Universidad de Murcia

Facultad de Química

Departamento de Química Inorgánica

COMPLEJOS DE Pd(II) Y Pd(IV) DERIVADOS DE LA 2,6-DIACETILPIRIDINA. APLICACIONES CATALÍTICAS

TESIS DOCTORAL

Francisco Juliá Hernández

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COMPLEJOS DE Pd(II) Y Pd(IV) DERIVADOS DE LA 2,6-DIACETILPIRIDINA. APLICACIONES CATALÍTICAS

Memoria presentada para optar al grado de Doctor por la Universidad de Murcia por el Licenciado Francisco Juliá Hernández

En cumplimiento de los requisitos necesarios para obtener la mención de “Doctorado Europeo” y siguiendo la normativa de “Redacción de la tesis doctoral en otro idioma” reglada por la Universidad de Murcia, todos los capítulos y epígrafes de esta tesis están redactados en inglés, excepto la portada, el índice y un resumen final, que se presentan en castellano.

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Que la Tesis Doctoral titulada "**Complejos de Pd(II) y Pd(IV) derivados de la 2,6-diacetilpiridina. Aplicaciones catalíticas**", ha sido realizada por D. Francisco Juliá Hernández, bajo la inmediata dirección y supervisión de D. José Vicente Soler y Dª Aurelia Arcas García, y que la Comisión Académica ha dado su conformidad para que sea presentada ante la Comisión de Doctorado.

Murcia, a 31 de Enero de 2012

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D. José Vicente Soler y Dª. Aurelia Arcas García, Catedráticos de Universidad del Área de Química en el Departamento de Química Inorgánica, AUTORIZAN:

La presentación de la Tesis Doctoral titulada "**Complejos de Pd(II) y Pd(IV) derivados de la 2,6-diacetilpiridina. Aplicaciones catalíticas**", realizada por D. Francisco Juliá Hernández, bajo su inmediata dirección y supervisión, y que presenta para la obtención del grado de Doctor por la Universidad de Murcia.

En Murcia, a 31 de Enero de 2012

Fdo: Prof. Dr. José Vicente Soler

Fdo: Prof. Dra. Aurelia Arcas García

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La realización de esta Tesis Doctoral me ha supuesto un esfuerzo continuado durante más de cuatro años. En este periodo han sido frecuentes las fases de euforia, tristeza, ilusión y desánimo. **Me gustaría agradecer** a todas aquellas personas que de una manera u otra, han hecho que los momentos malos no fueran tan malos; y los buenos, muy buenos. En especial:

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"It is my earnest desire that some of you should carry on this scientific work and keep for your ambition the determination to make a permanent contribution to science."

Marie Curie

On the Discovery of Radium Speech

Poughkeepsie, NY, 1921

A mi familia

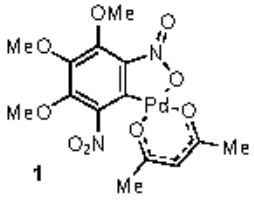
ÍNDICE/INDEX

ABBREVIATIONS

acac	acetylacetonate
APT	Attached Proton Test
Ar	arilo
bpy, bipy	2,2'-bipyridine
br	broad
^{t}Bu, *t*-Bu	tert-butyl
^{t}Bubpy, tbbpy, dbbpy	4,4'-*tert*-butyl-2,2'-bipyridine
Bz	benzyl
Bzdiaz	2',2',4'-trimethyl-2',3'-dihydro-1*H*-1',5'-benzodiazepine
ca.	approximately
CCDC	Cambridge Crystallographic Data Center
d	doublet
dd	doublet of doublets
dec	decomposition
DFT	Density Functional Theory
dmso	dimethylsulfoxide
dppm	diphenylphosphino methane
dppmo	bis(diphenylphosphino)methanemonoxide
eq, equiv	equivalent
ESI-MS	EletroSpray Ionization – Mass Spectrometry
GC/MS	Gas Chromatography – Mass Spectrometry
HMBC	Heteronuclear Multiple Bond Correlation
HMQC	Heteronuclear Multiple Quantum Correlation
HRMS	High Resolution Mass Spectrum
IR	Infrared
L	Ligand, liter
m	multiplet
mba	4-methoxybenzylamine

Me	methyl
MOM	methoxymethyl ether
Mp	melting point
NMR	Nuclear Magnetic Resonance
OAc	acetate
OTf, TfO	triflate, CF_3SO_3
pda	*o*-phenylendiamine
Ph	phenyl
ppm	parts per million
py	pyridine
rt	room temperature
s	singlet
S	solvent
t	triplet
TBDMS	*tert*-butyldimethylsilyl
THF	tetrahydrofuran
THP	tetrahydropyran
TMS	tetramethylsilane
tht	tetrahydrothiophene
UV	ultraviolet
vs	"versus"
XRD	X-Ray Diffraction
Xy	xylyl, 2,6-dimethylphenyl

Chapter I



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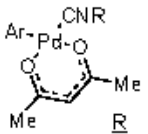

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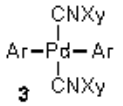

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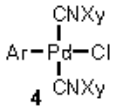

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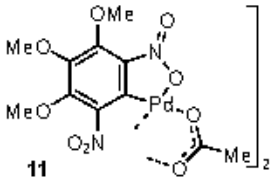

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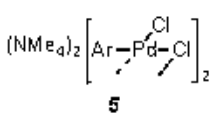

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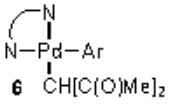

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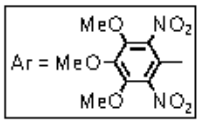
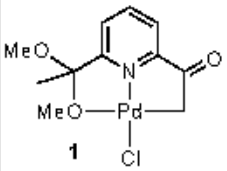


Chapter II - Section II.1



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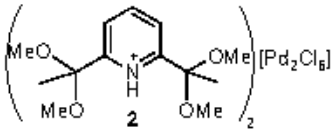

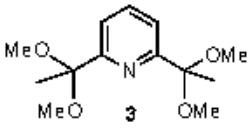

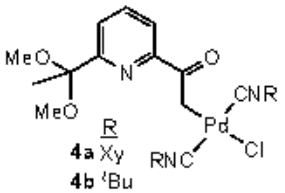

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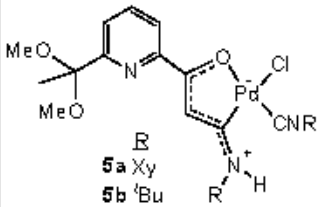

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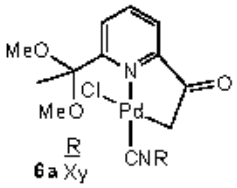

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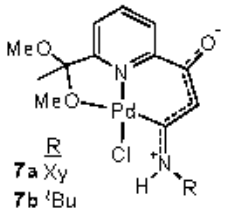

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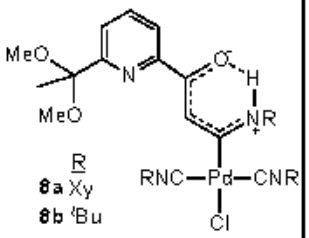

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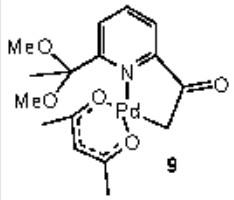

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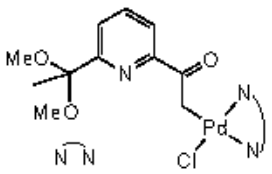

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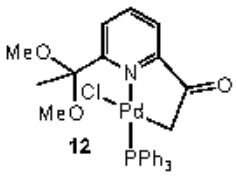

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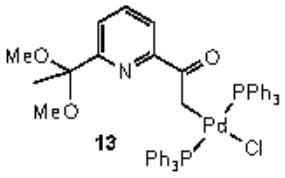

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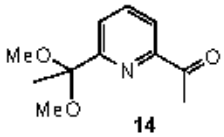

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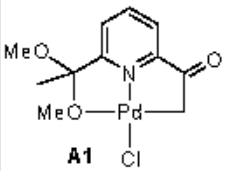

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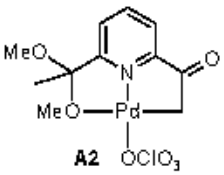

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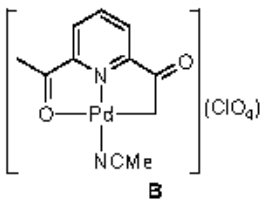

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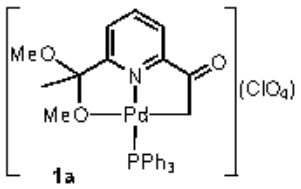

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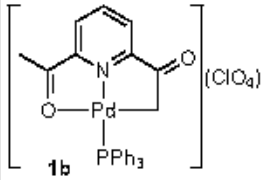

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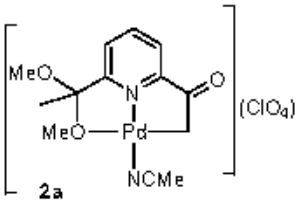

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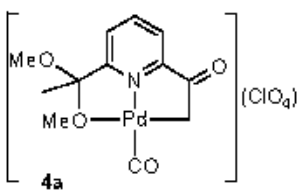

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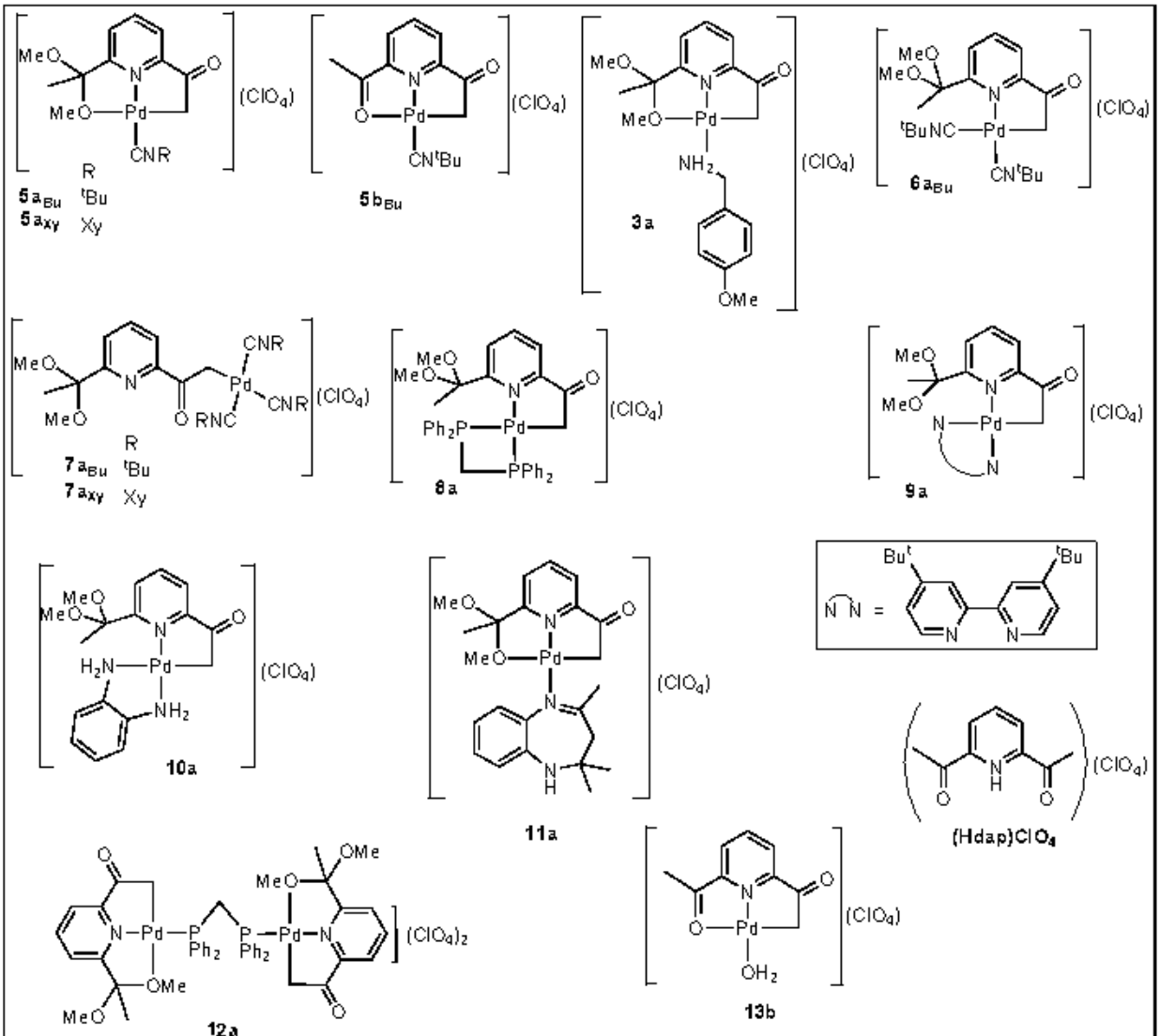

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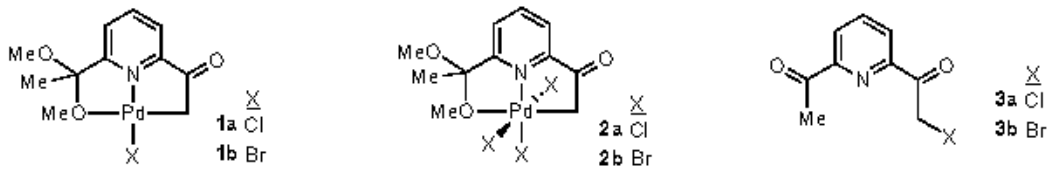

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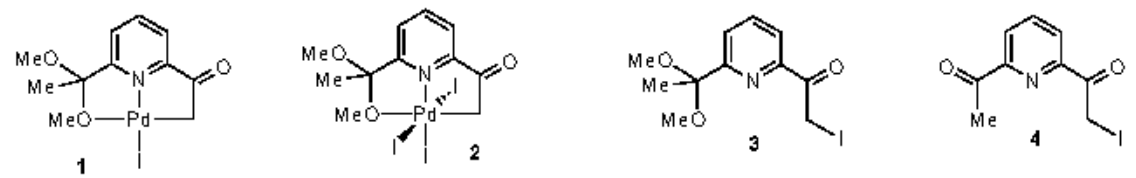

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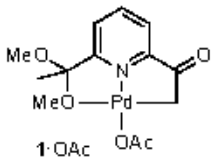

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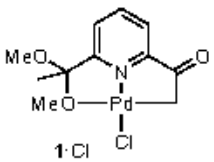

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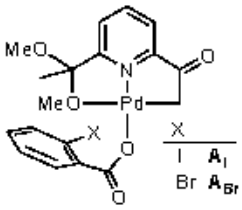
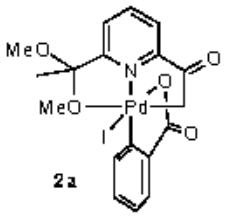


X	
I	**A**$_{I}$
Br	**A**$_{Br}$



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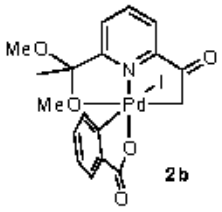

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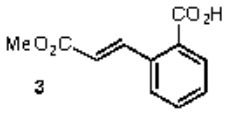

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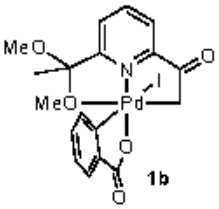
Chapter IV - Section IV.2



