (II), in order to obtain benzaldehyde, ii) the condensation reaction of this benzaldehyde with benzylamine to get the imine **a** and, iii) the cyclometallation reaction of imine **a** with $Pd(OAc)_2$ to lastly obtain the desired cyclopalladated imine, **1a**.

Precedent studies support the viability of these proposed one-pot and three-components systems (**I** and **II**) for the synthesis of compound **1a**. [24-27] These researches report, that a **System III** composed by a mixture composed of 4-nitroaniline, one arylcarbaldehyde and $Pd(OAc)_2$ in acetic acid with a moderate temperature, that can vary from 60 to 90 ºC and relatively long time reacting, between one and three days, give, in a satisfactory yield, the corresponding dinuclear acetate-bridged *endo*-palladacycle within: i) a five-membered metallacycle bonded to the *ortho*-aromatic carbon of the phenyl group (compounds **1b – 1e**) [24, 25], ii) a six-membered metallacycle bonded to the aliphatic carbon atom substituted in the phenyl group (compound **1f**) and iii) a six-membered metallacycle bonded to the aromatic carbon atom of the anthracenyl group (compound **1g**) [26] (Figure 10).

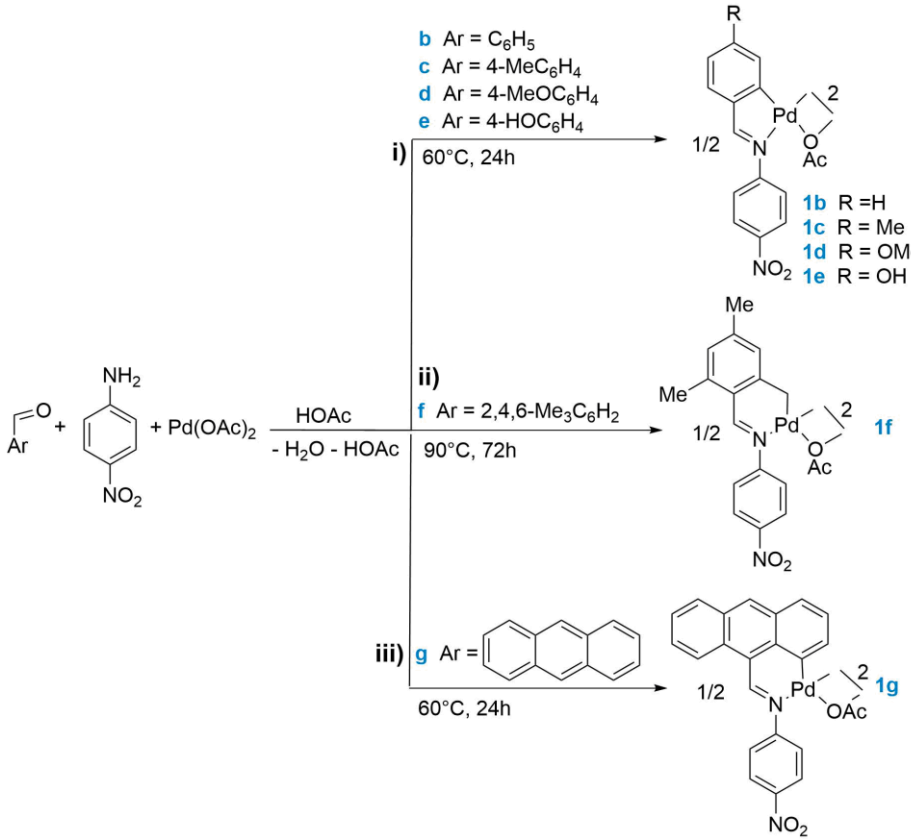
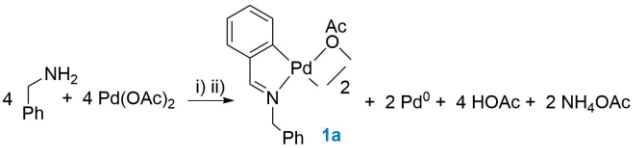


Figure 10: Imine cyclopalladated compounds obtained from **System III**. [24-26]

Besides, when benzylamine and $Pd(OAc)_2$ were treated in a one-to-one molar ratio in refluxing glacial acetic acid for 45 minutes, was possible to isolate compound **1a** in 14% yield (The global reaction in Figure 11 give detailed information about its experimental performance) [27]. Furthermore, for the plausibility of the oxidation reaction of benzylamine with Pd (II) in **System II**, the sequence of reactions, proposed time ago in a communication conference, could explain the obtention of benzaldehyde: i) the coordination of benzylamine with Pd (II), ii) the β-elimination followed by iii) the reductive elimination to get the phenylmethanimine (Ph-CH=N-H) and lastly, vi) the hydrolysis of this formed imine to the benzaldehyde (Figure 12). [28]



i) Benzylamine/$Pd(OAc)_2$ molar ratio = 1, refluxing HOAc, 45 min.
ii) Column chromatography (stationary phase = silica gel-60; mobile phase = $CHCl_3$:MeOH (100:6 v/v). 14% yield

Figure 11: Global reaction of the synthesis of compound **1a** by a benzylamine and $Pd(OAc)_2$ mixture.

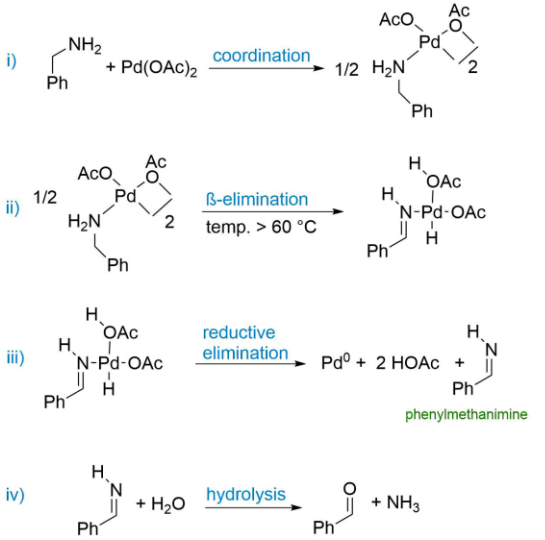
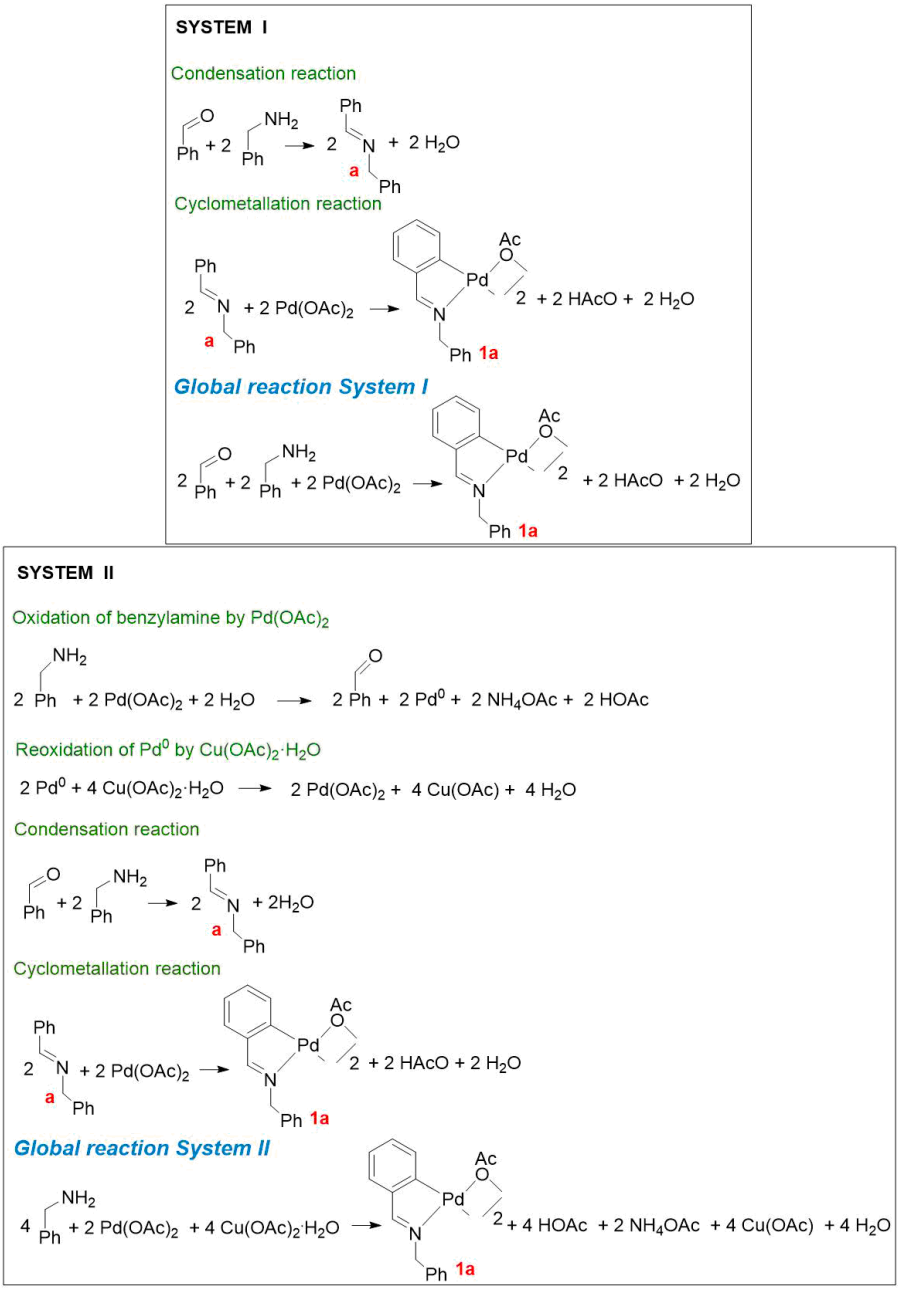


