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Grau de Química

Treball Final de Grau

Activation of CH bonds of imines by transition metal compounds.

Activació d'enllaços CH d'imines amb compostos de metalls de transició.

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June 2018

UNIVERSITAT DE BARCELONA

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El que sabem és una gota d'aigua; el que ignorem és l'oceà.

Isaac Newton

Als meus avis, pel seu incondicional suport, ara i sempre. A tots els meus amics que han fet possibles aquests 4 anys. A l'Ariadna Lázaro ,companya de laboratori, per tots els seus consells i per fer les hores de laboratori més amenes. A la Dra. Margarita Crespo per deixar-me treballar en el seu impecable laboratori. I sobretot, al Dr. Jaume Granell, per guiar-me en aquest treball, per totes les hores de dedicació i les coses apreses.

Moltes gràcies a tots.

REPORT

CONTENTS

1. SUMMARY

In this work, we describe the synthesis of some metallacycles by reaction between aromatic imines and palladium acetate. In this process, a carbon-palladium bond is formed by the activation of an *ortho* CH bond (a cyclometallation reaction).

The reaction between the imines $ClC_6H_4CHNCH_2C_6H_5$ or $C_6H_5CHNCH_2C_6H_5$ and palladium acetate afforded the cyclometallated compounds $[Pd(\mu\text{-}AcO)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$ and $[Pd(\mu\text{-}AcO)(C_6H_4CHNCH_2C_6H_5)]_2$ which contains an acetate bridged ligand. In a second reaction, the halogen bridged metallacycle, $[Pd(\mu\text{-}Cl)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$, was obtained by reaction between the acetate bridged compound $[Pd(\mu\text{-}AcO)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$ and LiCl. The monomer $[PdCl(o\text{-}ClC_6H_3CHNCH_2C_6H_5)(PPh_3)]$ was obtained by the reaction between $[Pd(\mu\text{-}Cl)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$ and PPh_3. Monomers $[PdCl(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ and $[PdBr(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ were obtained through a one pot reaction, by reaction between the corresponding acetate bridged compound and LiCl (or LiBr) and PPh_3, in order to increase the yield of the process.

Finally, the monomer $[Pd(C_7H_9N)(o\text{-}RC_6H_3CHNCH_2C_6H_5)(PPh_3)]$, in which the halogen ligand is substituted by the 2,4-lutidine, has been tried to obtain, without success, by different reactions and conditions.

The products have been characterized by IR, ^1H NMR and ^{31}P NMR and the following remarkable features have been found: i) the compounds with a chloro in *ortho* position present an interaction between this atom and the imine proton; ii) the acetate bridged compounds present an “open book” structure; iii) the P atom of the PPh_3 is coupled with the HC=N proton showing the *trans* disposition between the phosphine and the methinic proton.

Keywords: Organometallics, palladium, imine, cyclometallation, metallacycles.

2. RESUM

En aquest treball, es descriu la síntesis de metal·lacicles a partir de la reacció entre imines aromàtiques i acetat de pal·ladi. En el procés, es forma un enllaç carboni-pal·ladi fruit de l'activació de l'enllaç *orto* C-H de l'anell aromàtic.

A partir de les dues imines, $ClC_6H_4CHNCH_2C_6H_5$ i $C_6H_5CHNCH_2C_6H_5$, i a través de la reacció amb $Pd(AcO)_2$, s'han obtingut els compostos ciclometal·lats de pal·ladi amb pont acetat corresponents, $[Pd\{\mu\text{-}AcO\}\{o\text{-}ClC_6H_3CHNCH_2C_6H_5\}]_2$ i $[Pd\{\mu\text{-}AcO\}\{C_6H_4CHNCH_2C_6H_5\}]_2$. En una segona reacció, el metal·lacicle amb pont halogen, $[Pd\{\mu\text{-}H\}\{o\text{-}ClC_6H_3CHNCH_2C_6H_5\}]_2$, s'obté a partir de la reacció del compost pont acetat $[Pd\{\mu\text{-}AcO\}\{o\text{-}ClC_6H_3CHNCH_2C_6H_5\}]_2$ amb LiCl. El monòmer $[PdCl(o\text{-}ClC_6H_3CHNCH_2C_6H_5)(PPh_3)]$ s'obté a partir de la reacció de $[Pd\{\mu\text{-}H\}\{o\text{-}ClC_6H_3CHNCH_2C_6H_5\}]_2$ amb PPh_3 . Els monòmers $[PdCl(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ i $[PdBr(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ s'obtenen a través de la reacció "one pot", on es fa reaccionar el corresponent compost pont acetat amb LiCl (o LiBr) i PPh_3, per tal d'incrementar el rendiment del procés.

Finalment s'ha intentat obtenir a través de diferents condicions de reacció, sense èxit, el monòmer $[Pd(C_7H_9N)(o\text{-}RC_6H_3CHNCH_2C_6H_5)(PPh_3)]$ on es substitueix l'halogen per la 2,4-lutidina.

Els productes han estat caracteritzats per RMN de ^1H i ^{31}P i IR i s'han pogut definir les següents característiques trobades: i) els compostos amb un Cl en posició *ortho* presenten una interacció del Cl amb el protó de la imina; ii) els compostos amb pont acetat presenten una estructura de "open book"; iii) l'àtom de P de la PPh_3 s'acobla amb el protó del HC=N fet que demostra la disposició *trans* entre el lligand PPh_3 i el protó metínic.

Paraules clau: Organometàl·lics, pal·ladi, imina, ciclometal·lació, metal·lacicles.

3. INTRODUCTION

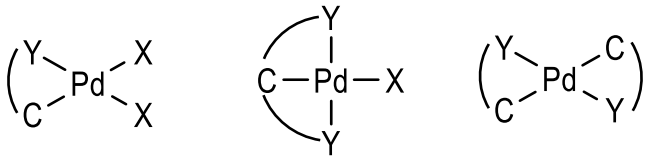
Organometallic chemistry was born in 1760, in a military pharmacy in Paris, when Louis Claude Cadet de Gassicourt was investigating inks based on arsenic-containing cobalt salts discovered a fuming, stinking liquid composed by cacodyl oxide and tetramethyldiarsine [1]. In recent years, organometallic chemistry has experimented an enormous growth in research areas and industry applications. Among the transition-metal organometallic family, organopalladium compounds are one of the most easily prepared and handled transition-metal complexes. The Nobel Prize in Chemistry 2010 was awarded jointly to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki for *"palladium-catalysed cross couplings in organic synthesis"*. Carbon-based organic chemistry is the basis of life and is responsible for numerous fascinating naturals phenomes, and due to the discoveries by the three organometallic chemist the organopalladium chemistry has made a big step forward [2].

3.1. CYCLOPALLADATED COMPOUNDS

One of the most studied group of organopalladium derivatives are the palladacycles or cyclopalladated compounds. Palladacycles contains at least one Pd-C bond stabilized by at least one donor atom (N, P, As, O, Se, or S) [3].

3.1.1. Types of Palladacycles

Due to the fact that C-ligand bond can be a different electron number donor, palladacyles are classified into anionic four-electron donor (CY), six-electron donor (YCY) or four-electron donor dimetallated $(CY)_2$ (Figure 1).



CY- Type YCY- Type $(CY)_2$- Type

Figure 1. Anionic four-electron donor (CY), anionic six-electron donor (YCY) and anionic four-electron donor dimetallated$(CY)_2$ palladacycle.