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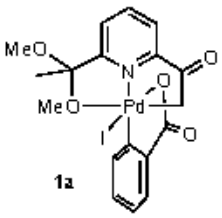

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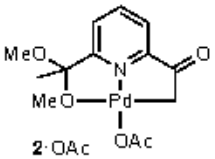

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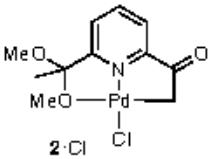

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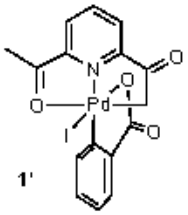
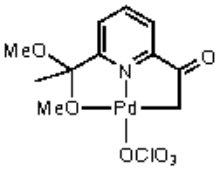
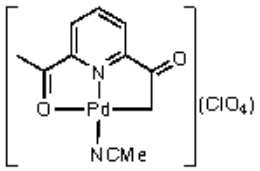


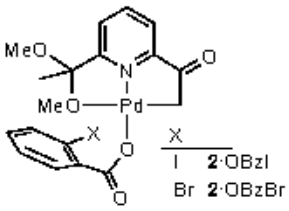
1'



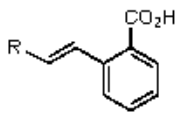
2·$OClO_3$



[**2'**·MeCN]ClO_4

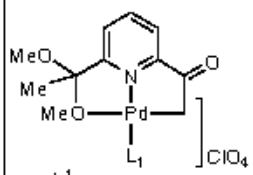


X	
I	**2**·OBzI
Br	**2**·OBzBr

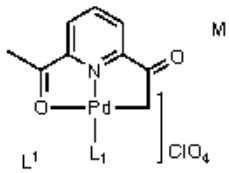


X	
CO_2Me	**3a**
CO_2Et	**3b**
Ph	**3c**

Chapter V



L^1	
MeCN	**A1**
PPh_3	**A2**



L^1	
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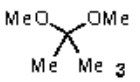
PPh_3	**2**



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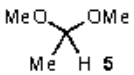

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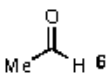

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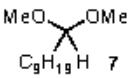

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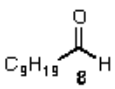

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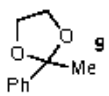

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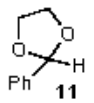

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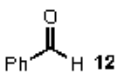

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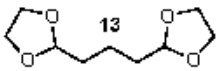

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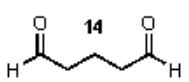

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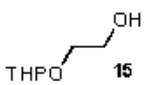

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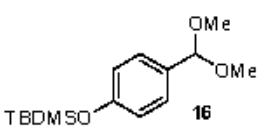

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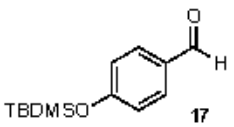

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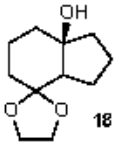

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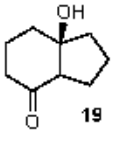

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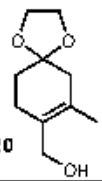

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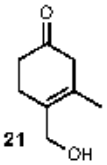

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PREFACE

This thesis represents a culmination of work and learning that has taken place over a period of almost four years and a half. The completion of this PhD has allowed me not only to improve my experimental skills, but my introduction to the scientific life by reading the literature, attending conferences and visiting a foreign research centre for three months. I think this formation has been a good starting point to carry on my scientific career in the near future.

This dissertation is framed within the main research lines of the *Grupo de Química Organometálica* in the Universidad de Murcia. The study of the behaviour of Pd–C bonds in organometallic complexes towards unsaturated molecules has been and still is one of the main aims in the group. The knowledge about the nature of this bond has important implications in the development of new methodologies in organic synthesis and catalytic processes, which are strongly useful in the preparation of compounds with biological or industrial applications.

By the time you read this memory, you will observe that there is a conductive line in the presentation of the results. In the first chapters, we describe the synthesis and reactivity of some Pd(II) compounds derived from 3,4,5-trimethoxy-2,6-dinitrophenyl and 2,6-diacetylpyridine. These results correspond to a fundamental research, in which we studied the nature of the Pd–C bond in these complexes, reporting some insertion reaction with isocyanides. As a result, we have reported the first family of ketonyl pincer type Pd(II) complexes.

Next, we gave one more step considering the preparation of Pd(IV) complexes. Starting from the Pd(II) derivatives with the ligand 2,6-diacetylpyridine monodimethylketal, we obtained the first pincer type Pd(IV) compounds by oxidation reactions with halogens (Cl_2, Br_2 and I_2).

Giving in mind these good results, we decided to extend the study of oxidation reactions and apply the knowledge gained to the investigation of a catalytic reaction mechanism. We selected the Heck coupling reaction because of their important applications in organic synthesis, recognized with the 2010 Nobel Prize in Chemistry, and the actual controversy between Pd(0)/Pd(II) and Pd(II)/Pd(IV) catalytic cycles. Actually, we prepared the first Pd(IV) complex synthesized from the oxidative addition of a haloarene to Pd(II), that corresponds to the first step in a Pd(II)/Pd(IV) mechanism. What is more important, we described several

experimental proofs and detected two Pd(IV) intermediates *in situ*, in accordance to this catalytic cycle.

Finally, we studied the properties of some of the compounds we prepared as catalyst in the hydrolysis of acetals and ketals. We reached good results with one complex derived from the ligand 2,6-diacetylpyridine and the results of this investigation have been protected with the application of a patent. The conductive line I mentioned, starts from a fundamental research and, having in our hands this experience, we were able to apply it to the study of a reaction mechanism. Also, we have developed a final application of a complex prepared as catalyst in one of the most used reaction in organic multistep synthesis.

Regarding the organization of the memory, this dissertation has been submitted in order to fulfil the requirements for the "European Doctorate" and in accordance to the "Redacción de la Tesis Doctoral en otro idioma" regulation of the Universidad de Murcia. Therefore, all chapters and epigraphs are written in English, except the title, index and a summary at the end of the memory which are presented in Spanish.

The chapters I-V of the memory, which describe the results of the research, are written in a journal article format, containing its own abstract, introduction, results and discussion, conclusions and references. The chapter VI corresponds to a summary of the work I have done during my short stay at La Sapienza - Università di Roma under the supervision of Dr. Mauro Bassetti.

Chapter I. Synthesis of Bis(2,6-dinitroaryl) Palladium(II) Complexes.

Chapter II. Organometallic Complexes of Pd(II) Derived from 2,6-Diacetylpyridine and 2,6-Diacetylpyridine Dimethylketal.

- *Section II.1*. Organometallic Complexes of Pd(II) Derived from 2,6-Diacetylpyridine Dimethylketal.

- *Section II.2*. Synthesis and Hydrolysis of Cationic 2,6-Diacetylpyridine Dimethylketal Palladium(II) Complexes. The Cyclopalladation of 2,6-Diacetylpyridine. Palladium-Catalyzed Synthesis of a 1,5-Benzodiazepine.

Chapter III. Organometallic Trihalopalladium(IV) Complexes. Reductive Elimination Reactions.

- *Section III.1*. Quantitative Synthesis and Full Characterization of the First Isolated and Stable Pincer Palladium(IV) Complexes. Quantitative and Regioselectiive Synthesis of the C–X (X = Cl, Br) Reductive Elimination Products.

- *Section III.2*. Synthesis, Isolation, and Characterization of an Organometallic Triiodopalladium(IV) Complex. Quantitative and Regioselective Synthesis of Two C–I Reductive Elimination Products.

Chapter IV. Pd(II)/Pd(IV) Catalytic Cycle in a Heck-Type Arylation of Olefins.

- *Section IV.1*. Synthesis of a Palladium(IV) Complex by Oxidative Addition of an Aryl Halide to Palladium(II) and Its Use as Precatalyst in a C–C Coupling Reaction.

- *Section IV.2*. Providing Support in Favor of the Existence of a Pd(II)/Pd(IV) Catalytic Cycle in a Heck-Type Reaction.

Chapter V. Pd(II)-Catalyzed Deprotection of Acetals and Ketals Containing Acid Sensitive Functional Groups.

Chapter VI. Kinetics and Activation Parameters of the Dimerization of Terminal Alkynes Catalyzed by [Ru(*p*-cymene)Cl_2]$_2$ in Acetic Acid.

The Supporting Information for this dissertation is available on a CD which is attached to the end of the memory. It includes, divided into chapters and sections, the CIF files corresponding to the crystal structures and all the spectroscopic data of the new compounds.

This thesis had not been realized without the help of financial support:

- Ministerio de Ciencia e Innovación and FEDER. Project CTQ2007-60808/BQU.

- **Fundación Séneca (04539/GERM/06 and 03059/PI/05) for financial support and a grant to the author of this thesis.**

The results presented in this memory have been published, or submitted for publication in these high impact international journals:

- **Chapter I**. J. Vicente, A. Arcas, M.-D. Gálvez-López, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2008**, *27*, 1582.

- **Chapter II – Section II.1**. J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2010**, *29*, 3066.

- **Chapter II – Section II.2**. F. Juliá-Hernández, A. Arcas, J. Vicente *Organometallics Submitted*.

- **Chapter III – Section III.1**. J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Chem. Comm*. **2010**, *46*, 7253.

- **Chapter III – Section III.2**. J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Inorg. Chem*. **2011**, *50*, 5339.

- **Chapter IV – Section IV.1**. J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Angew. Chem. Int. Ed*. **2011**, *50*, 6896.

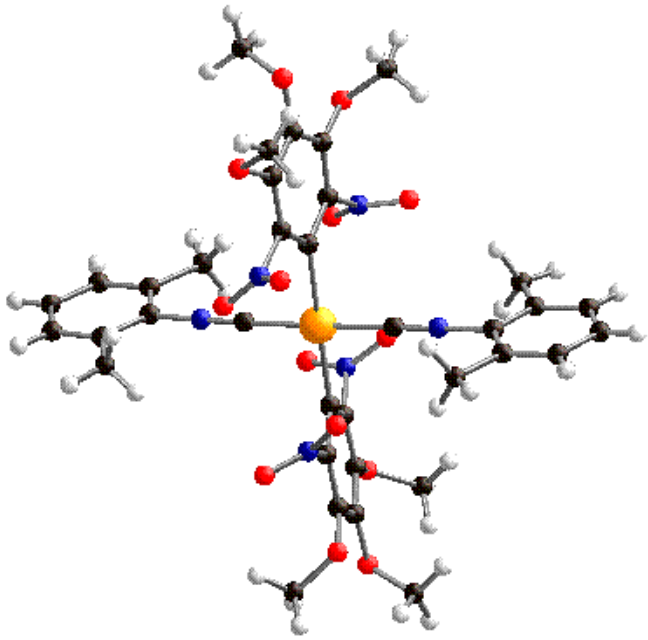
- **Chapter IV – Section IV.2**. F. Juliá-Hernández, A. Arcas, J. Vicente *Chem. Eur. J. Submitted*.

- **Chapter V**. F. Juliá-Hernández, A. Arcas, J. Vicente *Manuscript in preparation.*
  Patent Application No. 201031021.

- **Chapter VI**. M. Bassetti, C. Pasquini, F. Juliá-Hernández *Manuscript in preparation.*

CHAPTER I

Synthesis of Bis(2,6-dinitroaryl) Palladium(II) Complexes



The results of this chapter have been published in:

J. Vicente, A. Arcas, M.-D. Gálvez-López, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2008**, *27*, 1582.

SUMMARY CHAPTER I

In the **Chapter I** of this memory, we described the synthesis and reactivity of aryl Pd(II) complexes derived from the ligand 3,4,5-trimethoxy-2,6-dinitrophenyl. Previously, members of our group reported one Pd(II) complex with this ligand acting as pincer, κ^3-$C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5-C^1,O,O', another one with the chelating ligand κ^2-$C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5-C^1,O, and a series with the monocoordinated ligand κ^1-$C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5-C^1. However, some attempts to prepare other complexes with the pincer or chelating ligands failed. Thus, we decided to prepare new Pd(II) complexes with this ligand, to investigate the reactivity of such compounds towards unsaturated molecules and try to synthesize pincer complexes.

Reactions of a Pd(II) complex with the chelating ligand κ^2-$C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5-C^1,O, described by members of our group, with isocyanides were carried out. However, unexpectedly, a rare example of disproportionation was found when the starting monoaryl complex reacted with 4 equivalents of XyNC, yielding a diaryl complex. The preparation of a diaryl from a monoaryl Pd(II) complex was an unprecedented reaction so we found interesting to look into the reaction mechanism. We tried to prepare an expected intermediate of the reaction by two different ways, but we always yielded the final diaryl complex. Finally, we concluded that the formation of such compound could be explained in terms of a transphobia effect and we proposed a reaction pathway.

The results reported in this chapter represent my introduction into research, from books to the lab. In that period of time I acquired the necessary training to start a new research line. We decided to use a new ligand that would allow us to prepare pincer-type palladium complexes. We thought that 2,6-diacetylpyridine would be an interesting candidate because this compound had not yet been metalated, the double metalation would afford complexes with two CH_2 groups in trans and, in any case, in our group there is a great interest in the chemistry of acetonyl metal complexes.

ABSTRACT

The reaction of [Pd(κ^2-Ar)(*O,O*-acac)] (κ^2-Ar = κ^2-*C,O*-$C_6(NO_2)_2$-2,6-(OMe); **1**) with one equiv of RNC gives [Pd(κ^2-Ar)(*O,O*-acac)(CNR)] [R = Xy (**2a**), ^{t}Bu (**2b**)] and with four equiv of XyNC, *trans*-[Pd(κ^1-Ar)$_2$(CNXy)$_2$] (κ^1-Ar = κ^1-*C,O*-$C_6(NO_2)_2$-2,6-(OMe); **3**). These complexes has also been obtained (1) by reacting Tl(acac) with one equiv of *trans*-[Pd(κ^1-Ar)Cl(CNXy)$_2$] (**4**), obtained in turn by reacting *trans*-$(NMe_4)_2$[Pd(κ^1-Ar)Cl(μ-Cl)]$_2$ (**5**) with four equiv of XyNC or (2) by reacting [Pd(κ^1-Ar)(*C*-acac)(phen)] (**6**) with four equiv of XyNC. Reaction of palladium complex **5** with two equiv of $Hg(OAc)_2$ affords *trans*-[Pd(κ^2-Ar)(μ-OAc)]$_2$ (**11**). The crystal structures of **2a**, **2b**, **3**, **5** and **11** have been determined.