Figure 12: Proposed sequence of reactions for the oxidation of benzylamine by $Pd(OAc)_2$.

5. RESULTS AND DISCUSSION

Scheme 1 gives the expected concatenated reactions individually and their global reactions for **Systems I** and **II** for the three-component and one-pot synthesis of compound **1a**. Each global reaction establishes the stoichiometry of the three components to get their most usefulness to produce **1a**, hence, the molar ratio in **System I** between $Pd(OAc)_2$, benzylamine and benzaldehyde was 1:1:1. For **System II**, the molar ratio between benzylamine, $Pd(OAc)_2$ and $Cu(OAc)_2 \cdot H_2O$ was set at 2:1:2. Furthermore, both systems were performed in a closed reactor containing usually atmospheric air, whereby the time and temperature conditions of the reactions were altered.

System I and **II** were carried out in acetic acid, since protonic solvents are well known to accelerate the rate of the cyclopalladation reaction of imines. [29] It should be noted that in **System II**, $Cu(OAc)_2 \cdot H_2O$ was chosen as the oxidant for the supposed Pd(0) formed in the oxidation of benzylamine to benzaldehyde by Pd (II). These copper (II) compounds, either $Cu(OAc)_2 \cdot H_2O$ or $CuCl_2$, were effective in the reoxidation of Pd(0) in-situ, without interfering with the other process components from catalytic cycles [30] such as in the oxidative cyclization of indoles from anilines [31] and in the Wacker process, where the oxidation of ethylene to acetaldehyde occurs by the oxygen of the air and using catalytic amounts of Pd (II) with $CuCl_2$ as an oxidant.[32] It is noteworthy that neither expensive ligands nor strong acids/bases are needed.



Scheme 1: Expected concatenated individual reactions and the global reaction proposed (**System I** and **II**).

Figure 13 gives the molecular structure of the principal and secondary experimental compounds obtained from **Systems I** and **II**. Samples of compounds **1a**, **2a** and **I** were found in the laboratory and were prepared according to the previously described methods in the literature [16,27,33], therefore, their purity could be established by ^{1}H NMR in $CDCl_3$. These compounds were used as a reference compound for their comparison via TLC analysis with the experimental crude obtained, moreover, each compound (**1a**, **2a** and **I**) underwent their splitting reaction with py-d_5 to obtain compounds **3a**, **4a** and **II** respectively and were characterised by ^{1}H NMR in $CDCl_3$/py-d_5 solution. Hence, they were used for better ^{1}H NMR spectra comparison of the crudes, in $CDCl_3$/py-d_5 solution as well. In addition, protons from the *ortho*-metallated phenyl are labelled in Figure 13 for the following discussion, and all procedures followed for the treatment of the crudes and their characterization data are detailed in the **Experimental Section**.

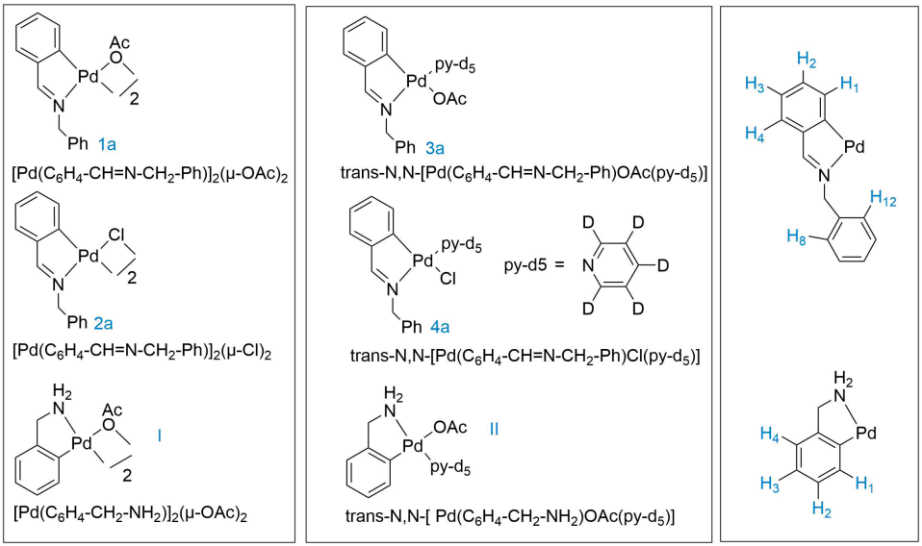
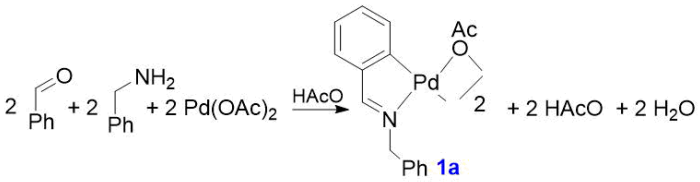


Figure 13**:** Lineal molecular structure of main and secondary compounds obtained in **Systems I** and **II**. Labelled protons from the *ortho*-metallated phenyl.

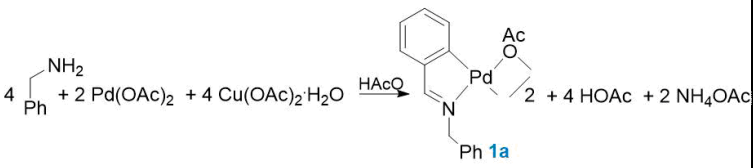
The summary below schematizes the results obtained for the proposed strategy in the synthesis of compound **1a** and it gives details about the reaction conditions executed in the three experiments for **System I** and in the two ones for **System II** (Table 1).