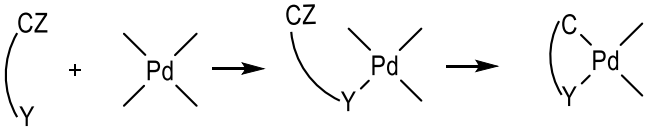
Anionic four-electron donor palladacycles usually exist as halogen or acetate bridged dimers and can be presented in two geometric isomers*: cisoid* and *transoid* conformations (Figure 2). Depending on the nature of the ligand, these compounds can be neutral, anionic or cationic. The metallated carbon is normally an aromatic sp^2 carbon usually forming a ring of between 3 and 11 links [4], however, sp^3 carbon or sp^2 vinylic carbon can be also found [5].

Cisoid-palladacycle Transoid-palladacycle

Figure 2. CY palladacycles geometrical isomers. (X= Halogen, OAc, etc.)

3.1.2. Methods of Preparation

There are several methods of synthesis of palladacycles. Five- or six-membered metallacycles are often formed as a result of the Pd-C stable bond formed. In the method explained below the formation of the Pd-C bond is facilitated by the coordination of the two-electron donor group (Scheme 1).



Scheme 1. Pd-C bond formation by two-electron donor group coordination. (Y= NR_2, SR, PR_2, etc. CZ= CH, CX, CM, C=C, C≡C)

The most important methods are: C-H bond activation, oxidative addition, transmetallation and alkoxy- and carbopalladation of alkenes and halopalladation of akynes.

3.1.2.1. C-H Activation

Cyclopalladation reactions can take place through a variety of mechanisms and the *ortho*-palladation method is the most easy and direct. The most current process takes place by mixing Pd^{2+} salts with base or palladium acetate in acetic acid or benzene. As a result of the investigation of Ryabov and co-workers about the cyclometallation of palladium with acetate ligand, it has been proposed an electrophilic mechanism for the reaction. The palladium acetate plays a dual role as an electrophilic activator of the arene and intramolecular base for the deprotonation [6].

In the first step the palladium is bonded to a donor electronegative atom (N in this case) and then one acetate group becomes a monodentate ligand, **A** (Figure 3), in a second step one oxygen atom of the other η^2-acetate is displaced by one *ortho*- C-H bond of the arene through a concerted state where the *ortho*-H, the Pd and the acetate ligand are interacting, **B** (Figure 3). After that, involving a six-membered transition state, with a minimal activation barrier, the *ortho*-H is transferred to the acetate ligand and a new Pd-C arene bond is formed, **C** (Figure 3). Finally, the H-acceptor acetate twist away from the new Pd-C bond and donates the H to the second acetate ligand [7].

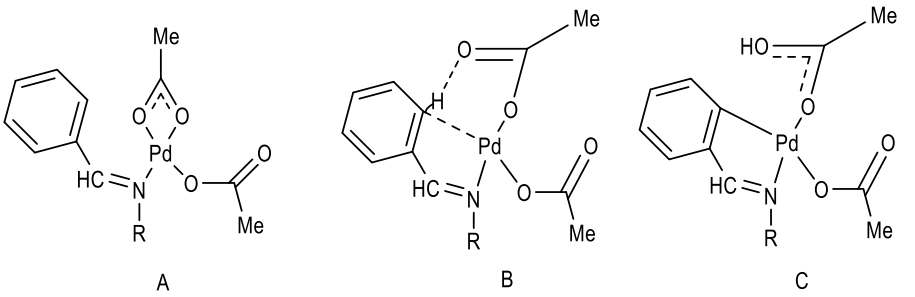
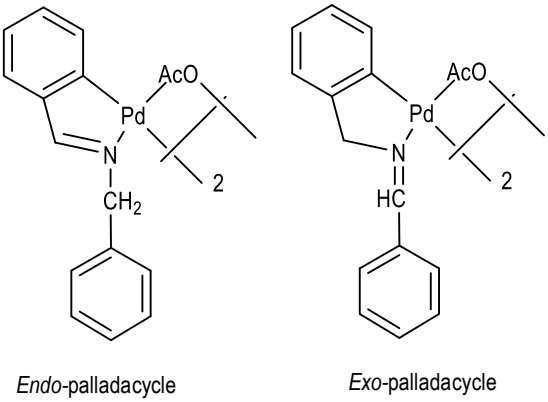


Figure 3. Mechanism of cyclometallation by palladium acetate.

The palladation of oxazolines and imines takes place in a regioselectivity way forming *endo*-palladacycles, corresponding to the isomer which contains the C=N bond inside the metallacycle, as opposed to the *exo*- isomer which contains the C=N bond outside the metallacycle (Figure 4). It has been reported that the *endo*- palladacycles are the thermodynamic isomers [8-9].



Endo-palladacycle *Exo*-palladacycle

Figure 4. *Endo*- and *Exo*- isomers.

3.1.3. Structural Aspects

Depending of the structural and electronic aspects of the palladated carbon, the nature of the donor group, the sizes of the ring, etc, the Pd-C bond distance can vary between 1.985 and 2.295 Å. Furthermore, because of the *trans* influence of the Pd-C bond which is stronger than the *trans* influence of the Pd-Heteroatom bond, the Pd-Halogen bond in *trans* is longer than the *cis* Pd-Halogen bond.

Halogen dimer palladacycles usually crystallizes in the *transoid* geometry, however, chloro-palladation of heterosubstitued alkynes crystallizes in the *cisoid* geometry. The acetate-bridged dimeric palladacycles present an "open-book" structure which allows to have the *cisoid* and *transoid* geometry in equilibrium (Figure 5).

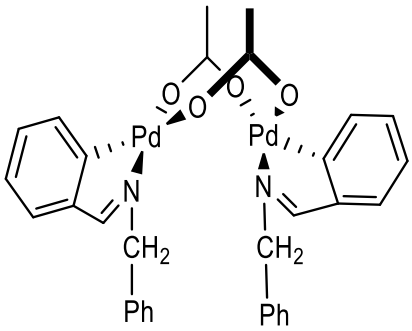


Figure 5. Example of a *cisoid* isomer with open book structure

The monomeric palladacycles formed through the splitting bridge reaction with Lewis bases ligands such as pyridines or phosphines usually have the *cis* isomer regarding the Pd-C bond.

3.1.5. Applications

There are many interesting applications of palladacycles. Homogeneous catalysis, and antitumor drugs are two of the more important applications among others.

The first use of the palladacycles in homogeneous catalysis was in the hydrogenation of C=C bonds. Followed by the use in the selective reduction of nitro-aromatic compounds, nitro-alkenes, nitriles, alkynes, alkenes and aromatic carbonyl compounds. Over the recent years it

has been appeared a new application of the palladacycles as catalyst precursors for C-C coupling reactions, in particular of the Suzuki- and Heck- reaction type.

Nowadays cancer is one of the deadliest diseases of the world, therefore, research aimed at obtaining better treatments has a great interest. Organometallic and transition metal complexes including palladacycles compounds are nowadays potential anticancer agents and due to the success of cis-platin as an anticancer drug the research and synthesis of this compounds has gained interest. The antidrug activity goes through the formation of palladium-DNA adducts that are capable of inducing cell death [10-11].

4. OBJECTIVES

The aim of this work is the synthesis and characterization of some palladium metallacycles. The specific objectives are:

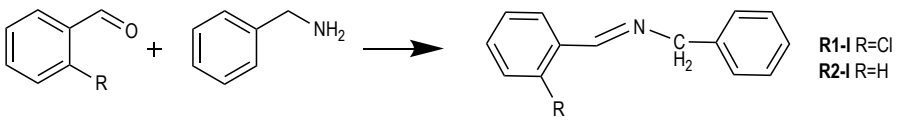
- The synthesis of aromatic imines by a condensation reaction.
- The synthesis of acetate-bridged cyclopalladated compounds by the activation of the C-H bond of the imines prepared before.
- The synthesis of the halogen-bridged cyclopalladated compound through the substitution of the acetate bridge by a halogen.
- The synthesis of the mononuclear cyclopalladated compounds by splitting reactions of the bridged dimers with triphyenilphosphine.
- Characterization of the compounds by spectrometric techniques as IR, ^{1}H-NMR and ^{31}P-NMR.