INTRODUCTION

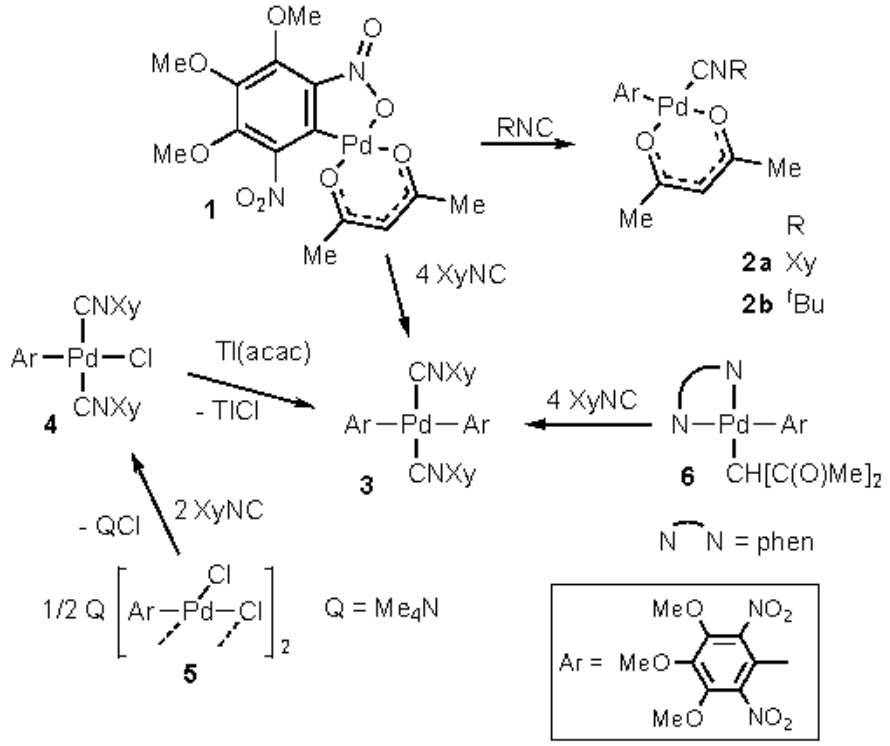
We have reported the synthesis of monoaryl palladium complexes [Pd](Ar) (Ar = C_6H_3Me-2,NO_2-6,[1] $C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5,[2] $C_6H_4NO_2$-2,[3] $C_6H_4(NO_2)_3$-2,4,6,[4] C_6H(CHO)-2-$(OMe)_3$-3,4,5,[5, 6] C_6HR-6-$(OMe)_3$-2,3,4 (R = CHO,[5-7] CH_2OEt,[8] C(O)NHBu^t),[9] C_6H_3R-2-R'-5 (R = R' = $CH(OMe)_2$, $CH(SCH_2CH_2S)$,[10] CHO, CO_2H, R = CHO, R' = CO_2H[11] through transmetallation reactions using the corresponding mercurial [$HgAr_2$] or [Hg(Ar)Cl]. Except for Ar = $C_6H_4NO_2$-2,[3] no diaryl complexes were obtained even when their syntheses were attempted by using an excess of mercurial.[1, 10, 11] Monoaryl palladium complexes are also the result of the reaction between other aryl mercurials and Pd(II) complexes,[12-14] except in one case.[14] In contrast, [Pt](Ar)$_2$ (Ar = $C_6H_4NO_2$-2,[15] $C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5)[6], is always the product of the transmetallation reaction and all attempts to obtain [Pt](Ar) by reacting [$HgAr_2$] with $(Me_4N)_2[Pt_2Cl_6]$ or $K_2[PtCl_4]$ in a 1:1 molar ratio, were unsuccessful. Instead, [Pt](Ar)$_2$ and the starting platinum complex were isolated.[15, 16] However, complexes [Pt](Ar) (Ar = Ph, 2-arylazoaryl, $C_6H_3NH_2$-2-NO_2-5)[12, 17, 18] and [Pt](Ar)$_2$ (Ar = Ph)[17] have been prepared using organomercurials. These data suggest that transmetallation reactions with aryl mercurials can only monoarylate palladium complexes, except in a few cases, and mono o diarylate platinum complexes depending on the nature of the aryl ligand. The synthetic challenge of preparing [Pd](Ar)$_2$ and [Pt](Ar) when Ar = $C_6(NO_2)_2$-2,6-$(OMe)_3$-3,4,5, for which all attempts with the corresponding mercurial were unsuccessful, is the object of the present article. We have successfully used mercurials to prepare nitrophenyl complexes of other metals such as Au[19] and Rh.[20]

The most general method for the synthesis of [Pd](Ar)$_2$ is the use of the corresponding Li or Mg derivative but we ruled out this method because of the presence of nitro groups in the aryl ligand. In fact, LiC$_6$H$_4$NO$_2$-2 is very unstable[21] and has only been used to prepare a family of complexes *cis*-[Pt(Ar)(C$_6$H$_4$NO$_2$-2)L$_2$] (L = PPh$_3$, R = C$_6$H$_4$R'-x where x = 2, 4, R' = OMe, Me, CF$_3$, NO$_2$; L$_2$ = cod, x = 4, R' = OMe, Me), a synthesis that functions only at very low temperatures.[22] We report here the preparation of [Pd](Ar)$_2$ complexes from a [Pd](Ar) complex by a new method that we have discovered in an experiment designed to study the consequences of forcing two carbon donor ligands to be coordinated mutually trans. We have shown that when a pair of C-donor/P-donor or C-donor/C-donor ligands in a Pd(II) complex is forced to be trans, the resulting species tends to be unstable, and some transformation (*transphobia*[23, 24] effect) is expected to prevent the attainment of such an arrangement. For example, a C–P[24, 25] or C–S[26] coupling process (or the C–C coupling in the well-known Suzuki, Stille and other catalytic reactions) or the insertion of dioxygen into a C–Pd bond have been reported.[24] We have also shown that the resistence to being trans (*transphobia*) of C-donor/C-donor ligands pairs is greater than that for C-donor/P-donor ligands. The concept of transphobia is being used successfully by other authors mainly to discuss geometrical preferences in Pd(II) complexes.[27]

RESULTS AND DISCUSSION

[Pd(κ^2-Ar)(*O,O*-acac)] (**1**) reacts with one equiv of isocyanides to give the adducts [Pd(κ^1-Ar)(*O,O*-acac)(CNR)] [R = Xy (**2a**), ^{t}Bu (**2b**); Scheme 1]. We have reported reactions of **1** with other neutral ligands to give adducts [Pd(κ^1-Ar)(*O,O*-acac)L] [L = PPh$_3$, py, tht, bis(diphenylphosphino)methanemonoxide (dppmo)] and [Pd(κ^2-Ar)(*O,O*-acac)(phen).[2] When **1** was reacted with four equiv of XyNC in acetone, several fast changes of color were observed (to orange via colorless, green and yellow) and after 5 min a colorless solid begin to precipitate. After 1 h of stirring, concentration of the solution precipitated *trans*-[Pd(κ^1-Ar)$_2$(CNXy)$_2$] (**3**) in 82% yield as a colorless solid. In the orange filtrate, a complex mixture of products was detected by ^{1}H NMR, among which **3** was identified. An X-ray crystallographic study of a few crystals obtained from this filtrate was carried out. Although a complete crystallographic analysis was not possible because of poor data quality the presence of a palladium atom in a square planar environment with two cis XyNC ligands was shown with certainty. The other two coordination positions were occupied by a complex chelate ligand

apparently resulting from the insertion of XyNC into Pd–$C_{(acac)}$ bonds in which three isocyanides and two acac ligands were involved. When this reaction was carried out in CH_2Cl_2, the same fast changes of color were observed, although the green persisted longer (~2 min), but complex **3** was also isolated. When **1** was reacted with two equiv of XyNC, the yield of **3** decreased (19%) and **2a** also was obtained. Addition of four equiv of ^{t}BuNC to an acetone solution of **1** also led to several rapid color changes (to pale yellow via orange and yellow) but only a complex mixture of products was isolated.



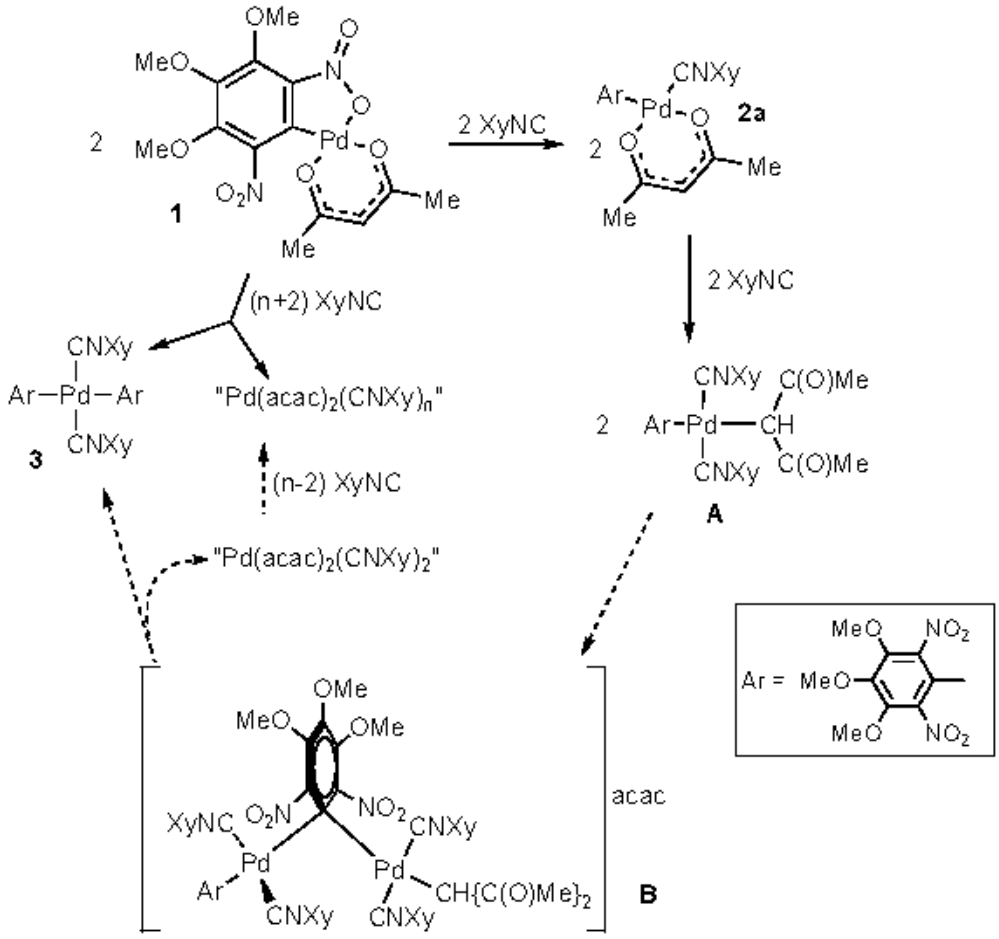
Scheme 1

The above reactions were designed with the purpose of obtaining a complex with four carbon donor ligands [Pd(κ^1-Ar)(*C*-acac)(XyNC)$_2$] (**A**). We hypothesize that the great C/C transphobia, *T*(C/C), should destabilize the complex, favoring an isocyanide insertion into the Pd–C_{acac} bond or inducing some C–C coupling process (see Introduction). However, instead, a new transphobia effect was observed in the 1:4 reaction: a disproportionation reaction leading to **3** and a mixture in which, at least, a product of stoichiometry "Pd(acac)$_2$(CNXy)$_5$" (**X**) was obtained (see above). Formation of **3** containing four C-donor ligands suggests that *T*(Ar/*C*-acac) in the intermediate complex **A** is greater than *T*(Ar/Ar) or *T*(CNXy/CNXy) in **3**. The

formation of **3** as a stable complex in spite of the four C–Pd bonds must be attributed to the strong Ar–M bonds. ^{1}H NMR spectra of complex **3** at 20, 30, 40, 50 and 60 °C in $CDCl_3$ during 45 min show no decomposition or isomerization process. The low yield of **3** in the 1:2 reaction suggests that formation of **X** is a fast process consuming part of the XyNC required for the synthesis of **3**.

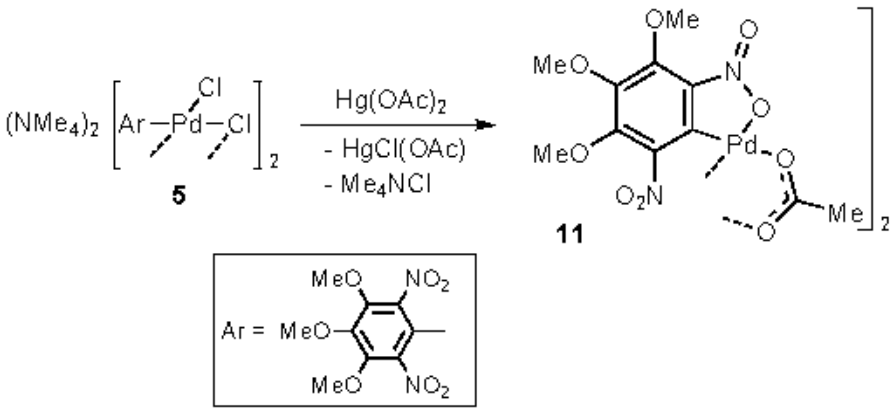
A Proposal for the Reaction Pathway of Formation of 3 from 1. It is reasonable to assume that the first step in this process is formation of complex **2a**, which in turn reacts with XyNC to give the desired complex **A** (Scheme 2). We assume this complex to be trans because, with exclusively C-donor ligands, this seems the geometry with the lower steric hindrance between Ar and acac ligands. Formation of **3** requires an intermolecular transmetallation reaction that could occur through a dinuclear complex such as **B**. The replacement of the acac ligand could be favored by the strong *T*(Ar/*C*-acac) and the trans geometry of **A**. Complexes with bridging aryl ligands have been postulated as intermediates in the formation of diaryl from monoaryl complexes.[28] A few palladium complexes containing bridging aryl ligands have been isolated.[29] Cleavage of the weakest Ar–Pd bond, i.e. that trans to the acac ligand, and coordination of the replaced acac ligand would give **3** and a highly reactive species *trans*-[Pd(*C*-acac)$_2$(CNXy)$_2$] (because of the strong *T*(*C*-acac/*C*-acac)) which would insert XyNC to give, among other products, complex "Pd(acac)$_2$(CNXy)$_5$" (**X**). We have studied the reaction between [Pd(acac)$_2$] and XyNC under different reaction conditions but we have not yet isolated any pure compound from the mixtures of complexes that we obtain. We have reported that isocyanides insert into the C–Pd bond of acetonyl complexes giving ß-ketoenamino derivatives.[30] A similar insertion followed by tautomerization could have occurred in the synthesis of **X**.

To support this proposal we have attempted the synthesis of **A** by two other routes. Thus, 1) we have prepared *trans*-[Pd(κ^1-Ar)Cl(CNXy)$_2$] (**4**), from *trans*-Me$_4$N[Pd(κ^1-Ar)Cl(μ-Cl)]$_2$ (**5**) and excess of XyNC, and reacted it with one equiv of Tl(acac) and 2) we have reacted *cis*-[Pd(κ^1-Ar)(*C*-acac)(phen)] (**6**) with four equiv of XyNC. In agreement with the above proposed mechanism, both reactions led to the isolation of complex **3** instead of **A**. The low stability of this intermediate contrasts with that of the related complexes **4** and **6** in which, for all trans pairs of groups, $T < T$(Ar/*C*-acac).



Scheme 2

The reaction of palladium complex 5 with two equiv of $Hg(OAc)_2$ does not proceed via transmetallation or formation of a Pd–Hg compound but simply with a ligand substitution of chloro by acetato to give the dinuclear complex $[Pd(\kappa^2\text{-}Ar)(\mu\text{-}O_2CMe)]_2$ (11; Scheme 3).



Scheme 3

Crystal Structures. Crystals apparently suitable for an X-ray crystallographic study were obtained for **10**. However, although a complete crystallographic analysis was not possible because the rings with the nitro and methoxy groups were badly disordered, the position of the ligands was established with certainty to be that indicated in Scheme 3.