System I



Experiment	Reactants molar ratio	Atmosphere	Temp (ºC)	Time (hours)	Compound	Yield (%)
1	1:1:1	air	60	48	**1a**	41
2	1:1:1	air	75	72	**1a**	63
3	1:1:1	N_2	70	96	**1a**	64

System II



Experiment	Reactants molar ratio	Atmosphere	Temperature (ºC)	Time (hours)	Compound	Yield (%)
4	2:1:2	air	90	48	**2a**	11
5	2:1:2	air	Reflux	1	**1a**	5

Table 1: Executed experiments from **Systems I** and **II**.

5.1. SYSTEM I

In **System I**, both reactions of condensation and cyclopalladation underwent positively effective in the synthesis of compound **1a** in one procedure, isolating this compound in reasonable yields (41% to 64%).

For this system, **Experiments 1** and **2** were performed in a closed reactor with air as the atmosphere and had a noticeable benefit by increasing the temperature and the time of the reaction, since the yield increased from 41% in **Experiment 1** (60 ºC for 48 h) to 63% in **Experiment 2** (75 ºC for 72 h). To improve this system further, we decided to check if atmospheric oxygen interfered since the benzaldehyde could be oxidized to benzoic acid in the presence of oxygen and sunlight. [34] Therefore, **Experiment 3** was set in a N_2 atmosphere at 70ºC for four days. There were no significant variations in this **Experiment 3** contrasted with **Experiment 2**, not only in the appearance during the reaction but also in the treatment of the

crude, and compound **1a** was isolated in a 64% yield. Hence, the amount of oxygen present in the closed reactors from the previous experiments did not affect in the obtention of **1a**.

The three experiments performed in **System I** changed their appearance similarly, from the commencement a dark orange precipitate appeared and as the reaction progressed, it became a darker brownish solution. Figure 14 gives the appearance of the reaction crude obtained from **Experiment 1**. In future experiments, these insoluble materials should be filtrated, isolated and characterised to establish their composition. The darker colours that all experiments presented at the end of the reaction suggested the formation of little amounts of Pd(0) in this system. As reported, palladium (II) has an oxidant character and a facile reduction to palladium(0), which has been observed in cyclopalladation reactions, mainly in harsh reaction conditions as refluxing acetic acid. [3,27,35]

Figure 14**:** Appearance of the reaction crude obtained in **Experiment 1**.

In addition, during the TLC study of the fractions from the column chromatography in the three experiments, a less polar compound was observed, however, only in **Experiment 2** it could be filtered, concentrated and characterised by ^{1}H NMR as compound **2a** (Detailed information is given in **Experimental Section**). This compound has formed via the metathesis reaction of **1a** with adventitious chloride anions during the synthesis or the treatment of compound **1a**.

From previous studies related to the mechanism of the cyclopalladation reaction and our results obtained, we reason plausible conclusions about the reactions that could be operating in **System I** schematized in Figure 15. [27,28,33,36]

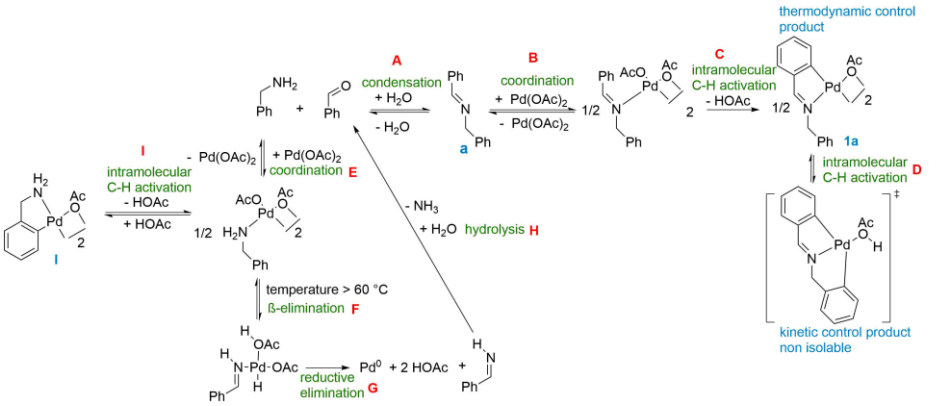


Figure 15: Plausible reactions operating in **System I**

On the one hand, they reported the study of a solution of imine **a** and $Pd(OAc)_2$ in a $CDCl_3$:Pd(OAc-d_3) solution of a two-to-one molar ratio and proved that: i) in few minutes, the solution was mainly constituted by benzaldehyde, deuterated benzylamine ($C_6H_5CH_2$-ND_2) and Pd(OAc-d_3), and ii) after two weeks, the solution was composed principally of benzaldehyde and the deuterated cyclopalladated compounds **1a** ([$Pd(C_6H_4$-CH=N-CH_2-Ph]$_2$(μ-OAc-d_3)$_2$) and **I** ([$Pd(C_6H_4$-CH_2-ND_2)(μ-OAc-d_3)$_2$). In addition, a ^{1}H NMR spectrum of imine **a** showed the presence of the imine **a**, benzaldehyde and benzylamine in an approximate ratio of 1:1:1. These data supported the proposed reactions **A**, **B**, **C**, **E** and **I** for **System I**. [33]

Besides, the treatment of compound **1a** in DAcO at 60 ºC for 24 hours produced a compound **1a** with the deuterated atoms located in the *ortho* positions of the phenyl group (Ph-CH_2-), however, the reaction between imine **a** and $Pd(OAc)_2$ afforded the compound **1a** with a bigger deuterium content than before. This result indicates that intramolecular C-H activation occurs even once the cyclopalladation reaction is over, exchanging the *ortho*-H of the phenyl group for deuterated atoms via the intermediate compound formed in reaction **D**. Nevertheless, this kinetical compound is neither detectable nor isolable. [33]

On the other hand, the reaction between benzylamine and $Pd(OAc)_2$ in refluxing acetic acid for 45 min formed compound **I**, besides, compound **1a** was isolated in a 14% yield, suggesting that the formation of compound **I** is a reversible process (Reaction **I**). Especially under harsh conditions, reactions **E**, **F**, **G** and **H** that benzylamine could undergo explain the obtention of a little amount of Pd(0) reported. Besides, the treatment of benzylamine with $Pd(OAc)_2$ in DAcO at 60 ºC for 24 hours and characterised by ^{1}H NMR in a $CDCl_3$/py-d_5 solution gave a mixture of

compound **II** and deuterated compound **II** with formula *trans*-***N,N***-[Pd(3-$DC_6H_3CH_2NH_2$)(OAc)(py-d_5), in where the deuterated atom is located in the *ortho* position of the metallated phenyl group, concerning Reactions **E** and **I**. [27,28]

Moreover, the ^{1}H NMR spectrum of **1a** obtained from the treatment of imine **a** with $Pd(OAc)_2$ in DAcO did detect the deuterium atom located in ortho-H of the phenyl group, as already said, however, it did not detect the deuterium atom in H4 from the metallated phenyl group. [33] Both data prove that the formation of compound **1a** in this system (Reaction **C**) was irreversible.

In summary, the experiments performed with **System I** manifest that in a system constituted by imine **a** and $Pd(OAc)_2$ in acetic acid, the reactions A, B and C showed in Figure 15 can be operative. Hereafter, these studies could pave the way for future developments in a one-pot method for the synthesis of imine cyclopalladated compounds derived from (E)-N-benzyl-1-phenylmethanimines.