5. RESULTS AND DISCUSSION

In order to synthesize and characterize the cyclopalladated compounds derived from imines, by the activation of the CH bond, two starting imines, o-$ClC_6H_4CHNCH_2C_6H_5$ (**R1-I**) and $C_6H_5CHNCH_2C_6H_5$ (**R2-I**), have been obtained through the reaction of *ortho*-chlorobenzaldehid and benzaldehid with benzylamine. The reaction of the imines (**R1-I** and **R2-I**) with $Pd(AcO)_2$ leads to the obtention of the $[Pd(\mu\text{-}AcO)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$ (**R1-A)** and $[Pd(\mu\text{-}AcO)(C_6H_4CHNCH_2C_6H_5)]_2$ (**R2-A**), dimers cyclopalladated compounds. The reaction of the acetate-bridged dimers cyclopalladated compounds (**R1-A** and **R2-A**) with LiCl leads to the obtention of the halogen-bridged dimer $[Pd(\mu\text{-}Cl)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$ **(R1-C)**. The monomer compound $[PdCl(o\text{-}ClC_6H_3CHNCH_2C_6H_5)(PPh_3)]$ (**R1-MC**) was obtained by reaction between PPh_3 and **R1-C**. **R1-MC** monomer was obtained as well through a one pot reaction where the $[Pd(\mu\text{-}AcO)(o\text{-}ClC_6H_3CHNCH_2C_6H_5)]_2$ (**R1-A)** was reacted with LiCl and PPh_3. Monomers $[PdCl(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ (**R2-MC**) and $[PdBr(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ (**R2-MB**) were obtained through the same one pot reaction where and **R1-A** and **R2-A** reacted with LiCl or LiBr , respectively, and PPh_3. Finally, a cyclopalladated monomer (**R1-L, R2-L**) with PPh_3 and 2,4-lutidine, as ligands, has been tried to obtain without success by different reactions and conditions.

5.1 STARTING IMINES

The imines o-$ClC_6H_4CHNCH_2C_6H_5$ (**R1-I**) and $C_6H_5CHNCH_2C_6H_5$ (**R2-I**) were obtained by reaction between *ortho*-chlorobenzaldehid or benzaldehid and benzylamine, refluxing in ethanol 1 h, in a 90% yield. Both compounds **R1-I** and **R2-I** are white oily materials at room temperature (Scheme 2).



Scheme 2. Obtention of **R1-I** and **R2-I** imines.

R1-I and **R2-I** compounds were characterised by ^{1}H NMR, and the data are in agreement with the proposed structures (Appendix 1). In particular, there are two common signals of both compounds that are interesting of the ^{1}H NMR spectra. Firstly, the singlet, which integrate one proton from the HCN, at 8.85 ppm of **R1-I** compound and at 8.38 ppm of **R2-I** compound. The different position of the singlet is due to presence of the *ortho* chloro substituent in the aromatic ring which interacts with the HC=N proton (Figure 6). Secondly the singlet, which integrate two protons from the N-CH_2, at 4.87 ppm and 4.83 ppm respectively.

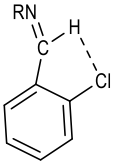


Figure 6. The *ortho*-chloro interaction with HC=N proton.

Nevertheless, there is a signal, different for each imine, which allows us to differentiate the two compounds. **R1-I** have one proton which have the presence of a chloro in ortho and produces a signal (dd) at 8.11-8.08 ppm (out of the aromatic zone). However, **R2-I** compound have a multiplet at 7.82-7.75 ppm from the two equivalent protons in the *ortho* position because of the lack of the chloro (Figure 7).

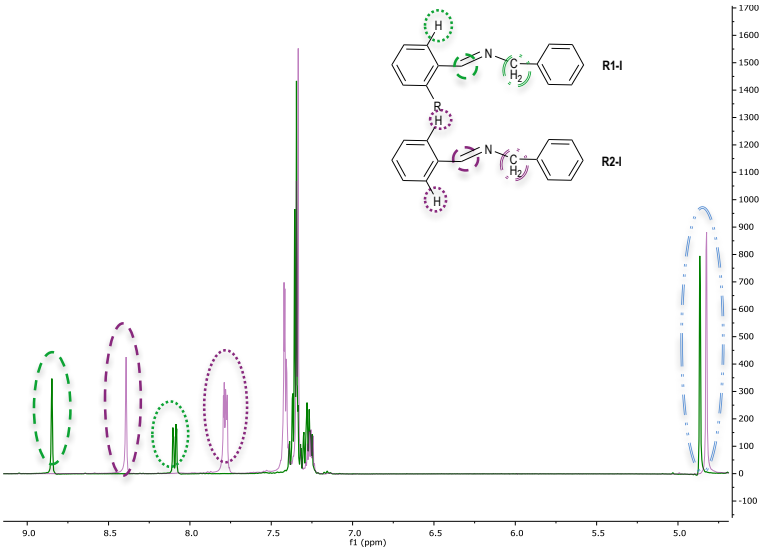
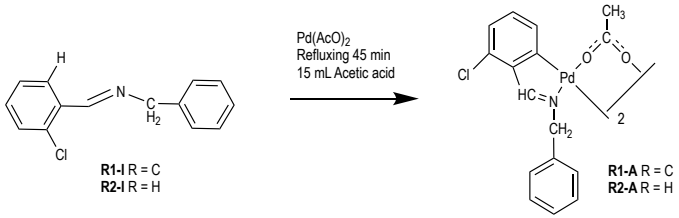


Figure 7. Overlap spectrum of **R1-I** —and **R2-I** —imines.

5.2 ACETATE-BRIDGED DIMER CYCLOPALLADATED COMPLEXES

The imines compounds (**R1-I** and **R2-I**) reacted with palladium acetate, in refluxing acetic acid during 45 min, and a yellow solid was obtained corresponding to the acetate-bridged dinuclear cyclopalladated complexes: [Pd(μ-AcO)(*o*-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ (**R1-A)** and [Pd(μ-AcO)($C_6H_4CHNCH_2C_6H_5$)]$_2$ (**R2-A**) (Scheme 3). The reaction take place in a first step through the coordination of the Pd with the N-donor atom and in a second step the C-H activation to form the acetate bridge. (see *3.1.2.1. C-H Activation* and Figure 3)



Scheme 3. Synthesis of acetate-bridged dimers cyclopalladated **R1-A** and **R2-A**.

^{1}H-NMR and IR spectra were recorded in order to verify the proposed structure of **R1-A** and **R2-A**. Complexes **R1-A** and **R2-A** present two intense bands, in their IR spectra (Appendix 2), assignable to the tension vibration of C=O of the acetate group. **R1-A** compound present the asymmetric stretching band at 1588.35 cm^{-1} and the symmetric band at 1405.39 cm^{-1}, and **R2-A** present de asymmetric band at 1588.17 cm^{-1} and the symmetric band at 1405.39 cm^{-1} (Figure 8). The difference between these frequencies indicates the coordination form of the acetate ligand: a) The terminal acetate ligand presents a difference of frequencies ($\Delta\nu$) bigger than the ionic acetate (164-171 cm^{-1}), b) The bidentate chelate acetate presents a difference of frequencies ($\Delta\nu$) inferior to the free acetate and c) values of the difference of frequencies ($\Delta\nu$) of the bismonodentate or bridge acetate ligand are similar to the ionic acetate (164-171 cm^{-1}) [12]. The difference of frequencies ($\Delta\nu$) of the bands from **R1-A** and **R2-A** complexes are 182.9 and 182.7 cm^{-1} respectively in good agreement to a bridged acetate ligand coordination. Furthermore, **R1-A** and **R2-A** spectra present the stretching symmetric band assigned to the CH_3 , of the acetate ligand, at 1365.35 and 1371.42 cm^{-1} respectively, and the stretching band assigned to the C=N at 1610.47 and 1614.16 cm^{-1}.