Complete crystallographic analysis was carried out for complexes **2a** (Figure 1), **2b** (Figure 2), **3** (Figure 3), **5** (Figure 4), and **11** (Figure 5). Solvent contents are given in Tables 1 and 2. All structures reveal a metal in a distorted square planar coordination. In the dinuclear complex **5**, the coordination planes are almost coplanar (angle between coordination planes: 1.8, 2.9 (**5**)) as has been found and theoretically predicted for most dinuclear complexes with two single-atom bridges.[31]

Bond distances at palladium in complexes are consistent with the trans influence scale. Thus, we observe (1) similar Pd–O(1) distances trans to XyNC and ^{t}BuNC [**2a** 2.0130(14), **2b** 2.0098(16) Å], (2) Pd–O bond distances *trans* to Ar [**2a** 2.0456(15), **2b** 2.0519(16) Å] longer than those trans to isocyanide [**2a** 2.0130(14), **2b** 2.0098(16) Å], (3) The Pd–O bonds trans to aryl (**11** 2.086(2) Å) longer than those trans to oxygen atoms (**11** 2.005(2)–2.019(2) Å), (4) Pd–CNXy bond distances trans to isocyanide [**3** 1.965(3) and 1.966(3) Å] longer than those trans to O [**2a** 1.925(2) Å], and (5) Pd–Ar bond distances trans to oxygen [**2a** 2.0002(2), **2b** 2.002(2) Å] shorter than trans to Ar [**3** 2.069(3), 2.071(3) Å]. In addition, the Pd–Cl bond distances in **5** follow the expected order: Pd–Cl bridging trans to Ar (2.4323(8), 2.4230(8), 2.4262(8), 2.4089(9) Å) > bridging trans to Cl (2.3199(8), 2.3464(8), 2.3222(8), 2.3395(8) Å) > terminal trans to Cl (2.2931(8), 2.2943(8), 2.3113(8), 2.3055(8) Å).

In **5**, two crystallographically independent, but very similar, units are present. One of them (**5a**) is represented in Figure 4. The anion dimer is not far from approximate inversion symmetry with four chloro ligands, two bridging and two terminal, and two mutually trans κ^1-Ar groups.

The crystal structure of **11** consists of dinuclear molecules that adopt an *anti* geometry, with the acetate bridges conferring an open-book shape upon the molecule. The planes of coordination around the Pd centers are stacked with a relatively short Pd–Pd distance of 2.8227(4) Å which is shorter than the expected for Pd–Pd covalent bond (3.00 Å) and lies in the range found in some other $[Pd]_2(\mu\text{-OAc})_2$ complexes (2.821–2.936 Å).[32]

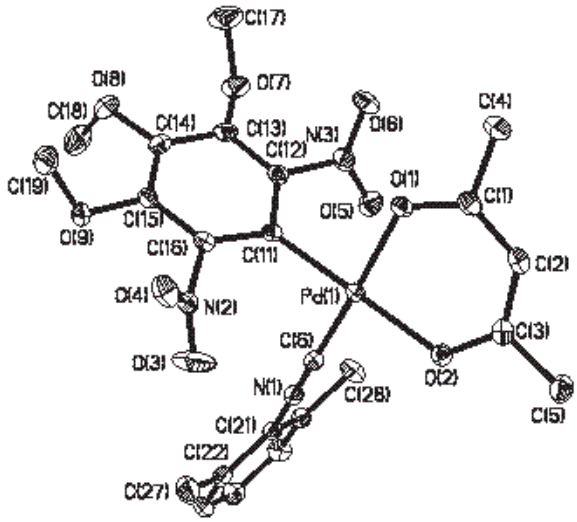


Figure 1. Ellipsoid representation of complex **2a** (50% probability). Selected bond lengths (Å) and angles (°): Pd(1)–C(6) = 1.925(2), Pd(1)–C(11) = 2.000(2), Pd(1)–O(1) = 2.0130(14), Pd(1)–O(2) = 2.0456(15), O(1)–C(1) = 1.280(3), O(2)–C(3) = 1.275(3), O(3)–N(2) = 1.208(3), O(4)–N(2) = 1.218(2), O(5)–N(3) = 1.227(2), O(6)–N(3) = 1.223(3), N(1)–C(6) = 1.145(3), N(1)–C(21) = 1.405(3), N(2)–C(16) = 1.475(3), N(3)–C(12) = 1.477(3), C(6)–Pd(1)–C(11) = 88.56(8), C(11)–Pd(1)–O(1) = 87.58(7), C(6)–Pd(1)–O(2) = 91.23(7), O(1)–Pd(1)–O(2) = 92.67(6).

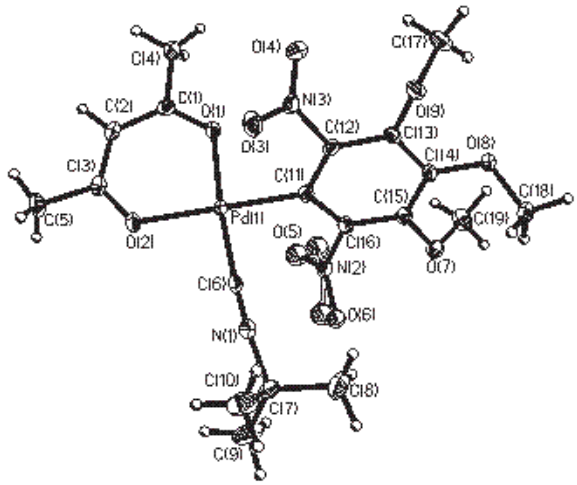


Figure 2. Ellipsoid representation of complex **2b** (50% probability). Selected bond lengths (Å) and angles (°): Pd(1)–C(6) = 1.927(2), Pd(1)–C(11) = 2.002(2), Pd(1)–O(1) = 2.0098(16), Pd(1)–O(2) = 2.0519(16), N(1)–C(6) = 1.143(3), N(1)–C(7) = 1.474(3), O(1)–C(1) = 1.280(3), O(2)–C(3) = 1.271(3), N(3)–O(4) = 1.222(3), N(3)–O(3) = 1.229(3), N(3)–C(12) = 1.477(3), N(2)–O(6') 1.126(6), N(2)–O(5) = 1.185(4), N(2)–O(6) = 1.279(4), N(2)–O(5') = 1.301(6), N(2)–C(16) = 1.482(3), O(7)–C(15) = 1.373(2), O(7)–C(19) = 1.443(3), O(8)–C(14) = 1.363(3), O(8)–C(18) = 1.444(3), O(9)–C(13) = 1.360(3), O(9)–C(17) = 1.449(3), C(6)–Pd(1)–C(11) = 86.68(9), C(11)–Pd(1)–O(1) = 88.02(8), C(6)–Pd(1)–O(2) = 92.92(8), O(1)–Pd(1)–O(2) = 92.36(6).

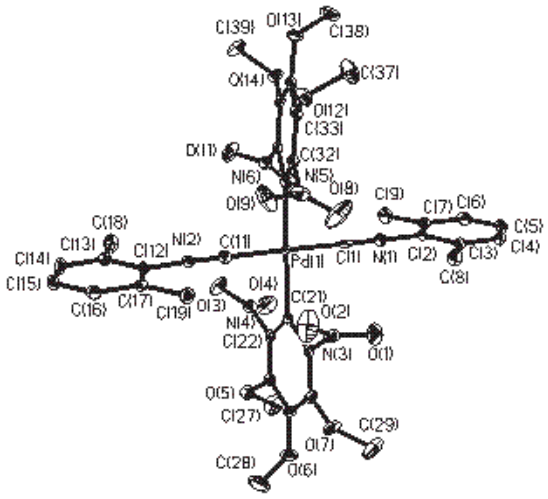


Figure 3. Ellipsoid representation of complex **3** (50% probability). Selected bond lengths (Å) and angles (°): Pd(1)–C(11) 1.965(3), Pd(1)–C(1) 1.966(3), Pd(1)–C(21) 2.069(3), Pd(1)–C(31) 2.071(3), O(1)–N(3) 1.219(3), O(2)–N(3) 1.207(3), O(3)–N(4) 1.220(3), O(4)–N(4) 1.224(3), O(5)–C(23) 1.367(3), O(5)–C(27) 1.440(4), O(6)–C(24) 1.370(3), O(6)–C(28) 1.432(4), O(7)–C(25) 1.369(3), O(7)–C(29) 1.445(4), O(8)–N(5) 1.215(3), O(9)–N(5) 1.215(3), O(10)–N(6) 1.218(3), O(11)–N(6) 1.219(3), O(12)–C(33) 1.371(3), O(12)–C(37) 1.433(4), O(13)–C(34) 1.368(3), O(13)–C(38) 1.444(3), O(14)–C(35) 1.371(3), O(14)–C(39) 1.446(3), N(1)–C(1) 1.149(3), N(1)–C(2) 1.405(3), N(2)–C(11) 1.151(3), N(2)–C(12) 1.404(3), N(3)–C(26) 1.479(3), N(4)–C(22) 1.474(3), N(5)–C(32) 1.472(3), N(6)–C(36) 1.477(3), C(11)–Pd(1)–C(21) 89.37(10), C(1)–Pd(1)–C(21) 89.97(10), C(11)–Pd(1)–C(31) 90.89(10), C(1)–Pd(1)–C(31) 89.73(10).

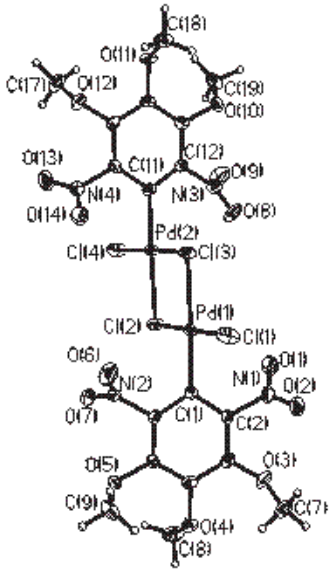


Figure 4. Ellipsoid representation of one of the two independent anionic complexes $[Pd_2(\kappa^1\text{–Ar})_2Cl_2(\mu\text{–}Cl)_2]^{2-}$ (**5a**) (50% probability). Selected bond lengths (Å) and angles (°) for the two independent complexes **5a** and **5b**. **5a**: Pd(1)–C(1) 1.979(3), Pd(1)–Cl(1) 2.2931(8), Pd(1)–Cl(2) 2.3199(8), Pd(1)–Cl(3) 2.4323(8), Pd(2)–C(11) 1.981(3), Pd(2)–Cl(4) 2.2943(8), Pd(2)–Cl(3) 2.3464(8), Pd(2)–Cl(2) 2.4230(8), C(1)–Pd(1)–Cl(1) 89.58(8), C(1)–Pd(1)–Cl(2) 90.94(8), Cl(1)–Pd(1)–Cl(3) 92.97(3), Cl(2)–

Pd(1)–Cl(3) 86.50(3), C(11)–Pd(2)–Cl(4) 89.28(9), C(11)–Pd(2)–Cl(3) 92.53(9), Cl(4)–Pd(2)–Cl(2) 92.09(3), Cl(3)–Pd(2)–Cl(2) 86.13(3). **5b**: Pd(1)–C(1) 1.970(3), Pd(1)–Cl(1) 2.3113(8), Pd(1)–Cl(2) 2.3222(8), Pd(1)–Cl(3) 2.4262(8), Pd(2)–C(11) 1.972(3), Pd(2)–Cl(4) 2.3055(8), Pd(2)–Cl(3) 2.3395(8), Pd(2)–Cl(2) 2.4089(9), C(1)–Pd(1)–Cl(1) 91.09(9), C(1)–Pd(1)–Cl(2) 87.99(9), Cl(1)–Pd(1)–Cl(3) 93.50(3), Cl(2)–Pd(1)–Cl(3) 87.45(3), C(11)–Pd(2)–Cl(4) 90.59(9), C(11)–Pd(2)–Cl(3) 89.75(9), Cl(4)–Pd(2)–Cl(2) 92.18(3), Cl(3)–Pd(2)–Cl(2) 87.46(3).

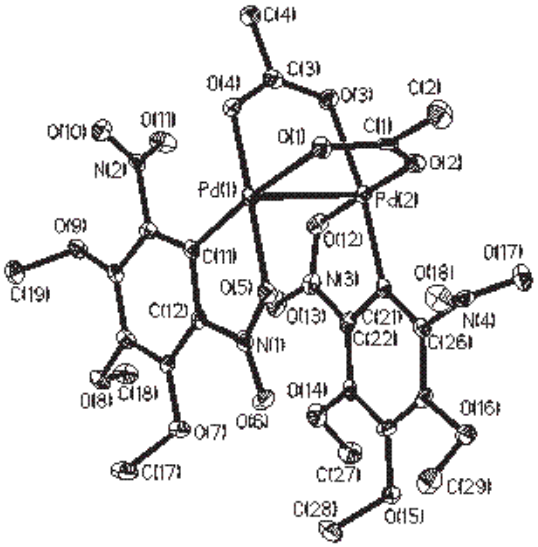


Figure 5. Ellipsoid representation of complex **11** (50% probability). Selected bond lengths (Å) and angles (°): Pd(1)–C(11) 1.955(3), Pd(1)–O(4) 2.005(2), Pd(1)–O(5) 2.019(2), Pd(1)–O(1) 2.086(2), Pd(1)–Pd(2) 2.8227(4), Pd(2)–C(21) 1.958(4), Pd(2)–O(12) 2.006(2), Pd(2)–O(2) 2.008(2), Pd(2)–O(3) 2.086(2), N(1)–O(6) 1.206(4), N(1)–O(5) 1.294(4), N(1)–C(12) 1.432(4), N(2)–O(10) 1.222(4), N(2)–O(11) 1.226(4), N(2)–C(16) 1.471(4), N(3)–O(13) 1.214(4), N(3)–O(12) 1.284(4), N(3)–C(22) 1.432(4), N(4)–O(18) 1.222(3), N(4)–O(17) 1.221(4), N(4)–C(26) 1.485(4), O(1)–C(1) 1.253(4), O(2)–C(1) 1.274(4), O(3)–C(3) 1.258(4), O(4)–C(3) 1.272(4), C(11)–Pd(1)–O(4) 97.03(12), C(11)–Pd(1)–O(5) 81.29(12), O(4)–Pd(1)–O(1) 89.08(10), O(5)–Pd(1)–O(1) 92.60(9), C(21)–Pd(2)–O(12) 81.28(12), C(21)–Pd(2)–O(2) 97.64(12), O(12)–Pd(2)–O(3) 91.37(10), O(2)–Pd(2)–O(3) 89.77(10).

Spectroscopic Properties. The NMR spectra of all complexes are in agreement with the proposed structures. Thus, at room temperature, the ^{1}H NMR spectra of complexes show the expected two (2:1) or three (1:1:1) methyl singlets per κ^1-Ar or κ^2-Ar groups, respectively. The IR spectrum of the chloro complex **4** shows a band assignable to ν(PdCl) at 314 cm^{-1}.

CONCLUSIONS

We report a rare example of disproportionation when [Pd(κ^2-Ar)(O,O-acac)] is reacted with four equivalents of XyNC, yielding *trans*-[Pd(κ^1-Ar)$_2$(CNXy)$_2$]. We attribute this to a new transphobia effect associated with formation of the intermediate [Pd(Ar)(*C*-acac)(XyNC)$_2$], the unstability of which arises from the strong *T*(aryl/*C*-acac). We have attempted to prepare this

intermediate by two other routes, confirming its instability and observing instead the formation of *trans*-[Pd(κ^1-Ar)$_2$(CNXy)$_2$]. This complex is the first [Pd](Ar)$_2$ with Ar = $C_6(NO_2)_2$-2,6-$(OMe)_3$; we had previously attempted to prepare, unsuccessfully, by a transmetallation using [$HgAr_2$].