Furthermore, the **System III** presented previously in Figure 10 composed by a mixture of 4-nitroaniline, arylcarbaldehyde and $Pd(OAc)_2$ in acetic acid gave better results than **System I** in the preparation of imine cyclopalladated compounds derived from (E)-N-(4-nitrophenyl)-1-arylmethanimines. A reaction from **System III** similar to the reaction from **System I**, for instance, it was the treatment of 4-nitroaniline, benzaldehyde and $Pd(OAc)_2$ in acetic acid at 90 ºC for 24 hours, in where compound **1b** was isolated in 80% yield. [24] The reason that may explain this difference is the lower nucleophilic character of the N atom from the 4-nitroaniline due to the electron-density withdraw character of the nitro group, hence, the rate of the condensation reaction with benzaldehyde could decrease. Besides, the N atom of the 4-nitroaniline is a harder Lewis base than benzylamine, hence, its affinity for the soft acid palladium (II) centre decreases. [20,21]

5.2. SYSTEM II

In **System II**, the global reaction detailed in Scheme 1 did not proceed as expected and the performed **Experiments 4** and **5** did not form compound **1a** in reasonable yields, these results are given in Table 1. This system is not yet efficient enough for producing compound **1a**, yet, it was noteworthy that milder conditions from **Experiment 4** (90 ºC for 48 hours) allowed the isolation of compound **2a** in 11% yield, while in **Experiment 5** (refluxing acetic acid for one hour) compound **1a** was achieved in 5 % yield.

The addition of $Cu(OAc)_2 \cdot H_2O$ to oxidise the formed Pd(0) by the oxidation of benzylamine to benzaldehyde was not as effective as we expected since the direct reaction, described previously in reference [27], between benzylamine and $Pd(OAc)_2$ afforded compound **1a** in 14% yield. Thus, $Cu(OAc)_2 \cdot H_2O$ had a damaging effect on the yield towards the obtention of compound **1a** for both experiments. The appearance of their reaction crude has an intense green yellowish colour and darker green areas that could contain Pd(0) (Figure 16). In addition, most of this material from the crude was retained fully at the beginning of the column chromatography as a big green band which could not be elute due to its high polarity.

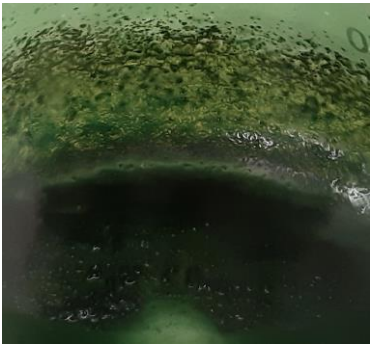


Figure 16: Appearance of the reaction crude obtained in **Experiment 5**.

On the one hand, in **Experiment 4**, the obtention of compound **2a** could be explained by the metathesis reaction that underwent the acetate-bridged compound **1a** via the substitution of these acetates for adventitious chlorides anions present in the synthesis procedure or the separation of **1a**. On the other hand, in **Experiment 5**, the increase of the polarity of the eluent after the separation of compound **1a** allowed the elution of a compound that could derivate from compound **I** with the formula $[Pd(C_6H_4\text{-}CH_2\text{-}NH_2)]_2(\mu\text{-}OAc)_2$ (detailed information is given in **Experimental Section**). Finally, more experiments are needed for **System II** in order to improve and understand the involved reactions, however, a more extended discussion of this system is given in the following section.

5.3. DISCUSSION TO IMPROVE THE EFFICIENCY OF SYSTEM I AND II

Firstly, all the experiments, performed in **System I**, had insoluble products at the start of the reaction (Figure 17) which could be any of the coordination compounds of benzylamine with Pd (II). These coordination compounds were reported with the general formula $[Pd(OAc)_2L_2]$ or their dimeric derivates (with the formula $[Pd(OAc)(\mu\text{-}OAc)L]_2$) obtained from the reaction with $[Pd(OAc)_2]_3$ (L = benzylamine). Moreover, they were isolated and proved to be precursors for the obtention of *ortho*-cyclopalladated compounds, for instance, compound **I**. Thus, these compounds were insoluble in usual organic solvents and assumed the thermodynamically stable *trans* geometry, therefore, our insoluble compounds formed could not be solubilized in acetic acid causing the decrease of the effectiveness in the production of compound **1a**. Similar compounds could extrapolate to **System II**, where $Cu(OAc)_2{\cdot}H_2O$ difficult their solubilization, even more, dropping the yield of **1a**. [37,38]

Figure 17: Appearance of the start of the reaction in **Experiment 1**.

Other metalating agents have been reported with good results for the obtention of cyclopalladated derivates of imine **a** or other cyclopalladated derivates. [3, 12, 37-39] As stated earlier, compounds with the formula $[Pd(OAc)_2L_2]$ (L = acetonitrile or dmso) has been proved their efficiency, likewise $PdCl_2$ or $K_2[PdCl_4]$, and they could improve **System I** in a better yielded synthesis of cyclopalladated derivates of imine **a**. Thereby, dmso or acetonitrile ligands in this metalating agents could compete for coordinating to palladium (II) centre, since chiral sulfoxide palladium complexes have been isolated in satisfactory yields, as well, or chloride ligands that could difficult this coordination in order to conduce the operating reactions in the system to the formation of compound derivates of imine **a** in enhanced yields, related to $Pd(OAc)_2$.

Secondly, concerning **System II**, several difficulties could be affecting the suggested synthetic path and more experiments are needed to understand and improve this system. On the one hand, the initial insoluble greenish precipitate (Figure 18) could be a stable Cu(II) coordination compound with benzylamine, since these types of compounds, either with chloride such as $[CuL_4Cl_2]$ (L = benzylamine), have been described in the literature. [40] Besides, other compounds could be interfering the progress of **System II** due to the reported oxidation of a derivative from benzylamine by CuX or CuX_2 (X = OAc, Cl or Br) giving place to the corresponding benzonitrile, benzylimine and benzaldehyde, with the action of oxygen air as well. [41] Moreover, an extra possibility is the stated potentially oxidation of benzaldehyde to benzoic acid via the O_2 and sunlight. These latter data support the low yield for this system, especially for **Experiment 5** which was performed in an open system in contact with air. [34]

Figure 18: Appearance of the start of the reaction in **Experiment 4**.

Recapitulating, the performed experiments in **System II** could be improved by using other Pd (II) and Cu(II) sources due to their different oxidation potentials according to the type of the ligand attached. For instance, chloride ligands could reduce the oxidant character of the metal centres and may achieve efficient selective production of compound **1a**. Furthermore, a metal-free oxidant such as benzoquinone could afford the oxidation of Pd(0) to Pd (II) without reacting with the organic components of the catalytic system. [42]

6. EXPERIMENTAL SECTION

6.1. INSTRUMENTS AND REAGENTS

^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ or $CDCl_3$/py-d_5 solution by Mercury 400 spectrometer at 298K. Chemical shifts (δ) were measured in ppm using $SiMe_4$ as an internal reference and coupling constants are expressed in Hz. IR spectra were collected with Nicolet iS5 FT-IR spectrometer and frequencies are given in cm^{-1}. Reagents and solvents were commercial compounds and they were used as received.

6.2. SYSTEM I

6.2.1. Experiment 1

An equimolar mixture of $Pd(OAc)_2$ (250 mg, 1.11 mmol), benzylamine (119 mg, 1.11 mmol) and benzaldehyde (118 mg, 1.11 mmol) in 10 mL of acetic acid was stirred at 60 ºC for 48 hours in a closed reactor containing atmospheric air. The suspension colour changed from dark orange to brown. After this period, the suspension was concentrated to dryness under vacuum by rotatory evaporation and the resulting residue was studied by TLC, using silica gel-60 supported on aluminium foil as stationary phase and different mixtures of CH_2Cl_2:MeOH as eluent to find a molar ratio for optimal separation. A sample of compound **1a**, found in the laboratory, was used in this TLC as a reference, after establishing its purity by ^{1}H NMR in a $CDCl_3$ solution. As well by ^{1}H NMR in $CDCl_3$/py-d_5 solution, where **1a** was converted into **3a** with formula *trans*-***N***,***N***-[Pd(C_6H_4-CH=N-CH_2-Ph)OAc(py-d_5)] by a fast splitting reaction due to the py-d_5. After the TLC verified the formation of **1a**, the crude of the reaction was eluted through a silica gel-60 column with a solution of CH_2Cl_2:MeOH in a 100:2 molar ratio. According to the previous TLC, the orange band (Figure 19) was supposed to be compound **1a**, hence, different fractions were collected and studied by TLC. Those fractions with the same pattern as **1a** were filtered, combined and concentrated under vacuum by rotatory evaporation. The addition of 5 mL of diethyl ether to the residue produced the precipitation of an orange yellowish powder, which was filtered and dried at the vacuum line. The ^{1}H NMR spectra in $CDCl_3$

(**Appendix A**) and in $CDCl_3$/py-d_5 (**Appendix B**) support that the isolated compound was **1a**, 41% yield (165 mg).