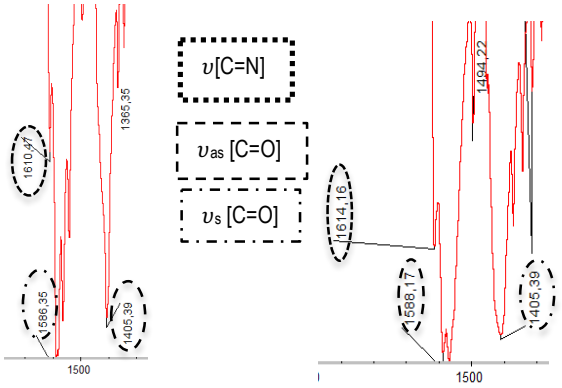


Figure 8. Piece of IR spectrum of **R1-A** (left) and **R2-A** (right).

One of the representative signals of the ^{1}H-NMR spectra of both compounds **R1-A** and **R2-A** (Appendix 3) is the singlet which integrate 3 H at 2.15 and 2.18 ppm, respectively, assigned to the CH_3 of the acetate bridged ligand. The fact that the spectra present a singlet assigned to the methyl means that the two methyls are equivalents therefore being a *trans* geometric isomer (See Figure 2). Moreover, the presence of two doublets at 4.53 and 3.92 ppm of **R1-A** spectrum and at 4.57 and 4.01 ppm of **R2-A** spectrum, assigned to one proton of the N-CH_2 each doublet, highlights the "open book" structure of both complexes (See Figure 5). Also at **R1-A** spectrum there is a singlet at 7.60 ppm assigned to the HC=N proton, which is out of the aromatic zone due to the *ortho*-chloro effect, however, the proton of the HC=N group of the **R2-A** compound can't be assigned because of the lack of the chloro effect displace the signal to the aromatic zone (Figure 9).

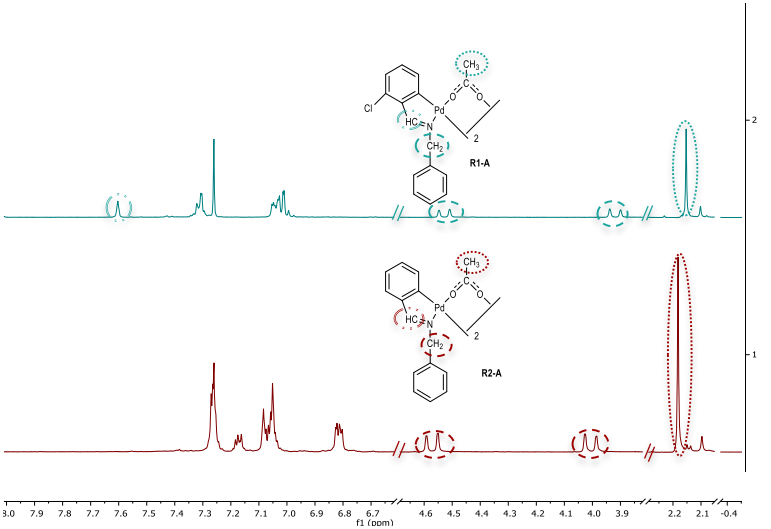
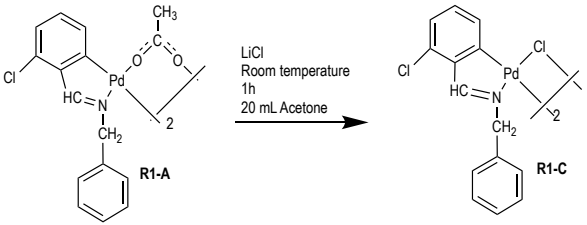


Figure 9. Comparison of the ^{1}H NMR spectra of compounds **R1-A** (up) and **R2-A** (down).

5.3 HALOGEN-BRIDGED DIMER CYCLOPALLADATED COMPLEXES

Through a substitution reaction of the [Pd(μ-AcO)(*o*-ClC$_6$H$_3$CHNCH$_2$C$_6$H$_5$)]$_2$ (**R1-A**) with LiCl, during 1 h in 20 mL of acetone, [Pd(μ-Cl)(*o*-ClC$_6$H$_3$CHNCH$_2$C$_6$H$_5$)]$_2$ **(R1-C)** compound was obtained (Scheme 4).



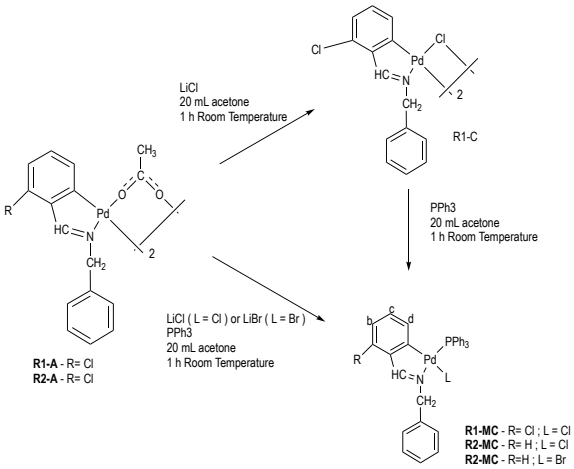
Scheme 4. Synthesis of halogen-bridged dimer cyclopalladated compound **R1-C**

Due to the insolubility of **R1-C** in common NMR solvents, the corresponding monomer compound [PdCl(py)(o-ClC$_6$H$_3$CHNCH$_2$C$_6$H$_5$)] was obtained by reaction with [D5]-Pyridine (directly into the NMR tube with a few drops) and the ^{1}H-NMR was recorded in order to verify the proposed structure (Appendix 4).

The absence of the signals corresponding to the acetate bridge (present in the reagent **R1-A** compound) and the two doublets corresponding to the CH_2 of the open book form indicates that the reaction has been carried out. The singlet at 8.21 ppm assigned to the HC=N proton, the singlet at 6.02 ppm assigned to the aromatic proton in *ortho* position respect the Pd, and the singlet at 5.16 ppm assigned to the two protons of the N-CH_2, allows us to verify the monomer structure with a chloro and a [D5]-pyridine as ligands.

5.4 MONOMERIC CYCLOPALLADATED COMPLEXES

Three monomers were obtained ([PdCl(o-$ClC_6H_3CHNCH_2C_6H_5$)(PPh_3)] (**R1-MC**), [PdCl($C_6H_4CHNCH_2C_6H_5$)(PPh_3)] (**R2-MC**) and [PdBr($C_6H_4CHNCH_2C_6H_5$)(PPh_3)] (**R2-MB**)) and characterized by ^1H NMR, ^{31}P NMR and IR. **R1-MC** compound was obtained in two different ways, by the reaction of **R1-C** with PPh_3 during 1h at room temperature in 20 mL of acetone, or by the one pot reaction of **R1-A** with LiCl and PPh_3 under the same conditions. **R2-MC** and **R2-MB** were both obtained by the one pot reaction of **R2-A** with LiCl or LiBr, respectively, and PPh_3 under the same reaction conditions (Scheme 5).