EXPERIMENTAL SECTION

General Procedures

The reactions were carried out without precautions to exclude light or atmospheric oxygen or moisture. The IR (Nujol/polyethylene), C, H and N analyses and melting point determinations were carried out as described elsewhere.[33] NMR spectra were recorded in a Varian Unity 300, Bruker AC 200 or Avance 300 or 400 spectrometers at room temperature. Chemical shifts were referred to TMS (^{1}H, ^{13}C{^{1}H}) or H_3PO_4 (^{31}P). The NMR probe temperature was calibrated using ethylene glycol ^{1}H NMR standard methods. The ligands κ^1-*C*-$C_6(NO_2)_2$-2,6-$(OMe)_3$ and κ^2-*C,O*-$C_6(NO_2)_2$-2,6-$(OMe)_3$ are represented by κ^1-Ar and κ^2-Ar. When the coordination mode of this aryl ligand is not known, it is formulated simply as Ar. Complexes [Pd(κ^2-Ar)(O,O-acac)] (**1**), $(NMe_4)_2$[Pd(κ^1-Ar)Cl(μ-Cl)]$_2$ (**5**),[2] and [Pd(κ^1-Ar)(*C*-acac)(phen)] (**6**) were prepared as reported previously. Single crystals of **5**•0.5Me_2CO were obtained by slow diffusion of Et_2O into a Me_2CO solution of **5**.

Synthesis

Synthesis of [Pd(κ^1-Ar)(acac)(CNXy)] (**2a**)**.** XyNC (7.5 mg, 0.06 mmol) was added to a solution of [Pd(κ^2-Ar)(O,O-acac)] (26.5 mg, 0.06 mmol) (**1**) in Me_2CO (6 mL). After 45 min, the resulting solution was concentrated (1 mL) and addition of *n*-pentane (4 mL) gave a suspension that was filtered off and air-dried to give complex **2a** as a pale yellow solid. Yield: 29.1 mg, 86%. Mp: 162.5–163.7 °C. IR (cm^{-1}): ν(CN) 2202; ν(CO) 1566. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (t, 1 H, *p*-H, $^2J_{HH}$ = 7.62 Hz), 7.09 (d, 2 H, *m*-H, $^2J_{HH}$ = 7.53 Hz), 5.40 (s, 1 H, CH), 3.99 (s, 6 H, OMe), 3.90 (s, 3 H, OMe), 2.38 (s, 6 H, Me Xy), 1.99 (s, 3 H, Me acac), 1.95 (s, 3 H, Me acac). Anal. Calcd for $C_{23}H_{25}N_3O_9Pd$•$C_2H_5O_{0.5}$: C, 47.44; H, 4.78; N, 6.64. Found: C, 47.51; H, 4.78; N, 6.64**.** Single crystals of **2a**•0.5Et_2O were obtained by slow diffusion of *n*-pentane into an Me_2CO/Et_2O solution of **2a**.

Synthesis of [Pd(κ^1-Ar)(acac)(CN^{t}Bu)] (**2b**). ^{t}BuNC (8.9 μL, 0.08 mmol) was added to a solution of **1** (35.6 mg, 0.08 mmol) in Me_2CO (5 mL). After 50 min, the resulting solution was concentrated (1 mL) and addition of *n*-pentane (4 mL) gave a suspension that was filtered off and air-dried to give complex **2b** as a pale yellow solid Yield: 29.7 mg, 71%. Mp: 153–154 °C. IR (cm^{-1}): ν(CN) 2218; ν(CO) 1580. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 5.35 (s, 1 H, CH), 3.99 (s, 6 H, OMe), 3.90 (s, 3 H, OMe), 1.97 (s, 3 H, Me), 1.91 (s, 3 H, Me), 149 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{19}H_{25}N_3O_9Pd$: C, 41.80; H, 4.58; N, 7.70. Found: C, 41.43; H, 4.80; N, 7.67. Single crystals of **2b** were obtained by slow diffusion of *n*-pentane into a Et_2O solution of **2b**.

Synthesis of trans-[Pd(κ^1-Ar)$_2$(CNXy)$_2$] (**3**). XyNC (39.5 mg, 0.30 mmol) was added to a solution of **1** (34.8 mg, 0.075 mmol) in Me_2CO (6 mL). After 1 h stirring the solution was concentrated (3 mL) and the resulting solid was filtered off and washed with Et_2O to give **3** as a colorless solid. Concentration of the filtrate afforded a second crop of **3**. Yield: 27.2 mg, 82%. Dec pt: 260–261 °C. IR (cm^{-1}): ν(CN) 2204. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 (t, 2 H, *p*-H, $^2J_{HH}$ = 7.5 Hz), 7.05 (d, 4 H, *m*-H, $^2J_{HH}$ = 7.5 Hz), 3.96 (s, 12 H, OMe), 3.89 (s, 6 H, OMe), 2.30 (s, 12 H, Me). Anal. Calcd for $C_{36}H_{36}N_6O_{14}Pd$: C, 48.96; H, 4.11; N, 9.52. Found: C, 48.61; H, 4.15; N, 9.56. Single crystals of **3** were obtained by slow diffusion of *n*-pentane into a $CHCl_3$ solution of **3**.

Synthesis of trans-[Pd(κ^1-Ar)Cl(CNXy)$_2$] (**4**). XyNC (98.5 mg, 0.75 mmol) was added to a suspension of **5** (191 mg, 0.19 mmol) in CH_2Cl_2 (7 mL). After 1 h stirring, the reaction mixture was filtered through anhydrous $MgSO_4$. The filtrate was concentrated (2 mL) and *n*-pentane was added (1 ml). The suspension was filtered and the filtrate was concentrated (*ca.* 2 mL) to give a solid that was filtered off, washed with *n*-pentane and air-dried, to give **11**, as a colorless solid. Yield: 137.9 mg, 55%. Mp: 150–151 °C. IR (cm^{-1}): ν(CN) 2203; ν(PdCl) 314. ^{1}H RMN (400 MHz, $CDCl_3$): δ 7.25 (t, 2 H, *p*-H, $^2J_{HH}$ = 7.7 Hz), 7.10 (d, 4 H, *m*-H, $^2J_{HH}$ = 7.6 Hz), 3.99 (s, 6 H, OMe), 3.91 (s, 3 H, OMe), 2.37 (s, 12 H, Me). Anal. Calcd for $C_{27}H_{27}N_4ClO_7Pd$: C, 48.99; H, 4.11; N, 8.47. Found: C, 48.97; H, 4.31; N, 8.51. Single crystals of **4** were obtained by slow diffusion of *n*-pentane into a $CDCl_3$ solution of **4**.

Synthesis of trans-[Pd(κ^2-Ar)(μ-OAc)]$_2$ (**11**). $Hg(OAc)_2$ (63.3 mg, 0.20 mmol) was added to a suspension of $(NMe_4)_2[Pd(\kappa^1\text{-Ar})Cl(\mu\text{-Cl})]_2$ (**5**) (101.1 mg, 0.10 mmol) in Me_2CO (6 mL). The resulting suspension was stirred for 30 min and then concentrated (2 mL) and filtered. The solid was treated with CH_2Cl_2 (5 mL), the mixture filtered through Celite, Et_2O (10 ml) was added to the filtrate and the suspension was filtered to give **11** as a red solid. Yield: 28 mg, 34%. Mp: 210-211 °C. IR (cm^{-1}): ν (CO) 1548, 1530. ^1H NMR (400 MHz, $CDCl_3$): δ 4.13 (s, 6 H, *p*-OMe), 3.96, 3.89 (two s, 6 H, *m*-OMe), 2.08 (s, 6 H, Me). Anal. Calcd for $C_{44}H_{48}N_8O_{36}Pd_2$: C, 31.24; H, 2.84; N, 6.63. Found: C, 31.26; H, 2.86; N, 6.63. Single crystals of **11** were obtained by slow diffusion of *n*-hexane vapor into a CH_2Cl_2 solution of **11**.

X-Ray Structure Determinations.

For clarity, solvent contents are omitted here, but are defined in Tables 1 and 2. Compounds **2a**, **2b**, **3**, **5** and **11** were measured on a Bruker Smart APEX machine diffractometer. Data were collected using monochromated Mo-Kα radiation in w scan mode. Absorption corrections were based on the multi-scan method (program SADABS). The structures of **2b**, **3**, **5** and **11** were solved by direct methods and **2a** by the heavy atom method. All were refined anisotropically on F^2. Restraints to local aromatic ring symmetry or light atom displacement factor components were applied in some cases. The ordered methyl groups were refined using a rigid groups, and the other hydrogens were refined using a riding mode. *Special features*. **2a**: the ether of solvation is disordered over an inversion center. **2b**: One of the nitro group is disordered over two positions, ca 60:40%. **5**: NMe_4 cations are disordered over two positions.

Table 1. Crystallographic Data for Complexes 2a, 2b, 3, 5 and 11.

	2a•0.5Et_2O	**2b**	**3**	**5**•0.5Me_2CO	**11**
formula	$C_{25}H_{30}N_3O_{9.5}Pd$	$C_{19}H_{25}N_3O_9Pd$	$C_{30}H_{30}N_6O_{14}Pd$	$C_{27.5}H_{45}Cl_4N_6O_{14.5}Pd$	$C_{22}H_{24}N_4O_{18}Pd_2$
M_r	630.92	545.82	883.11	1046.30	845.25
cryst habit	colorless, block	colorless, prism	colorless, needl	orange, lath	red, needle
cryst size (mm)	0.20 × 0.16 × 0.08	0.24 × 0.12 × 0	0.13 × 0.09 × 0	0.17 × 0.12 × 0.07	0.30 × 0.05 × 0.03
cryst syst	triclinic	monoclinic	monoclinic	triclinic	triclinic
space group	$P\bar{1}$	$P2_1/n$	$P2_1/c$	$P\bar{1}$	$P\bar{1}$
cell constants					
a, Å	10.0026(5)	16.322(2)	21.1560(9)	14.6377(6)	10.2492(5)
b, Å	10.5211(5)	8.2938(11)	11.2128(5)	16.8923(7)	11.6858(6)
c, Å	14.3597(7)	18.474(2)	16.2406(7)	18.0811(7)	14.5201(8)
α, deg	107.407(2)	90	90	73.573(2)	66.848(2)
β, deg	103.434(2	112.011(2)	92.797(2)	88.311(2)	72.464(2)
γ, deg	91.700(2)	90	90	71.063(2)	64.161(2)
V (Å^3)	1394.50(12)	2318.5(5)	3848.0(3)	4046.6(3)	1421.30(13)
Z	2	4	4	4	2
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073	0.71073
ρ (calc) (Mg m^{-}	1.503	1.56	1.52	1.72	1.98
μ mm^{-1}	0.72	0.853	0.558	1.222	1.358
F(000)	646	1112	1808	2112	840
T (K)	100(2)	100(2)	100(2)	100(2)	100(2)
θ_{max} (deg)	56	56	56	56	56
no. of reflns me	16229	24490	41574	47676	15553
no. of indep refl	6240	5320	7865	18222	5744
transmissions	0.945, 0.869	0.935, 0.821	0.962, 0.931	0.919, 0.819	0.960, 0.686
R_{int}	0.0232	0.0406	0.0511	0.0299	0.0355
no. rest/params	40 / 377	6 / 296	0 / 524	26 / 1007	0 / 423
$R_w(F^2$, all reflns)	0.0775	0.0726	0.0844	0.1006	0.0756
R(F, > 4σ(F))	0.0296	0.0306	0.0368	0.0424	0.0362
S	1.05	1.05	1.07	1.02	1.09
Largest diff peak (e Å^{-3})	0.97	0.82	0.64	1.22	0.616

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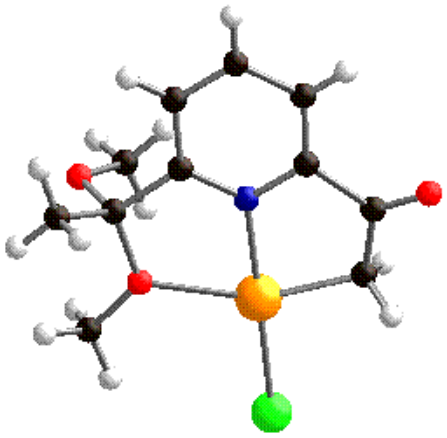
CHAPTER II

Organometallic Complexes of Pd(II) Derived from 2,6-Diacetylpyridine and 2,6-Diacetylpyridine Dimethylketal



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SUMMARY CHAPTER II

This Chapter shows the results corresponding to the synthesis and reactivity of Pd(II) complexes derived from 2,6-diacetylpyridine. More specifically, **Section II.1** is about the attempts to metallate 2,6-diacetylpyridine and the synthesis of the first ketonyl pincer-type Pd(II) complexes. This first section begins with the description of the failed reactions regarding the palladation of the ligand. We carried out several reactions with the most common palladium complexes used in metalation reactions and varying experimental conditions, but we always obtained a mixture of compounds or found no reaction. Finally, we were successful on the synthesis of a pincer Pd(II) complex when the reaction was performed in refluxing methanol using palladium dichloride as the starting material. In this way, we isolated a complex with the pincer ligand resulting from the deprotonation of the acetyl group of the dimethylmonoketal of 2,6-diacetylpyridine. Noteworthy, the ketalization of one of the acetyl groups allowed the metallation of the other one.

Starting from this *C,N,O* pincer complex, we carried out reactions with isocyanides, phosphines, and diimines. Reactions with the latter, the pincer ligand changed chelate or monodentate. With isocyanides, the products were the result of substitution and insertion reactions of the ligand into the Pd–CH_2 bond. The products of this insertion tautomerized from *β*-ketoimine to *β*-ketoenamine, affording complexes with new pincer, chelate or monodentate ligands. This work was highlighted in the 2011 Annual Reports on the Progress of Chemistry regarding Organometallic Chemistry.

In **Section II.2** we give account of our attempts to prepare cationic complexes. Thus, the reaction between the chloro pincer Pd(II) complex obtained in the metalation reaction was reacted with silver perchlorate affording the perchlorato derivative that was used as the starting material to prepare cationic Pd(II) complexes with P-, C- and N-donor ligands. Although isocyanides gave insertion reactions towards neutral complexes, we could not detect any of these reactions working with the corresponding cationic compounds.

Interestingly, most of the cationic complexes prepared suffer a hydrolysis process of the ligand, affording in some cases stable pincer-type complexes where the ligand results from deprotonation of the acetyl group in 2,6-diacetylpyridine, which were those we unsuccessfully attempted to prepare by metalation. These are the first complexes of any metal in which the 2,6-diacetylpyridine have been metallated.