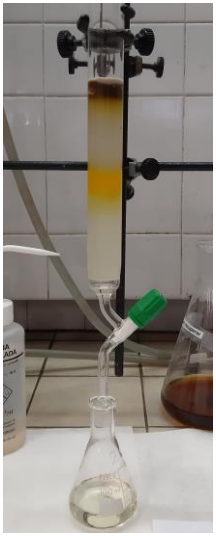


Figure 19: Performed column chromatography for the separation of compound **1a** (orange band) in **Experiment 1**.

6.2.2. Experiment 2

An equimolar mixture of $Pd(OAc)_2$ (250 mg, 1.11 mmol), benzylamine (119 mg, 1.11 mmol) and benzaldehyde (118 mg, 1.11 mmol) in 10 ml of acetic acid was stirred at 75 ºC for 72 hours in a closed reactor containing atmospheric air. After this period, the crude was treated as in **Experiment 1** and a ^{1}H NMR spectrum in $CDCl_3$ (**Appendix C**) was recorded characterising the isolated compound as **1a** in 63% yield (251 mg). In this experiment, a pale-yellow band eluted before the orange one and was collected in fractions 2 and 3 (Figure 20), which were filtered, combined and concentrated under vacuum. The small amount of the pale-yellow solid (**sample I**) was characterised by ^{1}H NMR in $CDCl_3$/py-d_5 (**Appendix D**), due to it solubilised partially in $CDCl_3$, and the spectrum suggested the formation of compound **2a** ([Pd(C_6H_4-CH=N-CH_2-Ph)]$_2$(μ-Cl)$_2$) in this experiment. The signals in the performed spectrum of the **sample I** could correspond to the mononuclear **4a** (*trans*-***N***,***N***-[Pd(C_6H_4-CH=N-CH_2-Ph)Cl(py-d_5)]) formed by py-d_5. Compound **2a** could have formed due to the metathesis reaction between the compound **1a** and adventitious chloride anions present during the synthesis and separation of compound **1a**.

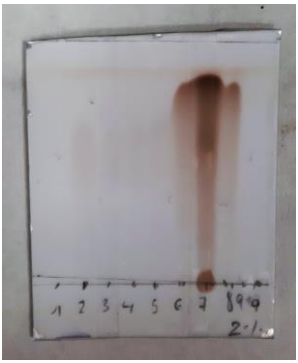


Figure 20: TLC study of the fractions obtained from the column chromatography in **Experiment 2**.

6.2.3. Experiment 3

An equimolar mixture of $Pd(OAc)_2$ (250 mg, 1.11 mmol), benzylamine(119 mg, 1.11 mmol) and benzaldehyde (118 mg, 1.11 mmol) in 10 mL of acetic acid was stirred at 70 ºC for four days in a closed reactor containing nitrogen atmosphere. The suspension colour changed as expected, hence, the crude was treated in a similar per-up as **Experiment 1** allowed the isolation of compound **1a** in 64% yield (258 mg). Compound **1a** was characterised by comparing the colour, the separated bands and a TLC analysis with the reference **1a**, already used in previous experiments (**Appendix E**).

6.3. SYSTEM II

6.3.1. Experiment 4

A mixture of 2:1:2 molar ratio of benzylamine (119 mg, 1.11 mmol), $Pd(OAc)_2$ (125 mg, 0.55 mmol) and $Cu(OAc)_2{\cdot}H_2O$ (222 mg, 1.11 mmol) in 10 mL of acetic acid was stirred at 90 ºC for 48 hours in a closed reactor containing atmospheric air. After this period, a dark green suspension was formed, and it was treated as in **Experiment 1**. The collected band was brighter than expected and after the conventional work-up, compound **2a** was isolated and characterised by ^1H NMR in $CDCl_3$/py-d_5 (**Appendix F**) and by IR (**Appendix G**) in 10% yield (21 mg). A sample of **2a** was found in the laboratory and was characterised by IR, which permitted the comparison of the spectra for its verification. In this experiment, most of the product was retained as a green band at the top of the column chromatography due to its high polarity (Figure 21).

Figure 21: Appearance of the column chromatography in **Experiment 4**.

6.3.2. Experiment 5

A mixture of 2:1:2 molar ratio of benzylamine (119 mg, 1.11 mmol), $Pd(OAc)_2$ (125 mg, 0.55 mmol) and $Cu(OAc)_2 \cdot H_2O$ (222 mg, 1.11 mmol) in 10 mL of acetic acid at reflux was stirred for one hour in an open system in contact with air. Despite the significant amount of black Pd(0) observed at the bottom of a greenish solution, the crude was treated as in **Experiment 1**. The product obtained was characterised by ^1H NMR in $CDCl_3$ (**Appendix H**) as compound **1a** in 5% yield (11 mg). In this experiment, the polarity of the eluent (CH_2Cl_2:MeOH) on the column chromatography was increased from the initial 100:2 volume ratio to a 100:6 volume ratio. A yellowish eluted band (Figure 22) was filtered, combined and concentrated under vacuum obtaining a small amount of a yellow sample (**sample II**), which was analysed in a $CDCl_3$/py-d_5 solution by ^1H NMR (**Appendix I**). The spectrum of **sample II** suggested the presence of compound **I** ($[Pd(C_6H_4\text{-}CH_2\text{-}NH_2)]_2(\mu\text{-}OAc)_2$) since the main signals observed were from its derivate compound **II** (*trans*-***N***,***N***-$[Pd(C_6H_4\text{-}CH_2\text{-}NH_2)OAc(py\text{-}d_5)]$) precedent from the splitting reaction with py-d_5. It should be remarked that in **sample II** the signal of the acetate-bridge did not appear. A sample of compound **I** found in the laboratory was converted to compound **II** to establish its purity by ^1H NMR in $CDCl_3$/py-d_5 solution (**Appendix J**) and permitted the comparison of the both spectra. Likewise **Experiment 4**, most of the product was retained as a green band at the top of the column chromatography due to its high polarity.

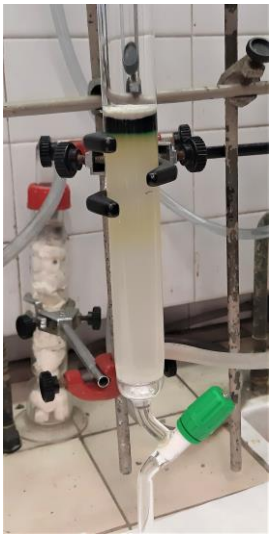
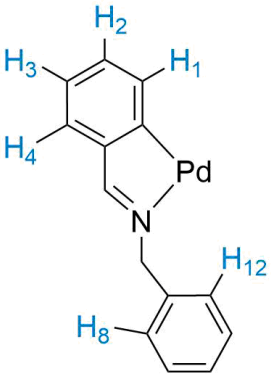


Figure 22: Appearance of **sample II** (yellowish band) after increasing the eluent polarity of the column chromatography in Experiment **5**.