Scheme 5. Synthesis of monomeric cyclopalladated compounds **R1-MC**, **R2-MC** and **R2-MB**

^{1}H NMR, ^{31}P NMR and IR spectra of compounds **R1-MC**, **R2-MC** and **R2-MB** were consistent with the structure proposed and provide very important information. The three ^{1}H NMR spectra of **R1-MC**, **R2-MC** and **R2-MB** (Appendix 5) contains a doublet at 8.46 ppm, 7.88 ppm and 7.90 ppm respectively assigned to the imine proton (HC=N) due to the coupling with P atom, the difference in the displacements is due to the presence of the chloro in *ortho* position. They also contain a multiplet at 7.60-7.67 ppm (**R1-MC**), 7.80-7.71 ppm (**R2-MC**) and 7.81-7.72 ppm (**R2-MB**) assigned to the aromatic protons of the PPh_3 in *ortho* position in relation to the P, and a singlet at 5.28 ppm (**R1-MC** and **R2-MC**) and at 5.41 ppm (**R2-MB**) assigned to the two protons of the N-CH_2. In the area of the spectra from 7.2 ppm to 6 ppm there is a set of signals assigned to the protons of the benzene directly bonded to the Pd (Figure 10).

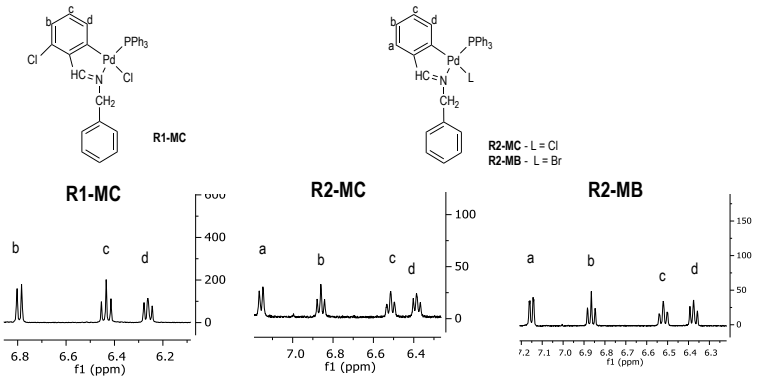


Figure 10. ^{1}H NMR spectrums of the aromatic protons of compounds **R1-MC**, **R2-MC** and **R2-MB**.

As can be seen in the figure 10, the spectrum of **R1-MC** compound doesn't have a signal for the H_a proton because of the presence of a chloro atom in *ortho* position of the aromatic ring. The electron with drawing character of the chloro cause the displacement, to larger ppm, of the other signals. The multiplicity of the signals is due to the coupling of the protons: H_a is coupled to H_b (doublet), H_b is coupled to H_a and H_c (triplet), H_c is coupled to H_b and H_d and H_d is coupled to H_c and the P of the PPh_3 (triplet). The triplet assigned to H_d, shows that the PPh_3 is in *trans* position in relation to the N.

The obtention of the *trans* isomer, in all cases, can be explained by the antisymbiotic effect. R. G. Pearson wrote, literally, in 1973: *"two soft ligands in mutual trans position will have a destabilising effect on each other when attached to class b metal atoms"* as an explanation of the antisymbiotic effect [13]. Therefore, in our case, given the possibility of coordinating the P (soft ligand), of the PPh_3, in trans to the N (hard ligand) or in *trans* to the aromatic carbon (soft ligand), the P is coordinated in trans to the N avoiding the antisymbiotic destabilizing effect.

^{31}P NMR spectrum (Appendix 6), of **R2-MC**, was recorded in order to discard the presence of a mixture of two isomers: *cis* and *trans.* The presence of only one signal, at 42.74 ppm, confirms the presence of only one isomer, the *trans* isomer, in agreement with the antisymbiotic effect.

IR spectrum (Appendix 7), of **R1-MC**, present a band at 1614 cm^{-1} assigned to the $\upsilon_{C=N}$. Characteristics bands of the PPh_3 can also be seen [14]: at 1477.99 and 1434.61 cm^{-1} a double band assigned to the υ_{C-C} and at 1096.59 and 508.95 cm^{-1} two bands assigned to an X-sens vibration. The form of the band at 508.95 cm^{-1} indicates that there are only one PPh_3 coordinated [15].

5.5 ATTEMPS TO OBTAIN 2,4-LUTIDINE DERIVATIVES

Two cyclopalladated monomers (**R1-L, R2-L**) (Figure 11) with PPh_3 and 2,4-lutidine, as ligands, has been tried to obtain without success. After trying different reactions conditions changing the reaction time, temperature and mechanism, from the reagents **R1-MC, R2-MC** and **R2-MB**, it has not been possible to obtain **R1-L** and **R2-L** in a high yield and purity.

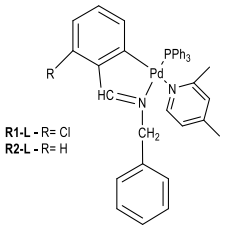


Figure 11. **R1-L** and **R2-L** structure.

6. EXPERIMENTAL SECTION

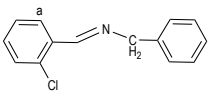
6.1. MATERIALS AND METHODS

NMR spectra were recorded in $CDCl_3$ at 298 K with Mercury 400 (^1H) and Bruker 400 Avance III HD (^{31}P) spectrometers. Chemical shifts are given in δ values (ppm) relative to TMS (^1H), and 85% H_3PO_4 ($^{31}P\{^1H\}$), and coupling constants are given in Hz. Multiplicity is expressed as: s (singlet), d (doublet), t (triplet), q (quadruplet), and m (multiplet). IR spectra were recorded in KBr dispersion, and band values are given in cm^{-1}.

6.2. PREPARATION OF STARTING REAGENTS

6.2.1. Preparation of o-$ClC_6H_4CHNCH_2C_6H_5$ – R1-I

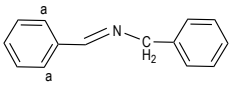
Compound *o*-$ClC_6H_4CHNCH_2C_6H_5$ was obtained after refluxing for 1 h a solution containing 190 mg (1.35 mmol) of 2-chlorobenzaldehyde and 150 mg (1.40 mmol) of benzylamine in 20 mL of ethanol. The solvent was evaporated in a rotary evaporator and a white oily material was obtained. Yield: 281 mg (91%)



^1H NMR ($CDCl_3$, 400 MHz): δ 8.85 (s, 1H, HC=N), 8.11-8.08 (dd, $J_{H\text{-}H}$ = 7.71, 1.8 Hz, 1H[a]), 7.39-7.25 (m, 8H, aromatic), 4.87 (s, 2H, N-CH_2).

6.2.2. Preparation of $C_6H_5CHNCH_2C_6H_5$ – R2-I

Compound $C_6H_5CHNCH_2C_6H_5$ was obtained after refluxing for 1 h a solution containing 516 mg (4.86 mmol) of benzaldehydes and 521 mg (4.86 mmol) of benzylamine in 20 mL of ethanol. The solvent was evaporated in a rotary evaporator and a white oily material was obtained. Yield: 806 mg (85%)

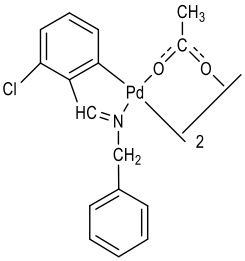


^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.39 (s, 1H, HC=N), 7.82-7.75 (m, 2H, H^a), 7.45-7.23 (m, 8H, aromatic), 4.83 (s, 2H, N-CH_2).