Section II.1: Organometallic Complexes of Pd(II) Derived from 2,6-Diacetylpyridine Dimethylketal

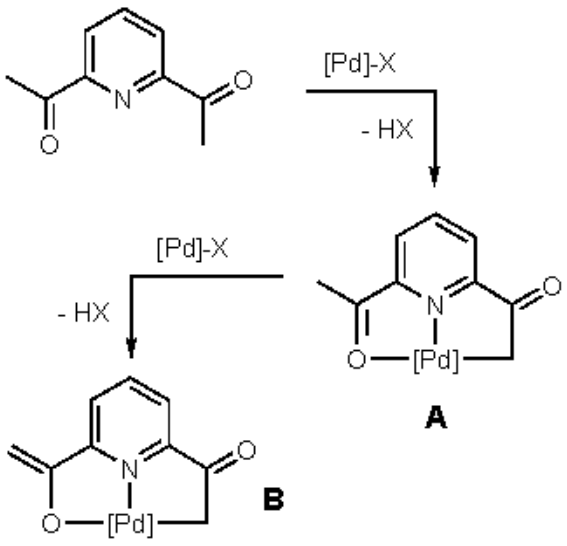
ABSTRACT

$PdCl_2$ reacts with 2,6-diacetylpyridine (dap) (1 : 1) in refluxing MeOH to give the pincer complex [Pd(O^1,N^1,C^1-L)Cl] (**1**) and $(QH)_2[\{PdCl_2(\mu\text{-}Cl)\}]_2$ (**2**), where L is the monoanionic ligand resulting from the deprotonation of the acetyl methyl group of the monoketal of dap and QH is $C_5H_3NH\{C(OMe)_2Me\}_2$-2,6, the diketal of $Hdap^+$. Reaction of **2** with NEt_3 (1:2) in MeOH affords the diketal of dap, Q = $C_5H_3N\{C(OMe)_2Me\}_2$-2,6 (**3**). Complex **1** reacts with two equiv of RNC at 0 °C to give *trans*-[Pd(C^1-L)Cl(CNR)$_2$] (R = Xy = 2,6-dimethylphenyl (**4a**), ^{t}Bu (**4b**)) but at room temperature affords [Pd(O^2,C^2-L_R)Cl(CNR)] (R = Xy (**5a**), ^{t}Bu (**5b**)). The ligand L_R results from the insertion of one isocyanide into the Pd–C bond plus a tautomerization process from *β*-ketoimine to *β*-ketoenamine, and coordinates in **5** through the carbonyl oxygen atom (O^2) and the inserted isocyanide carbon atom (C^2). The reaction of **1** with one equiv of RNC at 0 °C leads a mixture of [Pd(N^1,C^1-L)Cl(CNR)] (R = Xy (**6a**), ^{t}Bu (**6b**); 85–90%), **1** and **4**, but at room temperature gives the pincer complex [Pd(O^1,N^1,C^2-L_R)Cl] (R = Xy (7**a**), ^{t}Bu (7**b**)), resulting from the same insertion/tautomerization processes that lead to **5**. Complex 7 reacts at 0 °C (1) with 2 equiv of RNC to give *trans*-[Pd(C^2-L_R)Cl(CNXy)$_2$] (R = Xy (**8a**), ^{t}Bu (**8b**)) or (2) with one equiv of ^{t}BuNC to afford **5b**. The reaction of **1** (1) with [Tl(acac)] gives [Pd(N^1,C^1-L)(acac)] (**9**); (2) with chelating ligands L^L affords [Pd(C^1-L)Cl(N^N)] (N^N = 2,2'-bipyridine = bpy (**10**), 4,4'-di-tert-butyl-2,2'-bipyridine = dbbpy (**11**)); (3) with one equiv of PPh_3 gives, in the same way as with isocyanides, an equilibrium mixture of [Pd(N^1,C^1-L)Cl(PPh_3)] (**12**), **1** and *trans*-[Pd(C^1-L)Cl(PPh_3)$_2$] (**13**), which is the only product when two equiv of PPh_3 is added to the reaction mixture; (4) with excess PPh_3 affords the monoketal of dap, $C_5H_3N\{C(O)Me\text{-}2\}\{C(OMe)_2Me\text{-}6\}$ (**14**) and [Pd(PPh_3)$_4$]. The crystal structures of complexes **1**, **2**, **5b**, **6a** and 7**a** have been determined.

INTRODUCTION

We are currently involved in the synthesis of ketonyl metal complexes $[M]CH_2C(O)R$ (M = Pd, Pt, Au, Hg, Tl) because of the great stability that this alkyl ligand confers to their complexes, their interesting reactivity[1-4] and their roles as intermediates in organic synthesis.[2, 5] Recently, we have reported the synthesis and reactivity of $[Pd\{CH_2C(O)Me\}Cl]_n$, $[Pt\{CH_2C(O)Me\}Cl_2(\eta^2\text{-}C_2H_4)]$ and $[Pt_2\{CH_2C(O)Me\}_6(\mu\text{-}Cl)_3]^-$, studies that have allowed us to prepare unprecedented types of metal complexes.[3, 6]

We report here our attempts to prepare ketonyl palladium complexes derived from 2,6-diacetylpyridine (dap). Our interest centered on the possibility that this ligand would allow us to prepare complexes with mono- and dianionic ligands resulting from deprotonation reactions like those shown in Scheme 1. The reactivity of complexes of type **A** is expected to be similar to that of other palladium ketonyl complexes, although it could be modified by the coordination of the pyridine moiety. Cyclometalation of 2-acetylpyridine has been reported only for Rh(III) and Au(III),[7] and one Pd(II) complex has been prepared (but not isolated) by using a silyl enol ether of 2-acetylpyridine,[8] while [Te(O^1,N^1,C^1-L)Cl_3], obtained by reacting dap with $TeCl_4$, is the only reported complex with the ligand present in **A**.[9] However, the reactivity of these species has not been studied. Formation of mixed enolato/ketonyl *O,N,C*-complexes (**B**) is expected in those containing the dianionic ligand because the strong C/C[10] transphobia[11] would destabilize the *C,N,C* pincer isomer. This second functionality would confer on these complexes the expected reactivity of enolato metal complexes (aldol reactions, for example), but, more interestingly, the dual and unprecedented nature of these complexes could lead to novel types of reactivity.



Scheme 1

The study of the synthesis and reactivity of dap metal complexes has additional relevance because complexes of Fe(II) and Co(II) with bis(imino) derivatives of dap (PDI) are highly active catalysts for polymerization and oligomerization of olefins.[12] It has been reported that some of these PDI ligands prepared with two different amines have important effects on the

catalytic perfomance of their complexes.[13, 14] One additional reason for preparing complexes **A** would be their use as catalysts or for the synthesis of complexes with nonsymmetrical PDI-related monoanionic ligands.

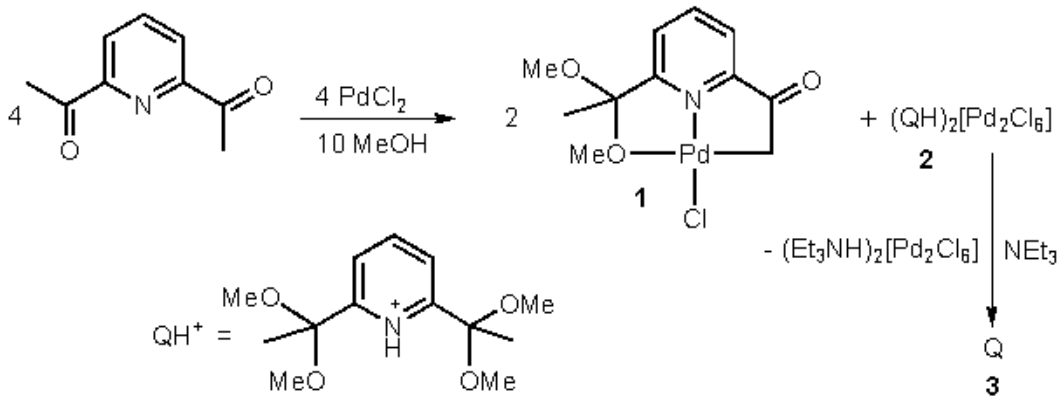
Pincer complexes have attracted great interest because of their important applications in organic synthesis, homogeneous catalysis, bond activation, and design of new materials.[15] In spite of the great number of reported Pd(II) pincer complexes, those of type **A** (C,N,O-pincer) are represented only by one family derived from 2-alkyl-substituted 8-quinolinols[16] or C_6H_4[NHC(Me)CHC(Me)O]-2 derivatives[4] and one complex derived from 8-alkylquinoline-2-carboxylic acid.[17]

Attempts to prepare complexes of type **A** were initially unsuccesful; instead we isolated a family of [*C,N,O*]-pincer ketonyl complexes derived from 2,6-diacetylpyridine dimethylketal when methanol was used as solvent. However, during the study of the reactivity of these complexes we discovered that some of their derivatives decompose to give the desired complexes, which provided us the necessary information for their rational synthesis. In this paper we report the synthesis of these dimethylketal derivatives and their reactivity toward isocyanides. There is only one related precedent for these complexes, the 2-lithium phenyl dimethylketal, which is described as a nonisolated intermediate obtained from the dimethylketal of 2-bromoacetophenone via metal–halogen exchange.[18]

RESULTS AND DISCUSSION

Reactions of 2,6-Diacetylpyridine with Palladium Compounds. Numerous attempts to prepare ketonyl palladium complexes derived from 2,6-diacetylpyridine (dap) failed. Thus, by reacting dap with the usual starting palladium(II) compounds ([$Pd(OAc)_2$], $PdCl_2$, [$PdCl_2(NCMe)_2$], $(NMe_4)_2[Pd_2Cl_6]$), using various solvents ($Me_2C(O)$, CH_2Cl_2, THF, MeCN) and reaction temperatures, in the absence of a base or adding Ag_2O, $Tl_2(CO_3)$ or K^{t}BuO, led to palladium metal or complex mixtures. We interpreted these negative results in terms of the low coordinative capacity of dap, in turn attributable to the electron-withdrawing character of both ortho acetyl substituents. It is well-known that coordination to the metal of a ligand assists the required C–H activation that affords a metalated complex of such a ligand. Indeed, a limited number of metal complexes with the dap ligand have been isolated[13, 22, 23] and the only reported crystal structure of a dap complex, $[Ag(O,N,O\text{-dap})_2]^{2+}$, shows that the Ag–N bond distances are much longer (2.316(6) Å) than those in $[Ag(py)_2]^+$ (2.126(4) and 2.133(4) Å).[23]

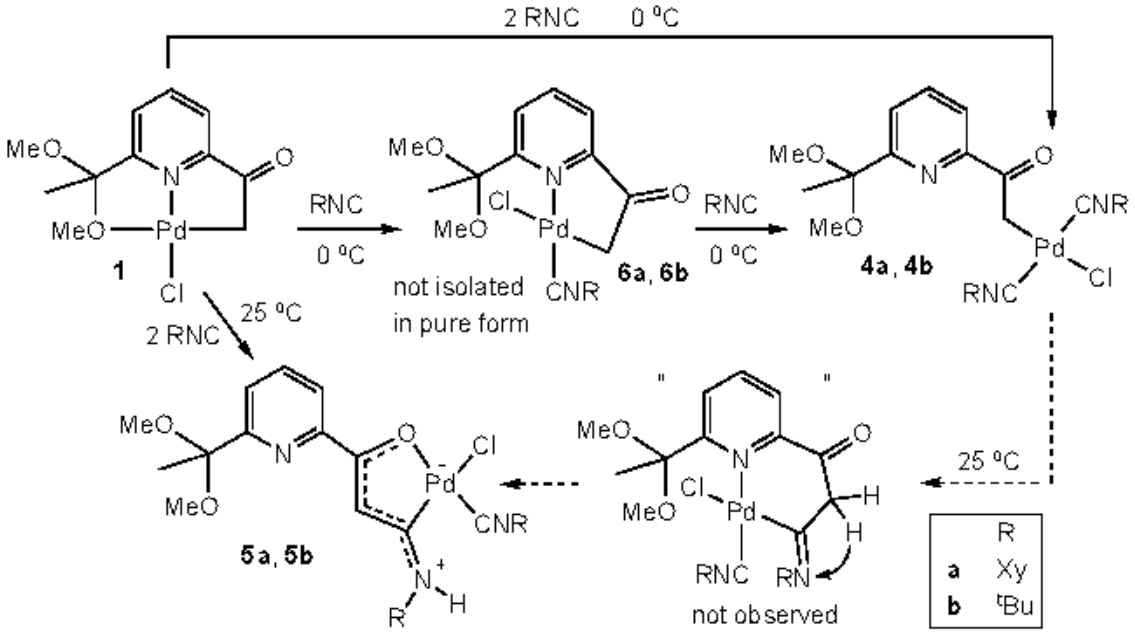
Finally, the only successful result was obtained by reacting dap and $PdCl_2$ (1 : 1) in refluxing MeOH, which gave a mixture of the pincer complex [Pd(O^1,N^1,C^1-L)Cl] (**1**), where L is the monoanionic ligand resulting from deprotonation of the acetyl methyl group of the monoketal of dap (Scheme 2), and $(QH)_2[PdCl_2(\mu\text{-}Cl)]_2$ (**2**) (Scheme 2), where QH is the diketal of $Hdap^+$. This mixture could be separated on the basis of the different solubility of its components in $CHCl_3$. The yield of **1** was improved (69%, based on the stoichiometry shown in Scheme 2) in the presence of NEt_3 in the molar ratio Pd:dap:NEt_3 = 1:1:0.4. An increase in the amount of NEt_3 caused decomposition to palladium metal, decreasing the yield of **1** and increasing that of **2**. Monoketalization methods of dicarbonyl compounds are scarce but some have been reported,[24] including a few giving ethyleneglycol monoketal derivatives of 2,6-diacetylpyridine.[25] Probably, $PdCl_2$ acts as an acid for the ketalization of one acetyl group. The electron-releasing capacity of the ketal group will favor the coordination of Pd to the pyridine N and, correspondingly, the palladation of the other acetyl group. The full ketalization of dap in the presence of the formed HCl will give the corresponding pyridinium salt, which reacts with $PdCl_2$ to afford complex **2**.



Scheme 2

The reaction of **2** with two equiv of NEt_3 at room temperature in MeOH for 1 day gives the diketal of dap, Q = $C_5H_3N\{C(OMe)_2Me\}_2$-2,6 (**3**; Scheme 2), in 93% yield. The synthesis of this compound has not been reported, and our attempts to synthesize it using *para*-toluenesulfonic acid as catalyst were unfruitful. When the reaction was carried out using an excess of NEt_3, impure **3** was obtained. This compound is soluble in organic solvents and is stable in the solid state and in solution.