6.4. PREPARATION OF REFERENCE COMPOUNDS 3A, 4A AND II

A suspension formed by nearly 7 mg of the found reference dinuclear cyclopalladated compounds **1a**, **2a** or **I**, 0.7 mL of $CDCl_3$ and two drops of deuterated pyridine was agitated for a few seconds. The resulting solutions were pale-yellow for compound **3a** or colourless for compounds **4a** and **II**, indicating the quantitative conversion of the dinuclear to the mononuclear cyclopalladated compounds. These obtained compounds **3a**, **4a** and **II** were characterised by ^1H NMR in $CDCl_3$/py-d_5 solution.

6.5. CHARACTERIZATION DATA

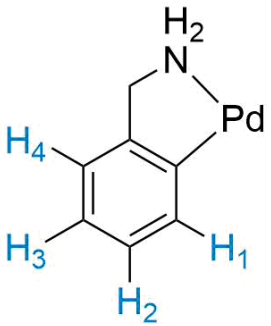


Compound 1a ([Pd(C_6H_4-CH=N-CH_2-Ph)]$_2$(μ-OAc)$_2$): Orange-yellowish powder. ^{1}H NMR in $CDCl_3$ solution (400 MHz) (selected data): δ 7.38 (unknown impurity), δ 7.18 - 7.16 (m, 1H, **3**), δ 7.09 – 7.03 (m, 4H), δ 6.83 - 6.80 (m, 2H, **8**, **12**), δ 4.59, 4.55, 4.02, 3.98 (AB quartet ($^3J_{HH}$ = 8, $^4J_{HH}$ = 2), 2H, **CH_2**), δ 2.18 (s, 3H, **OAc**).

Compound 2a ([Pd(C_6H_4-CH=N-CH_2-C_6H_5)]$_2$(μ-Cl)$_2$): Pale yellow powder. IR (cm^{-1}) (selected data): ω 3027 (st Csp^2-H), ω 2910, 2841 (st Csp^3-H), ω 1611 (st C=N)

Compound 3a (*trans*-*N*,*N*-[Pd(C_6H_4-CH=N-CH_2-C_6H_5)OAc(py-d_5)]): Yellowish solution. ^{1}H NMR in $CDCl_3$/py-d_5 solution (400 MHz) (selected data): δ 7.60 (s, 1H, **CH=N**), δ 7.10 – 7.08 (dd ($^3J_{HH}$ = 8, $^4J_{HH}$ = 2), 1H, **4**), δ 6.93 – 6.89 (t, $^3J_{HH}$ = 8 Hz, 1H, **3**), δ 6.84 – 6.80 (td ($^3J_{HH}$ = 8, $^4J_{HH}$ = 2), 1H, **2**), δ 6.16, 6.14 (d ($^3J_{HH}$ = 8), 1H, **1**), δ 4.79 (s, 2H, **CH_2**), δ 1.83 (s, 3H, **OAc**).

Compound 4a (*trans*-*N*,*N*-[Pd(C_6H_4-CH=N-CH_2-Ph)Cl(py-d_5)]): Pale yellow solution. ^{1}H NMR in $CDCl_3$/py-d_5 solution (400 MHz) (selected data): δ 7.76 (br. s, **1H**, **CH=N**), δ 7.12 – 7.11 (br. d ($^3J_{HH}$ = 8), 1H, **4**), δ 6.95 – 6.92 (t ($^3J_{HH}$ = 8), 1H, **3**), δ 6.88 – 6.85 (br t ($^3J_{HH}$ = 8), 1H, **2**), δ 6.10 (br s, 1H, **1**), δ 5.08 (br. s, 2H, **CH_2**).



Compound II (*trans*-*N*,*N*-[Pd(C_6H_4-CH_2-NH_2)OAc(py-d_5)]): Colourless solution. ^{1}H NMR in $CDCl_3$/py-d_5 solution (400 MHz) (selected data): δ 6.92 – 6.86 (m, 2H, **4**, **3**), δ 6.73 – 6.69 (td ($^3J_{HH}$ = 8, $^4J_{HH}$ = 2), 1H, **2**), δ 6.15 – 6.13 (d ($^3J_{HH}$ = 8), 1H, **1**), δ 4.98 (br s, 2H, **CH_2**), δ 4.11 – 4.08 (t, 2H, **NH_2**), δ 1.84 (s, 3H, **OAc**).

7. CONCLUSIONS

Based on the results obtained, **System I** is potentially functional for the one-pot method synthesis we were searching for. The tree experiments could allow the isolation of compound **1a** in reasonable yields and, with small variations in the design, **System I** could produce in high yields the compounds **1a**, **2a** or mononuclear derivates of these compounds (the general formula [Pd(C_6H_4-CH=N-CH_2-Ph)XL] (X = OAc or Cl, L = acetonitrile or dmso)]). This can be a more handling process than the two-step process described previously for the preparation of cyclopalladated derivates of (E)-N-benzyl-1-phenylmethanimines, in where the first step the imine was prepared and isolated for in the second step, undergoing the *ortho*palladation reaction with $Pd(OAc)_2$ to isolate the imine cyclopalladated compound. [16]

Considering **System II**, the proposed synthetic strategy was more challenging than in **System I** to produce compound **1a**, which only could be isolated in quite low yields. Nevertheless, with the proper corrections discussed above, **System II** could improve its efficiency and give more satisfactory yields in the production of cyclopalladated compound **1a** or its derivates. Besides, managing further experiments for the oxidation of benzylamine to benzaldehyde could be useful to improve the efficiency of **System II** because of the selective oxidation chemistry seen in the literature for Pd (II) and Cu(II) compounds. [30-32, 41, 42]

8. REFERENCES AND NOTES

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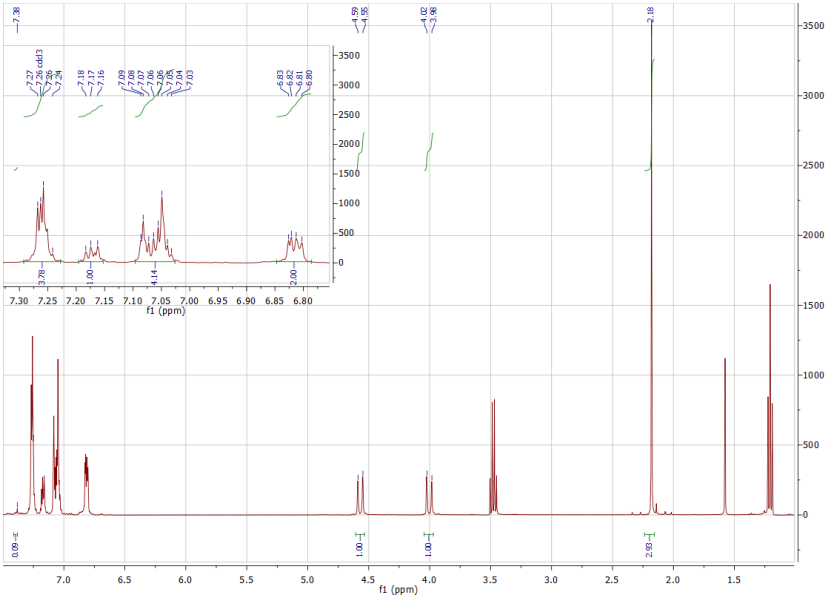
9. ACRONYMS