6.3. STUDY OF CICLOPALLADATES

6.3.1 Synthesis of [Pd(μ-AcO)(o-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ – R1-A

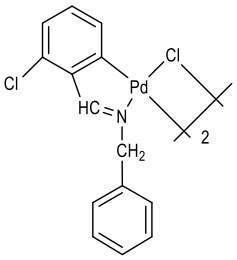
Compound [Pd(μ-AcO)(*o*-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ was obtained after stirring for 45 min at 100ºC a solution containing 103 mg (0.448 mmol) of o-$ClC_6H_4CHNCH_2C_6H_5$ and 105 mg (0.467 mmol) of $Pd(AcO)_2$ in 15 mL of acetic acid. The dark solid was filtered and discarded and the orange solution was evaporated in a rotary evaporator. The yellow solid obtained was washed with ethanol and filtered under vacuum. Yield: 115 mg (64%)



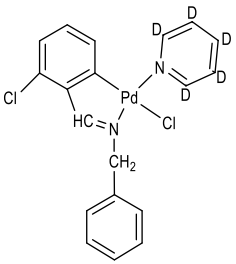
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60 (s, 1H, HC=N), 7.32-7.30 (m, 3H, aromatic), 7.05-6.99 (m, 5H, aromatic), 4.53 (d, $J_{H\text{-}H}$= 15.1 Hz, 1H, N-CH_2), 3.92 (d, $J_{H\text{-}H}$ = 15.1 Hz, 1H, N-CH_2), 2.15 (s, 3H, CH_3COO^-).
IR (cm^{-1}): υ_{as} (C=O) 1586.35, υ_s (C=O) 1405.39, υ (C=N) 1610.47

6.3.2 Synthesis of [Pd(μ-Cl)(o-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ – R1-C

Compound [Pd(μ-Cl)(*o*-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ was obtained after stirring for 1 hour at room temperature a solution containing 79 mg (0.0995 mmol) of [Pd(μ-AcO)(*o*-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ and 49 mg (1.55 mmol) of LiCl in 20 mL of acetone. The yellow solution was filtered and evaporated in a rotary evaporator. The yellow solid obtained was washed with ethanol and filtered under vacuum. Yield: 46 mg (62%)



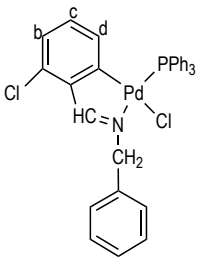
Due to the insolubility of this compound in common NMR solvents, the corresponding monomer compound ([PdCl(py)(o-$ClC_6H_3CHNCH_2C_6H_5$)]) was obtained by reaction with [D5]-Pyridine in a NMR-tube, and then the proton-NMR was recorded. Owing to the rapid exchange between the coordinated and free [D5]-Pyridine, the signal corresponding to the hydrogen in *ortho* position to palladium appears as a broad singlet.



^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21 (s, 1H, HC=N), 7.67-7.28 (m, 5H, aromatic), 6.97-6.87 (m, 2H, aromatic), 6.02 (s, 1H, aromatic ortho C-Pd bond), 5.16 (s, 2H, N-CH_2).

6.3.3 Synthesis of [PdCl(o-$ClC_6H_3CHNCH_2C_6H_5$)(PPh_3)] – R1-MC

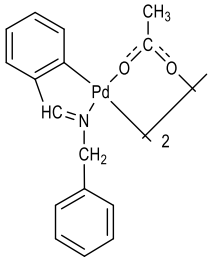
Compound [PdCl(o-$ClC_6H_3CHNCH_2C_6H_5$)(PPh_3)] was obtained after starring for 1h at room temperature a solution containing 856 mg (0.116 mmol) of [Pd(μ-Cl)(*o*-$ClC_6H_3CHNCH_2C_6H_5$)]$_2$ and 642 mg (0.244 mmol) of PPh_3 in 20 mL of acetone. The yellow solution was filtered and evaporated in a rotary evaporator. A yellow spongy solid was obtained and washed with diethyl ether and filtered under vacuum. Yield: 131 mg (89%)



^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, $J_{H\text{-}H}$= 8.0 Hz, 1H, HC=N), 7.60-7.67 (m, 6H aromatic, H *ortho*-Pd), 7.52-7.28 (m, 14H aromatic), 6.79 (dd, $J_{H\text{-}H}$= 8.0, 0.9 Hz, 1H, H_b)), 6.43 (t, $J_{H\text{-}H}$= 7.9 Hz, 1H, H_c), 6.26 (ddd, $J_{H\text{-}H}$= 7.7, 6.0, 0.9 Hz, 1H, H_d), 5.28 (s, 2H, CH_2N).
IR (cm^{-1}): υ (C=N) 1614.08, υ C-C (PPh_3) 1477.99 and 1434.61, X-sens (PPh_3) 1096.59, X-sens (PPh_3) 508.95

6.3.4 Synthesis of $[Pd(\mu\text{-}AcO)(C_6H_4CHNCH_2C_6H_5)]_2$ – R2-A

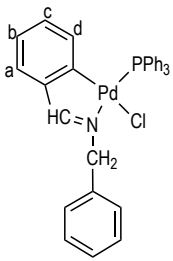
Compound $[Pd(\mu\text{-}AcO)(C_6H_4CHNCH_2C_6H_5)]_2$ was obtained after stirring for 45 min at 100 ºC a solution containing 200 mg (1.024 mmol) of $C_6H_5CHNCH_2C_6H_5$ and 230 mg (1.025mmol) of $Pd(AcO)_2$ in 15 mL of acetic acid. The dark solid was filtered and discarded and the orange solution was evaporated in a rotary evaporator. The yellow solid obtained was washed with ethanol and filtered under vacuum. Yield: 234 mg (60%)



^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26-6.80 (m, 3H, aromatic), 7.05-6.99 (m, 10 H, 9 H aromatic, HC=N), 4.57 (d, $J_{H\text{-}H}$= 16.1 Hz, 1H, N-CH_2), 4.01 (d, $J_{H\text{-}H}$ = 16.1 Hz, 1H, N-CH_2), 2.18 (s, 3H, CH_3COO^-).
IR (cm^{-1}): υ_{as} (C=O) 1588.17, υ_s (C=O) 1405.39, υ (C=N) 1614.16

6.3.5 Synthesis of $[PdCl(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ – R2-MC

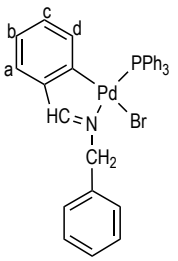
Compound $[PdCl(C_6H_4CHNCH_2C_6H_5)(PPh_3)]$ was obtained, by a one pot reaction, after stirring for 1 h at room temperature a solution containing 100 mg (0.132 mmol) of $[Pd(\mu\text{-}AcO)(C_6H_4CHNCH_2C_6H_5)]_2$, 33.6 mg (0.792 mmol) of LiCl and 139 mg (0.222mmol) of PPh_3 in 20 mL of acetone. The white solid obtained was filtered under vacuum. Yield: 133 mg (84%)



^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (d, $J_{H\text{-}H}$= 7.9 Hz, 1H, HC=N), 7.80-7.71 (m, 6H aromatic, H *ortho*-Pd), 7.48-7.29 (m, 14H aromatic), 7.16 (d, $J_{H\text{-}H}$= 7.6 Hz, 1H, H_a), 6.86 (t, $J_{H\text{-}H}$= 7.4 Hz, 1H, H_b), 6.51 (t, $J_{H\text{-}H}$= 7.6, Hc), 6.38 (t, $J_{H\text{-}H}$= 6.9 ,H_d), 5.28 (s, 2H, N-CH_2).
^{31}P {^{1}H} NMR ($CDCl_3$, 161,93 MHz): δ 42.74 (s, 1P, PPH_3)

6.3.6 Synthesis of [PdBr($C_6H_4CHNCH_2C_6H_5$)(PPh_3)] – R2-MB

Compound [PdBr($C_6H_5CHNCH_2C_6H_5$)(PPh_3)] was obtained, by a one pot reaction, after stirring for 1 h at room temperature a solution containing 100 mg (0.132 mmol) of [Pd(μ-AcO)($C_6H_5CHNCH_2C_6H_5$)]$_2$, 69 mg (0.794 mmol) of LiBr and 69 mg (0.263mmol) of PPh_3 in 20 mL of acetone. The white solid obtained was filtered under vacuum. Yield: 155 mg (91%)



^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.90 (d, J_{H-H}= 7.9 Hz, 1H, HC=N), 7.81-7.72 (m, 6H aromatic, H *ortho*-Pd), 7.47-7.30 (m, 14H aromatic), 7.15 (d, J_{H-H}= 7.7 Hz, 1H, H_a), 6.87 (t, J_{H-H}= 7.4 Hz, 1H, H_b), 6.52 (t, J_{H-H}= 7.7, H_c), 6.38 (t, J_{H-H}= 7.1, H_d), 5.41 (s, 2H, N-CH_2).