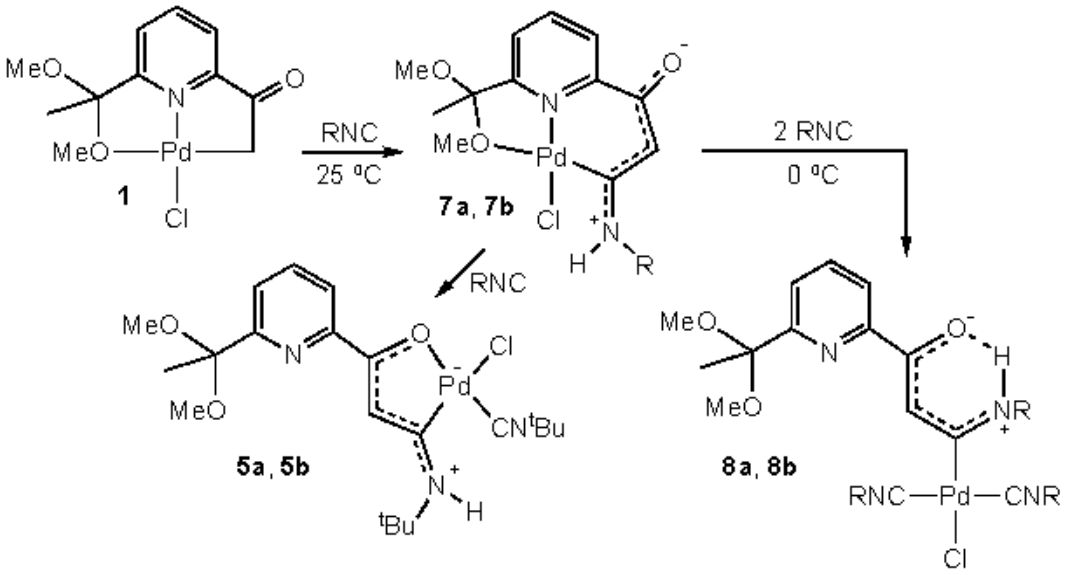
Reactions of 1 with Isocyanides. The reaction of **1** with two equiv of isocyanide at 0 °C (5 min for R = Xy, 20 min for R = ^{t}Bu) afforded *trans*-[Pd(C^1-L)Cl(CNR)$_2$] (R = Xy (**4a**), ^{t}Bu (**4b**); Scheme 3, solid arrow). However, at 25 °C this reaction led to the isolation of [Pd(O^2,C^2-L$_R$)(CNR)Cl] (R = ^{t}Bu, **5b**), whereas the corresponding product with R = Xy (**5a**) could only be isolated in impure form (see below). Complexes **5** are probably formed from **4** after insertion of one isocyanide into the Pd–C bond plus a tautomerization process from *β*-ketoimine to *β*-ketoenamine that converts the ligand C^1-L into O^2,C^2-L$_R$ (Scheme 3, dashed arrows). The reaction of complex **1** with one equiv of isocyanide gave a mixture of [Pd(N^1,C^1-L)Cl(CNR)] (Scheme 3, R = Xy (**6a**), ^{t}Bu (**6b**)), **4** and unreacted **1** (85:9:6 molar ratios).



Scheme 3

The reaction of **1** with one equiv of RNC at room temperature afforded the pincer complex [Pd(O^1,N^1,C^2-L$_R$)Cl] (R = Xy (**7a**), ^{t}Bu (**7b**); Scheme 4) probably resulting from the same insertion/tautomerization processes that led to **5** from **4**. Complex **7b** was better prepared in refluxing $CHCl_3$, but **7a** had to be prepared at room temperature over 10 days because refluxing in $CHCl_3$ (1.5 h) led to mixtures, whose main component was the Pd(I) complex $[PdCl(CNXy)_2]_2$. We have reported a similar behavior when studying the reactivity of $[Pd\{CH_2C(O)Me\}Cl]_n$ toward isocyanides.[6] Complexes **7** reacted at 0 °C (1) with 2 equiv of RNC to give *trans*-[Pd(C^2-L$_R$)Cl(CNXy)$_2$] (R = Xy (**8a**), ^{t}Bu (**8b**)) or (2) with one equiv of

RNC to afford **5**. This is a better way to prepare **5b** than that involving the reaction **1** with two equiv of ^{t}BuNC. The corresponding reaction with XyNC gave **5a** contaminated with 7**a** and **8a** (81:15:4), which is the same irresolvable mixture obtained by reacting **1** with two equiv of XyNC (see above), suggesting that complexes 7 are intermediates in the synthesis of **5** from **1** (Scheme 3).

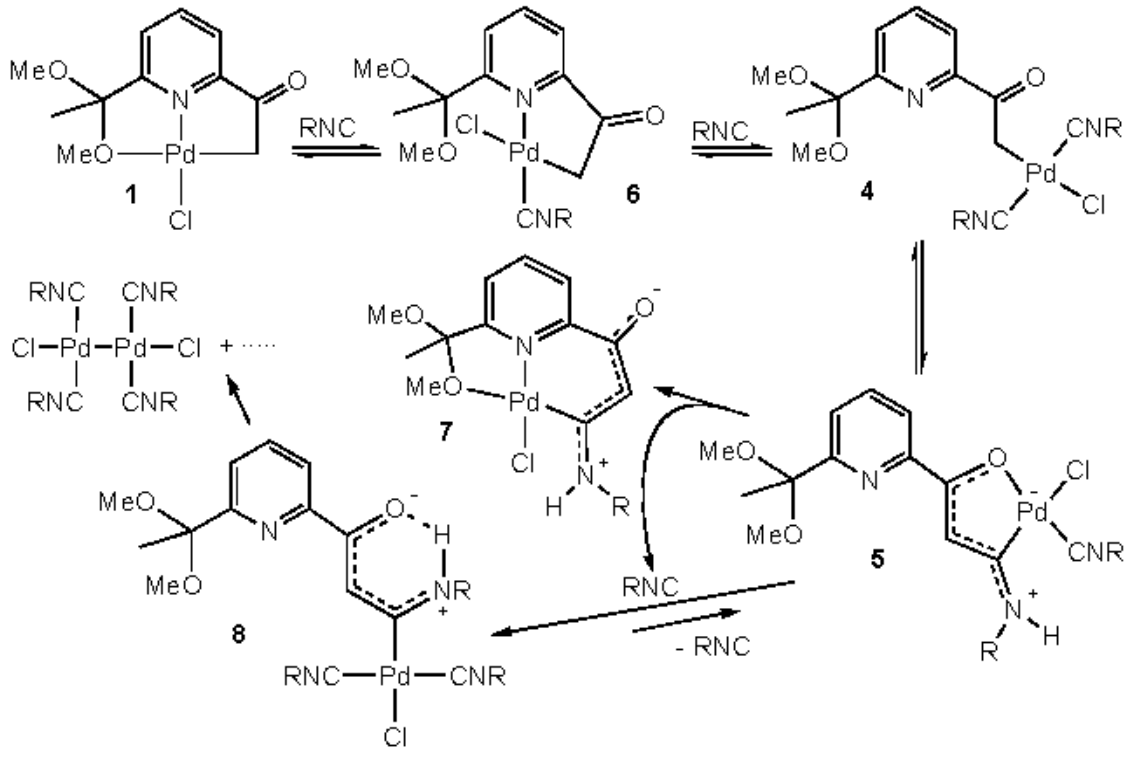


Scheme 4

Reaction Pathways. The reaction of **1** with one equiv of isocyanide was monitored by ^{1}H NMR at 0 °C (Scheme 3). The intermediate **6** was first observed but, as it reacts with isocyanide to afford **4**, it could only be isolated as a mixture of **6**, **4** and **1**.

The 10-day reaction of **1** with one equiv of XyNC at 25 °C was monitored by ^{1}H NMR showing the initial formation of **6a** along with minor amounts of **4a** (Scheme 5), their concentrations' decreasing and formation of 7**a** and traces of **5a** and **8a**. Through the 10-day period the concentration of 7**a** increased and that of **1** remained constant (ca. 4% of the initial concentration). These data and those shown above suggest that complexes **1** and **4**–**8** are related through the reactions shown in Scheme 5.

The ^{1}H NMR monitoring of the reactions of **1** with two equiv of the isocyanide at 25 °C showed formation of **4** and its conversion into **5**, as proposed above (Scheme 3). The final product was **5**, along with minor amount of 7, **8** and $[PdCl(CNR)_2]_2$. The reaction was faster with XyNC (Scheme 5).



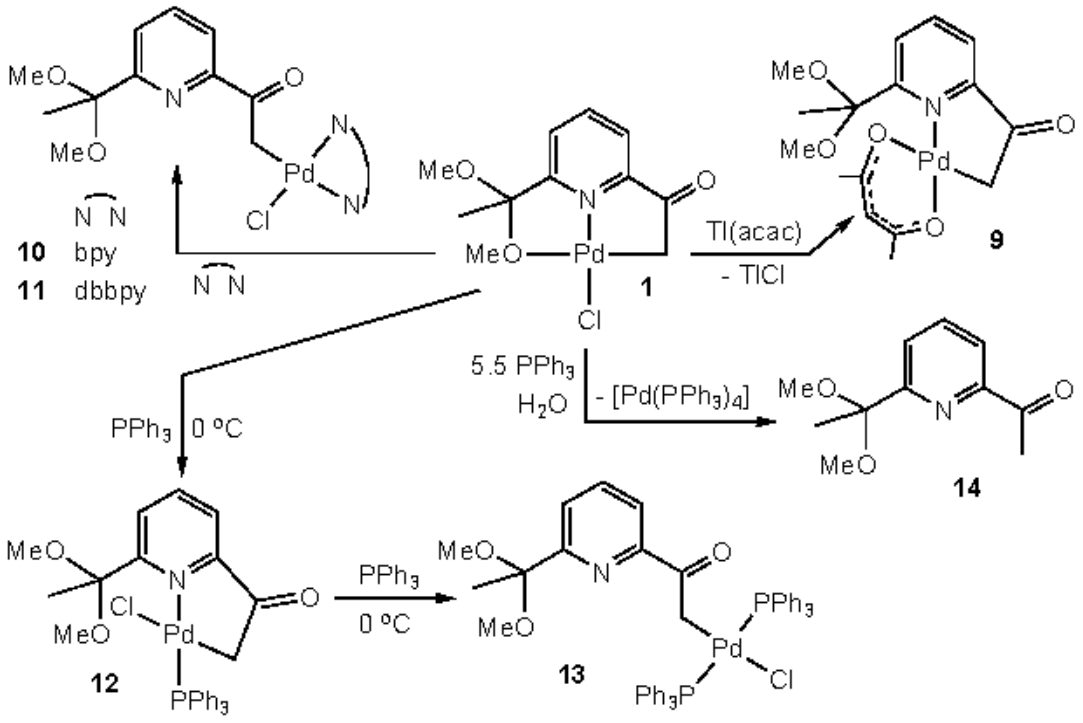
Scheme 5

A ^{1}H NMR study of the behavior of **4a** at 25 °C in $CDCl_3$ showed that it decomposes initially to **6a**, and later formation of **5a**, 7**a**, and **8a** was observed. After 2 days **4a** and **6a** had disappeared, while the amounts of **5a** and **8a** increased over 48 h and 25 min, respectively, and then decreased, and the omount of 7**a** increased continuously. Perhaps the transformation of **8a** into the Pd(I) complex $[PdCl(CNXy)_2]_2$ (**8a**:$[PdCl(CNXy)_2]_2$ = 4; minor amounts of **5a** and traces of 7**a** were also observed). This can explain why the attempt to prepare 7**a** by refluxing a 1:1 mixture of **1** and XyNC, gave mainly $[PdCl(CNXy)_2]_2$. Complex **4b** behaves similarly but all processes were much slower. Thus, after 4 days the **4b**:**6b**:7**b**:**5b**:**8b** molar ratios are 3:0:4:88:5.

Reactions of [Pd(O^1,N^1,C^1-L)Cl] (1) with P-, N- or O-donor Ligands. The reaction of complex **1** with PPh_3 gave similar results to that with isocyanides. Thus, at 0 °C the equimolecular reaction led to the expected product [Pd(N^1,C^1-L)Cl(PPh_3)] (**12**) along with **1** (5%) and *trans*-[Pd(C^1-L)Cl(PPh_3)$_2$] (**13**) (5%) (Scheme 6). This prevented the isolation of pure **12**. The reaction with two equivalents of PPh_3 gave complex **13** but it could not be obtained in an analytically pure form because traces of an impurity containing PPh_3 could not

be separated. The ^{1}H NMR spectrum of the reaction mixture obtained from **1** and an excess of PPh_3 (1:5.5) showed, almost instantly, the presence of a mixture of the monoketal of dap, $C_5H_3N\{C(O)Me\text{-}2\}\{C(OMe)_2Me\text{-}6\}$ (**14**), $[Pd(PPh_3)_4]$ and its dissociation products $[Pd(PPh_3)_3]$ and PPh_3 as well as traces of dap. This was formed by hydrolysis of **14**, because the traces of water initially observed in the spectrum disappeared. Probably, the formed hydroxo Pd(II) complex is reduced by PPh_3 to $[Pd(PPh_3)_3]$. The excess of PPh_3 precluded separation of the mixture by recrystallization, and TLC chromatography using silica gel led to the hydrolysis of **14** to give dap.

Complex **1** reacted with 2,2'-bipyridine (bpy) or 4,4'-di-tert-butyl-2,2'-bipyridine (dbbpy) to afford the adducts $[Pd(C^1\text{-}L)Cl(N\text{^}N)]$ (N^N = bpy (**10**), dbbpy (**11**)) (Scheme 6) and with [Tl(acac)] to give [Pd(L)(acac)] (**9**).



Scheme 6

Crystal Structures. The crystal structures of complexes **1** (Figures 1 and 2), **2** (Figures 3 and 4), **5b** (Figure 5), **6a** (Figures 6 and 7) and 7**a** (Figures 8 and 9) have been determined (Table 1). All show a nearly square-planar coordination around the palladium atom. Crystals apparently suitable for an X-ray crystallographic study were selected for **5a**. Although a complete crystallographic analysis was not possible, because of severely disordered methoxy

groups, the position of the ligands was established with certainty to be that indicated in Scheme 3.

In complex **1** (Figure 1), the three rings of the coordinated pincer ligand are almost coplanar, being the angle between the mean planes of the py ring and the palladacycles PdNCCO and PdNCC(O)C of 3.9° and 2.6°, respectively. The molecules are connected by Pd···Pd (3.3460(3) Å) and Pd···Cl (3.9016(6) Å) contacts (van der Waals radii of Pd: 2.05 Å and Cl: 1.8 Å[26]) giving dimers that form layers via C–H···Cl and C–H···O hydrogen bonds (Figure 2).

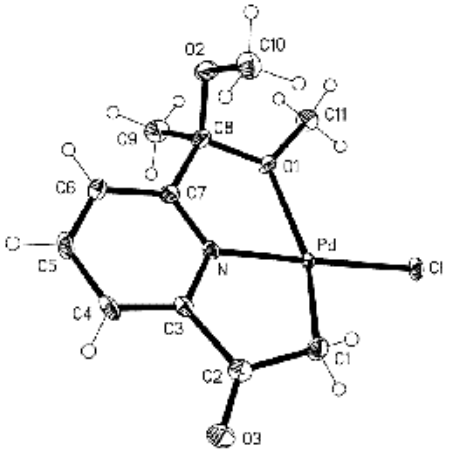


Figure 1. Ellipsoid representation of **1** (50% probability). Selected bond lengths (Å) and angles (deg): Pd-N 1.9752(19), Pd-C(1) 2.000(2), Pd-O(1) 2.2149(16), Pd-Cl 2.3040(5), Pd-Pd#1 3.3460(3), O(3)-C(2) 1.217(3), C(1)-C(2) 1.497(3), C(2)-C(3) 1.499(3), N-Pd-C(1) 83.85(9), N-Pd-O(1) 76.32(7), C(1)-Pd-Cl 96.63(7), O(1)-Pd-Cl 103.03(4).