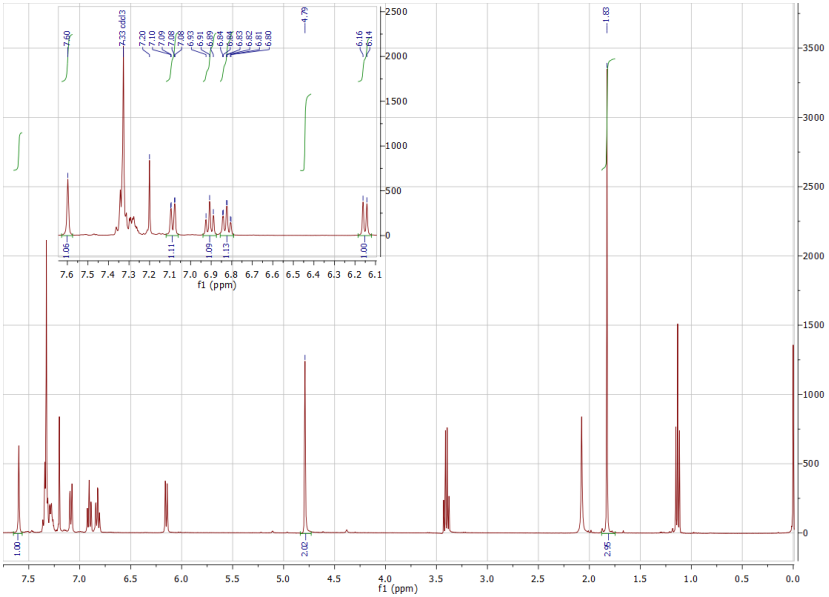
OAc	Acetate
Ph	Phenyl
$CDCl_3$	Deuterated chloroform
py-d_5	Deuterated pyridine
CH_2Cl_2	Dichloromethane
MeOH	Methanol
NMR	Nuclear Magnetic Resonance
IR	Infrared
br.	Broad
s	Singlet
d	Doublet
t	Triplet
m	Multiplet
dd	Doublet of doublets
td	Triplet of doublets
st	Stretching

APPENDICES

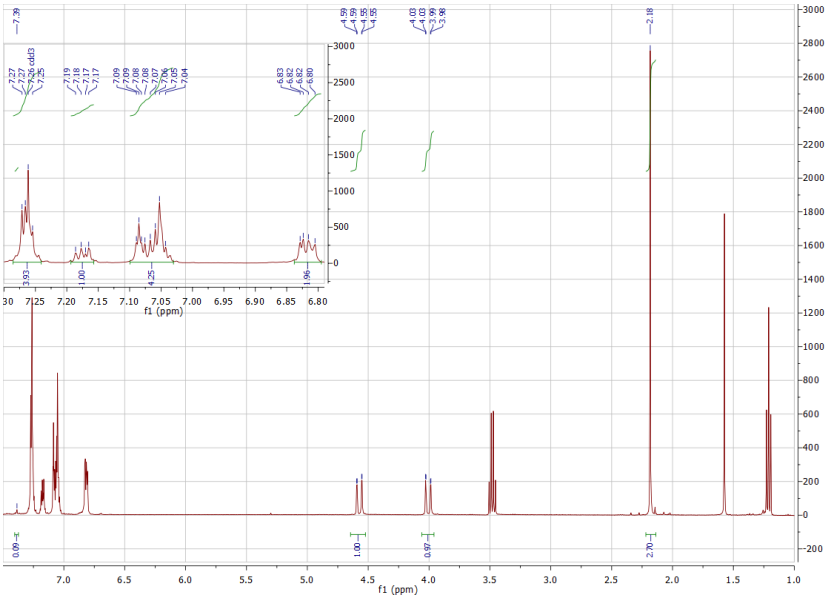
APPENDIX 1: ^{1}H NMR AND IR SPECTRA



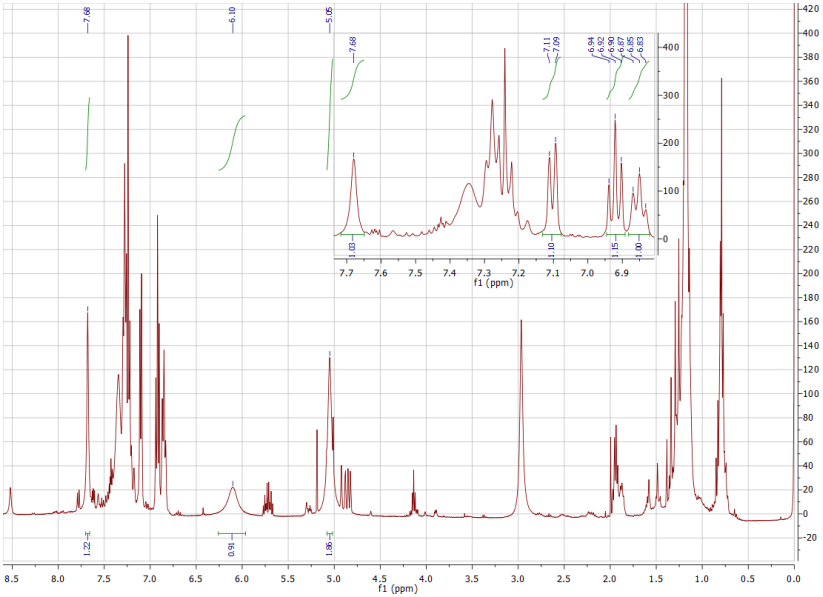
Appendix A: ^{1}H NMR spectrum in $CDCl_3$ of compound **1a** ($[Pd(C_6H_4\text{-}CH{=}N\text{-}CH_2\text{-}Ph)]_2(\mu\text{-}OAc)_2$) from **Experiment 1**.



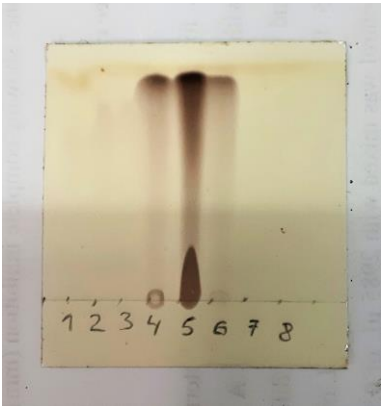
Appendix B: ^{1}H NMR spectrum in $CDCl_3$/py-d_5 of compound **3a** (*trans*-***N***,***N***-[Pd(C_6H_4-CH=N-CH_2-C_6H_5)OAc(py-d_5)]) obtained from **1a** in **Experiment 1**.



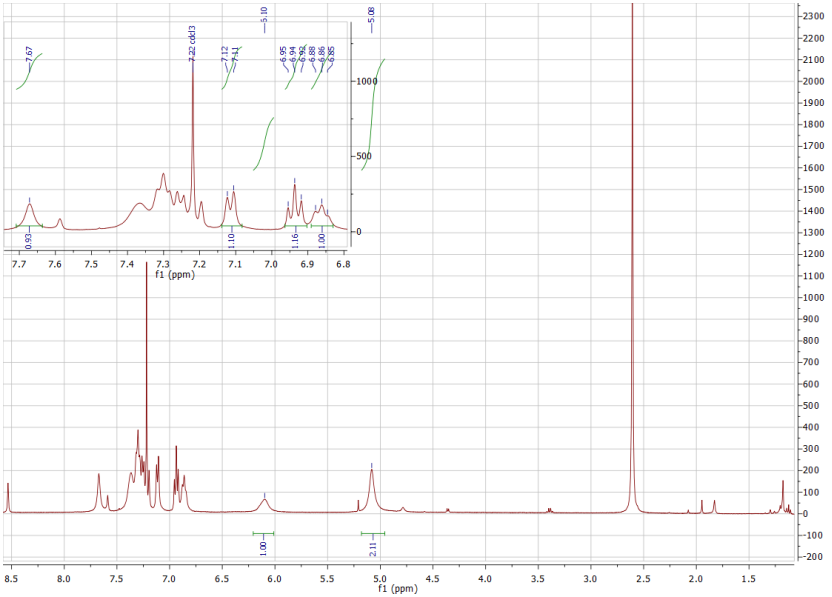
Appendix C: ^{1}H NMR spectrum in $CDCl_3$ of compound **1a** ([Pd(C_6H_4-CH=N-CH_2-Ph)]$_2$(μ-OAc)$_2$) from Experiment **2**.