7. CONCLUSIONS

The aim of this work has been achieved by the synthesis and characterization of six palladium metallacycles. In a more specific way:

- Two aromatic imines have been synthesized, by a condensation reaction, in a 90% yield and characterized.
- Two acetate-bridged cyclopalladated compounds have been synthesized, by the activation of the C-H bond of the imines prepared before, and an "open book" structure has been shown in ^{1}H NMR spectra.
- One halogen-bridged cyclopalladated compound has been synthesized through the substitution of the acetate bridge by two chloro ligands, in a medium yield, and the insolubility on common solvents has been observed.
- Three mononuclear cyclopalladated compounds have been synthesized by the splitting reaction of the bridged dimers with triphyenilphosphine in one pot conditions and in two steps. In both cases the reactions have been achieved with a high yield. Through the characterization with ^{1}H and ^{31}P NMR the formation of the *trans* isomer has been observed and the antisymbiotic effect explained.
- *Ortho*-chloro products have a N=CH···Cl interaction between de imine proton and the chloro atom.
- Cyclopalladated monomers with PPh_3 and 2,4-lutidine, instead of a halogen, have not been synthesized despite the attempts changing the reaction conditions.

8. REFERENCES AND NOTES

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9. ACRONYMS

AcO – Acetate Group

d – doublet

dd – doublet of doublets

ddd – doublet of doublets of doublets

DNA – Desoxyribonucleic Acid

[D5]-pyridine – pyridine pentadeuterated

IR – Infrared spectroscopy

$J_{H\text{-}H}$ – Coupling constant between two H

L – Ligand

m – Multiplet

NMR – Nuclear Magnetic Resonance

o – *ortho* position

py – pyridine

q – quadruplet

R – Substituent

s – Singlet

t – Triplet

υ - Stretching

υ_{as} – Asymmetric stretching

υ_{s} – Symmetric stretching

X – Halogen

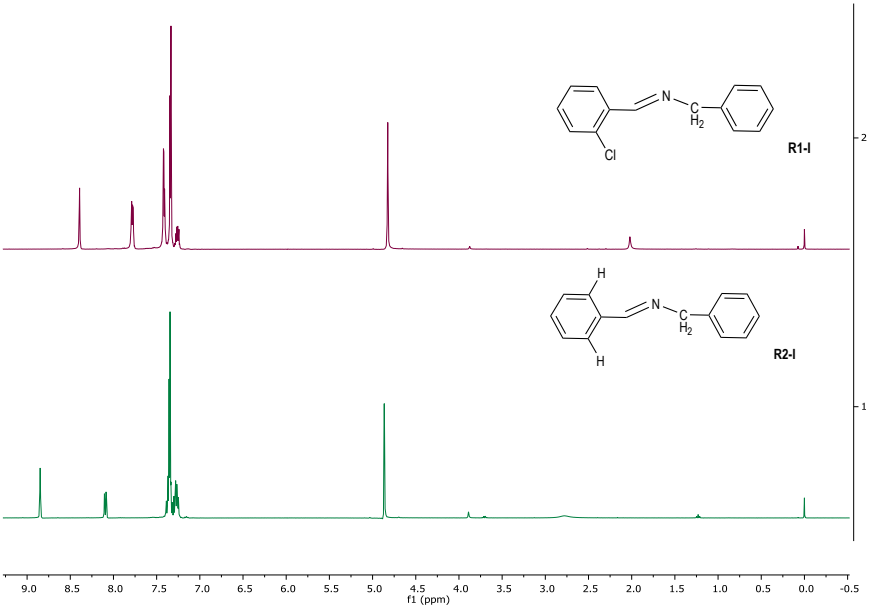
μ - Bridged ligand

η^2 – Bidentated ligand

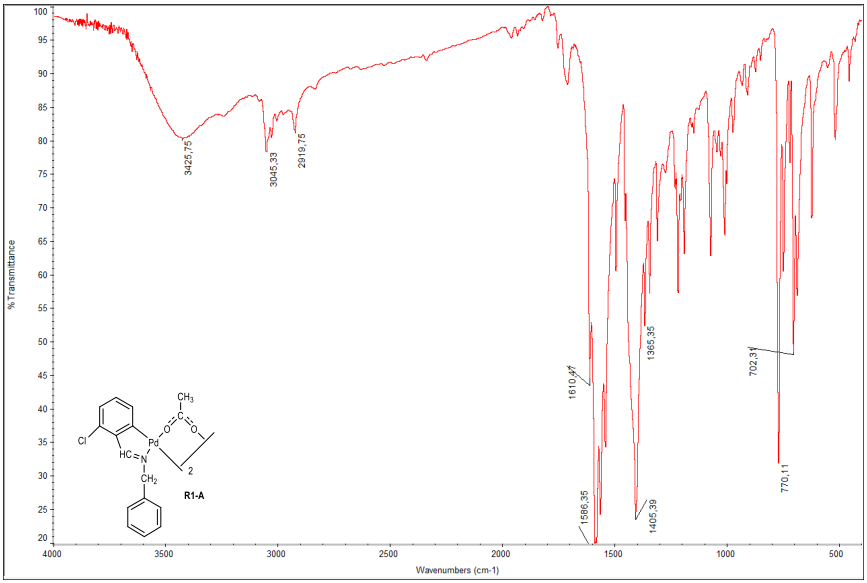
δ - Chemical shift

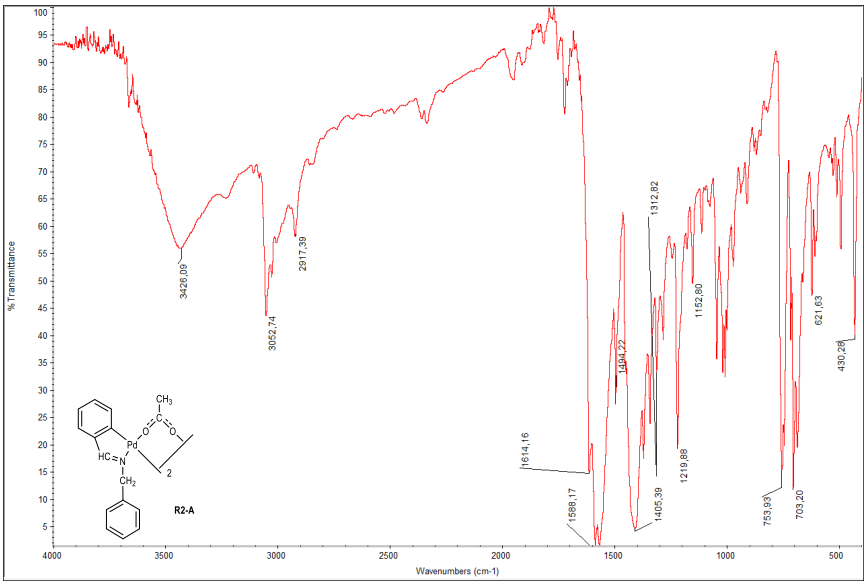
APPENDICES

APPENDIX 1: SPECTRA DATA OF R1-I AND R2-I

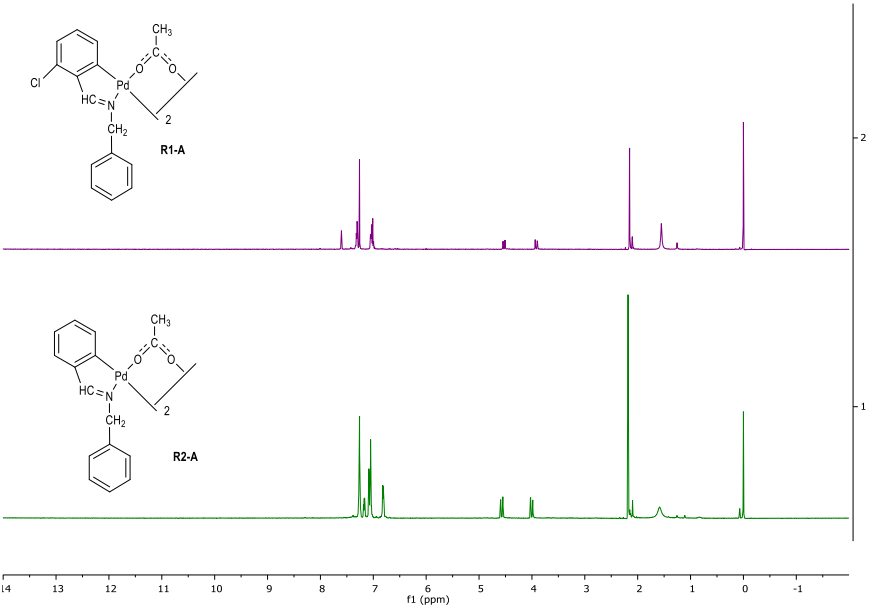


APPENDIX 2: IR SPECTRA OF R1-A AND R2-A

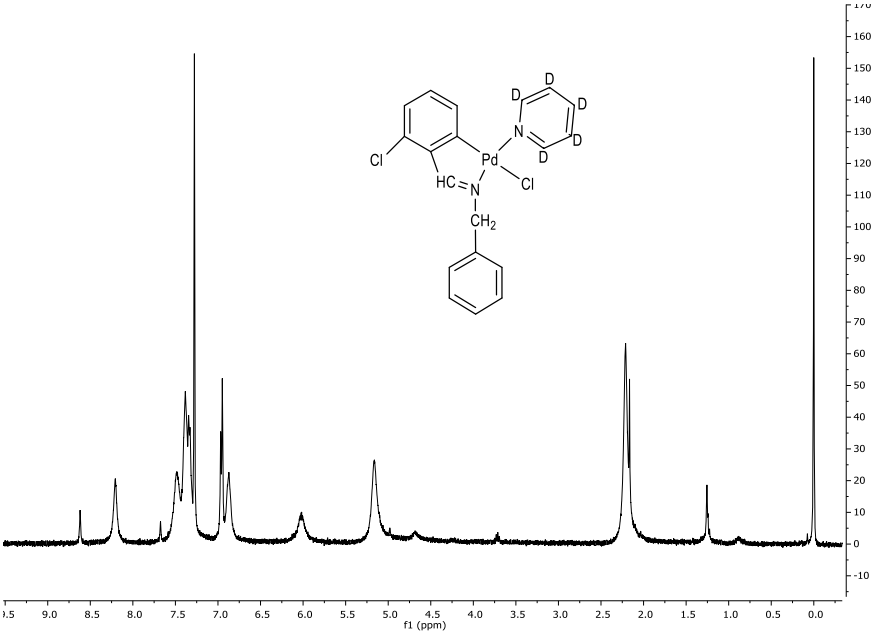




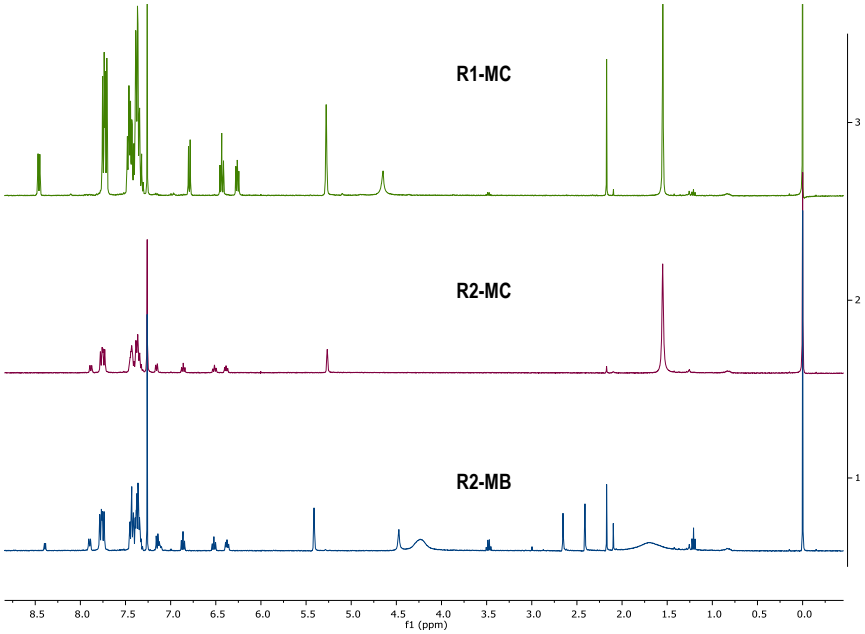
APPENDIX 3: ^{1}H-NMR SPECTRA OF R1-A AND R2-A

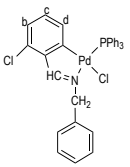


APPENDIX 4: ^{1}H-NMR SPECTRUM OF R1-C

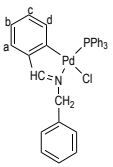


APPENDIX 5: ^{1}H-NMR SPECTRA OF R1-MC, R2-MC AND R2-MB

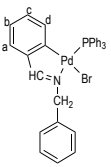




R1-MC

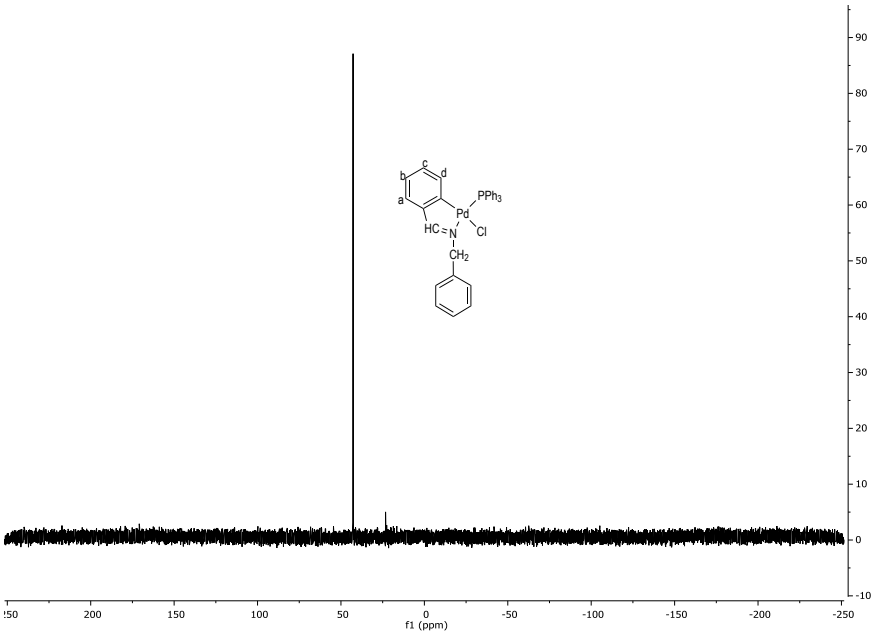


R2-MC



R2-MB

APPENDIX 6: ^{31}P-NMR SPECTRUM OF R2-MC



APPENDIX 7: IR SPECTRUM OF R1-MC