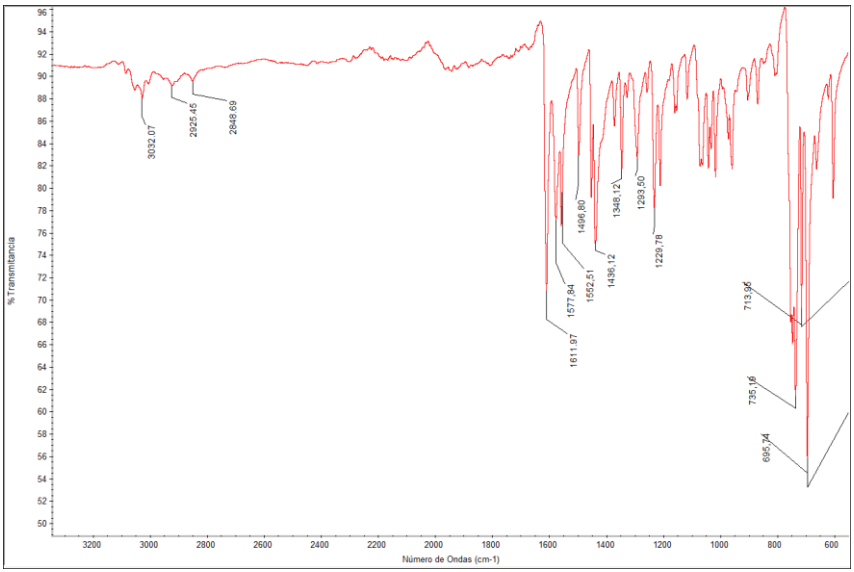
Appendix D: ^{1}H NMR spectrum in $CDCl_3$/py-d_5 of **sample I** from **Experiment 2**. Selected signals could characterise compound **4a** (*trans*-***N***,***N***-[Pd(C_6H_4-CH=N-CH_2-C_6H_5)Cl(py-d_5)]).



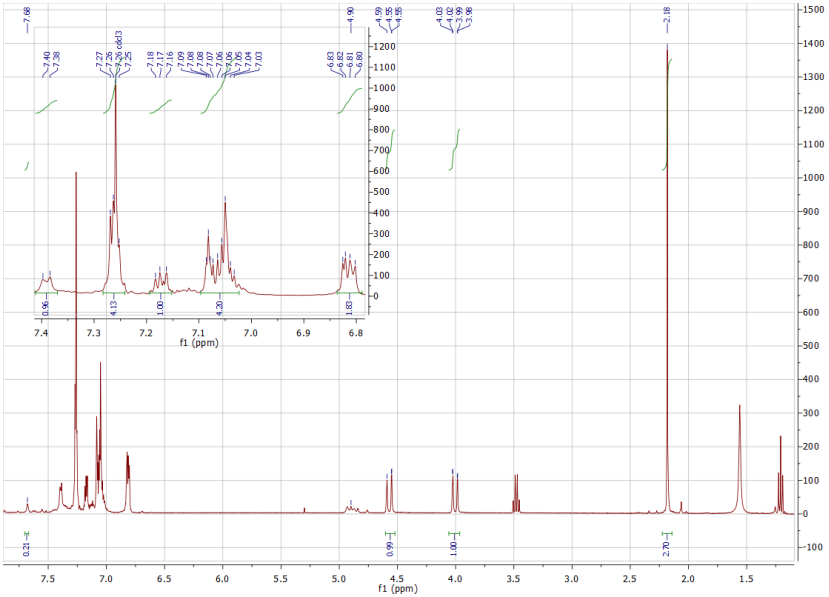
Appendix E: The TLC study for compound **1a** of the fractions from the column chromatography of **Experiment 3**.



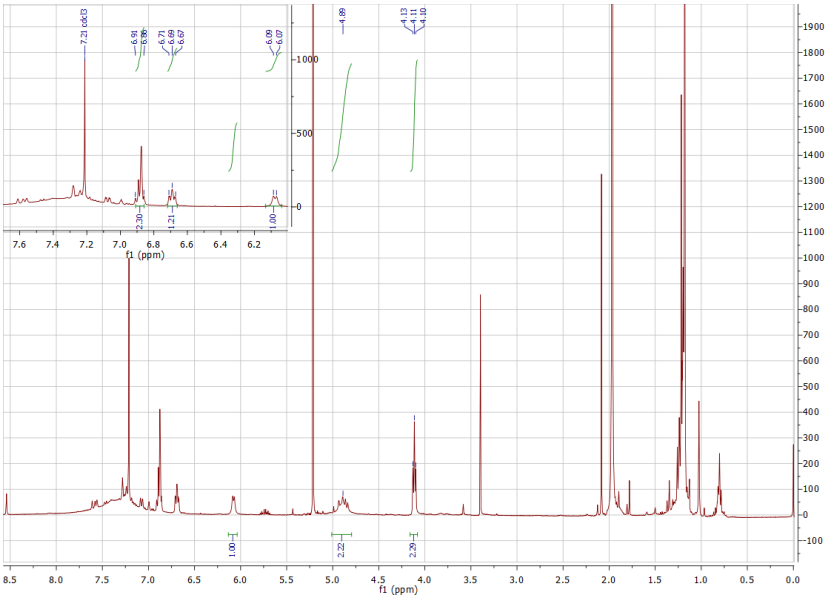
Appendix F: ^{1}H NMR spectrum in $CDCl_3$/py-d_5 of compound **4a** (*trans*-***N***,***N***-[Pd(C_6H_4-CH=N-CH_2-C_6H_5)OAc(py-d_5)]) obtained from **2a** in **Experiment 4**.



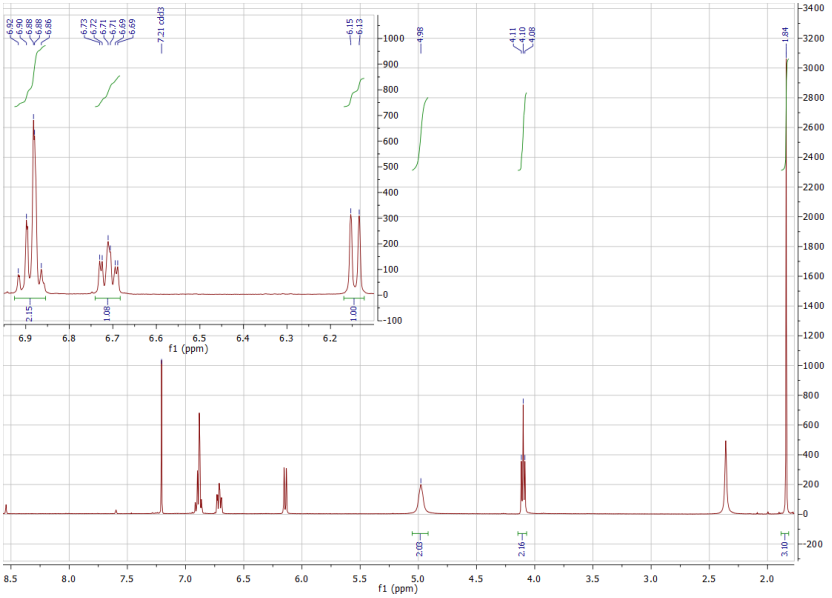
Appendix G: IR spectrum of compound **2a** ([Pd(C_6H_4-CH=N-CH_2-C_6H_5)(μ-Cl)$_2$]) from **Experiment 5**.



Appendix H: ^{1}H NMR spectrum in $CDCl_3$ of compound **1a** ([Pd(C_6H_4-CH=N-CH_2-C_6H_5)(μ-OAc)$_2$]) from **Experiment 5**.



Appendix I: ^{1}H NMR spectrum in $CDCl_3$/py-d_5 of **sample II** from **Experiment 5**. Selected signals could characterise compound **II** (*trans*-***N***,***N***-[Pd(C_6H_4-CH-NH_2)(OAc)(py-d_5)]).



Appendix J: ^{1}H NMR reference spectrum of compound **II** in $CDCl_3$/py-d_5.