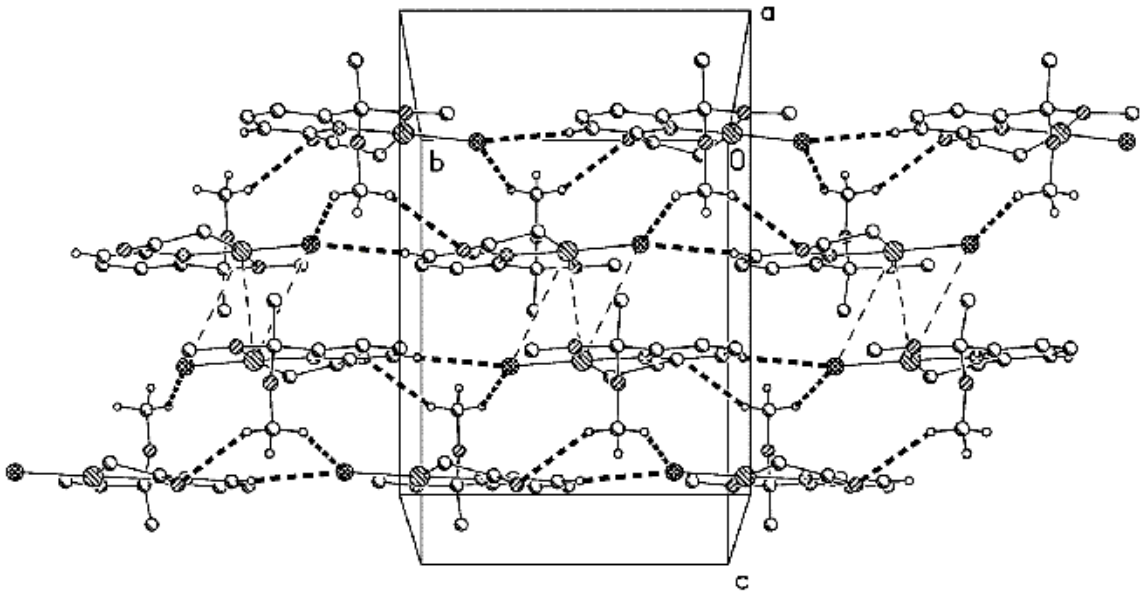


Figure 2. Packing diagram showing Pd···Pd and Pd···Cl contacts (thin dashed bonds), and C–H···Cl and C–H···O hydrogen bonds (thick dashed bonds) in complex **1**.

In complex 2 (Figure 3), the $[Pd_2Cl_6]^{2-}$ anion lies across an inversion center with each palladium atom in a square-planar enviroment. The geometrical parameters of the anion agree with those found in other $[Pd_2Cl_6]^{2-}$ salts.[27] Anions and cations are connected by hydrogen bonds between terminal Cl atoms of the anion and Me and MeO groups of cations (Figure 4).

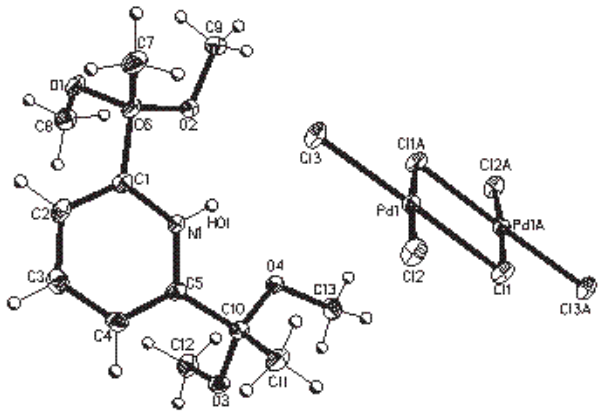


Figure 3. Ellipsoid representation of **2** (50% probability). Selected bond lengths (Å) and angles (deg): Pd(1)-Cl(3) = 2.2750(6), Pd(1)-Cl(2) = 2.2798(6), Pd(1)-Cl(1) = 2.3259(6), Pd(1)-Cl(1A) = 2.3287(6), N(1)-C(5) = 1.344(3), N(1)-C(1) = 1.353(3), O(1)-C(6) = 1.410(3), O(2)-C(6) = 1.405(3), O(3)-C(10) = 1.415(2), O(4)-C(10) = 1.407(3), C(1)-C(6) = 1.526(3), C(5)-C(10) = 1.525(3), Cl(3)-Pd(1)-Cl(2) = 92.25(2), Cl(2)-Pd(1)-Cl(1) = 91.53(2), Cl(3)-Pd(1)-Cl(1A) = 91.04(2), Cl(1)-Pd(1)-Cl(1A) = 85.26(2), Pd(1)-Cl(1)-Pd(1A) = 94.735(19), N(1)-C(1)-C(6) = 117.27(19), N(1)-C(5)-C(10) = 118.56(19), O(4)-C(10)-C(5) = 104.23(16).

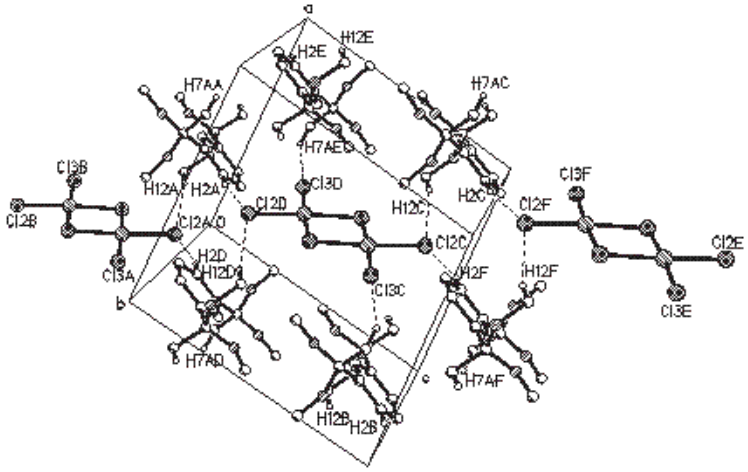


Figure 4. Packing diagram showing the hydrogen bonds between terminal Cl atoms of the anion and Me and MeO groups of cations in complex **2**.

In 5b (Figure 5), two crystallographically independent molecules are present in the unit cell with a strong intermolecular Pd–Pd interaction (3.1652(3) Å)[26] within the asymmetric

unit. The angle between the coordination planes of these two molecules is 6.6°. In 6a (Figure 6), the metal is in a very distorted square planar coordination; the mean deviation from the coordination plane is 0.12 Å, with the CH_2 carbon 0.16 Å and the chlorine atom 0.13 Å out of this plane. This distortion might be attributable to the steric hindrance of the uncoordinated ortho substituent. The chlorine atom lies +1.911 Å and C(9) –0.124 Å out of the plane of the pyridyl ligand and the palladium atom (mean deviation 0.070 Å). The molecules of 6a are connected through CH···OMe hydrogen bonds giving dimers that form double chains along the axis *a* via the hydrogen bond of one Me and the chlorine atom (Figure 7).

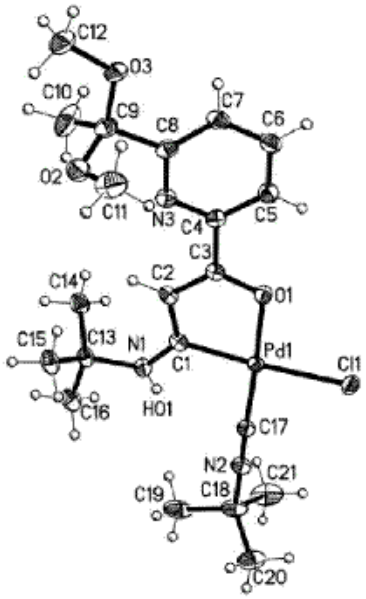


Figure 5. Ellipsoid representation of one of the two independent molecules in complex **5b** (50% probability). Selected bond lengths (Å) and angles (deg) for **$5b_1$**: Pd(1)-C(17) = 1.914(3), Pd(1)-C(1) = 1.988(3), Pd(1)-O(1) = 2.021(2), Pd(1)-Cl(1) = 2.3846(8), Pd(1)-Pd(1')= 3.1652(3), O(1)-C(3) = 1.293(4), C(1)-N(1) = 1.324(4), C(1)-C(2) = 1.412(4), N(1)-C(13) = 1.498(4), C(2)-C(3) = 1.386(4), C(3)-C(4) = 1.492(4), C(17)-N(2) = 1.150(4), C(17)-Pd(1)-C(1) = 95.89(12), C(1)-Pd(1)-O(1) = 82.15(10), C(17)-Pd(1)-Cl(1) = 88.92(8), O(1)-Pd(1)-Cl(1) = 93.00(6), C(17)-Pd(1)-Pd(2) = 82.29(8), C(1)-Pd(1)-Pd(1) = 81.80(8), O(1)-Pd(1)-Pd(1) = 99.98(6), Cl(1)-Pd(1)-Pd(1) = 99.87(2), C(3)-O(1)-Pd(1) = 111.24(18), C(2)-C(1)-Pd(1) = 111.2(2), C(3)-C(2)-C(1) = 114.2(3), O(1)-C(3)-C(2) = 120.9(3). **$5b_2$**: Pd(1')-C(17') = 1.912(3), Pd(1')-C(1') = 1.978(3), Pd(1')-O(1') = 2.048(2), Pd(1')-Cl(1') = 2.3956(7), O(1')-C(3') = 1.289(4), C(1')-N(1') = 1.326(4), C(1')-C(2') = 1.408(4), C(2')-C(3') = 1.389(4), C(3')-C(4') = 1.487(4), C(17')-Pd(1')-C(1') = 92.04(12), C(1')-Pd(1')-O(1') = 82.21(11), C(17')-Pd(1')-Cl(1') = 90.47(9), O(1')-Pd(1')-Cl(1') = 94.58(6), C(17')-Pd(1')-Pd(1) = 98.63(9), C(1')-Pd(1')-Pd(1) = 82.68(9), O(1')-Pd(1')-Pd(1) = 92.18(6), Cl(1')-Pd(1')-Pd(1) = 100.62(2), C(3')-O(1')-Pd(1') = 109.42(18), C(2')-C(1')-Pd(1') = 111.1(2), C(3')-C(2')-C(1') = 114.0(3), O(1')-C(3')-C(2') = 121.8(3).

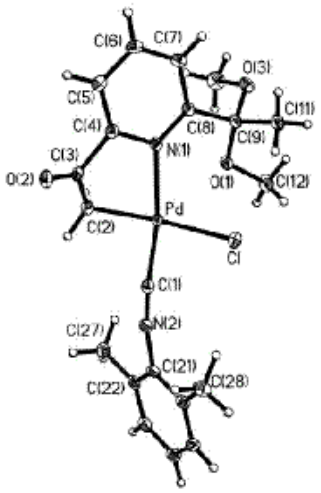


Figure 6. Ellipsoid representation of **6a** (50% probability). Selected bond lengths (Å) and angles (deg): Pd-C(1) = 1.9037(15), Pd-C(2) = 2.0558(14), Pd-N(1) = 2.1169(12), Pd-Cl = 2.4001(4), C(1)-N(2) = 1.156(2), N(2)-C(21) = 1.4044(18), C(2)-C(3) = 1.477(2), C(3)-O(2) = 1.2205(18), C(3)-C(4) = 1.505(2), C(4)-N(1) = 1.3557(18), N(1)-C(8) = 1.3462(18), C(8)-C(9) = 1.537(2), C(9)-O(1) = 1.4044(17), C(9)-O(3) = 1.4228(18), C(10)-O(3) = 1.432(2), C(12)-O(1) = 1.4358(18), C(1)-Pd-C(2) = 90.24(6), C(2)-Pd-N(1) = 79.90(5), C(1)-Pd-Cl = 87.31(5), N(2)-C(1)-Pd = 172.58(13), C(1)-N(2)-C(21) = 168.61(14), C(3)-C(2)-Pd = 94.11(9), C(2)-C(3)-C(4) = 111.86(12), N(1)-C(4)-C(3) = 112.59(12), C(8)-N(1)-Pd = 135.13(10), C(4)-N(1)-Pd = 105.73(9), N(1)-C(8)-C(9) = 120.67(13).

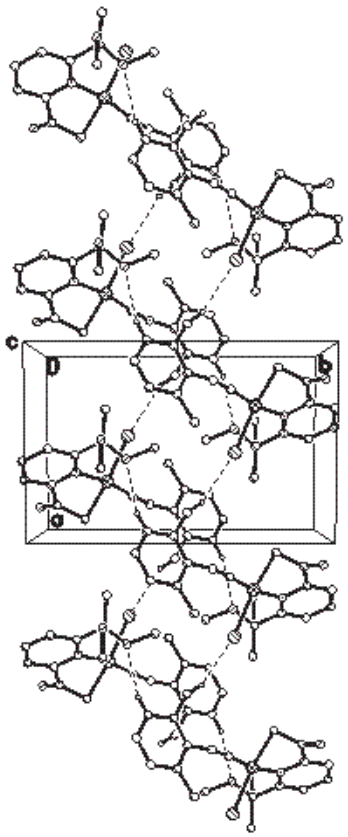


Figure 7. Packing diagram showing the hydrogen bonds in complex **6a**.

The structure of 7a (Figure 8) shows the metal in a slightly distorted square planar coordination, the mean deviation from the coordination plane being 0.081 Å. The complex has two palladacycles; the five-membered ring has an envelope conformation with the sp^3 carbon out of the ring-plane and the six-membered ring has a boat conformation, with the CO carbon and the palladium atom out of the plane. Each molecule has one classical intramolecular N-H ··Cl hydrogen bond and four non-classical C–H ··O hydrogen bonds affording a double chain (Figure 9).

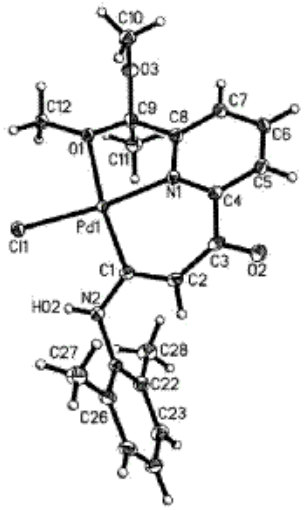


Figure 8. Ellipsoid representation of **7a** (50% probability). Selected bond lengths (Å) and angles (deg): Pd(1)-C(1) = 1.9492(17), Pd(1)-N(1) = 2.0257(15), Pd(1)-O(1) = 2.1673(12), Pd(1)-Cl(1) = 2.3022(5), O(1)-C(9) = 1.443(2), N(1)-C(4) = 1.349(2), N(1)-C(8) = 1.352(2), C(1)-N(2) = 1.351(2), C(1)-C(2) = 1.379(2), N(2)-C(21) = 1.443(2), C(2)-C(3) = 1.418(3), C(3)-O(2) = 1.242(2), C(3)-C(4) = 1.515(2), C(8)-C(9) = 1.534(2), C(9)-O(3) = 1.389(2), C(1)-Pd(1)-N(1) = 92.73(7), N(1)-Pd(1)-O(1) = 79.19(5), C(1)-Pd(1)-Cl(1) = 93.60(5), N(1)-Pd(1)-Cl(1) = 172.35(4), O(1)-Pd(1)-Cl(1) = 94.99(3), C(9)-O(1)-Pd(1) = 110.19(10), C(4)-N(1)-Pd(1) = 126.05(12), C(8)-N(1)-Pd(1) = 114.51(12), C(2)-C(1)-Pd(1) = 122.75(13), C(1)-N(2)-C(21) = 122.71(15), C(1)-C(2)-C(3) = 128.73(16), O(2)-C(3)-C(2) = 122.29(16), O(2)-C(3)-C(4) = 115.73(16), C(2)-C(3)-C(4) = 121.71(16), N(1)-C(4)-C(3) = 121.87(16), N(1)-C(8)-C(9) = 119.09(15), O(1)-C(9)-C(8) = 105.70(14), C(22)-C(21)-N(2) = 118.60(16).

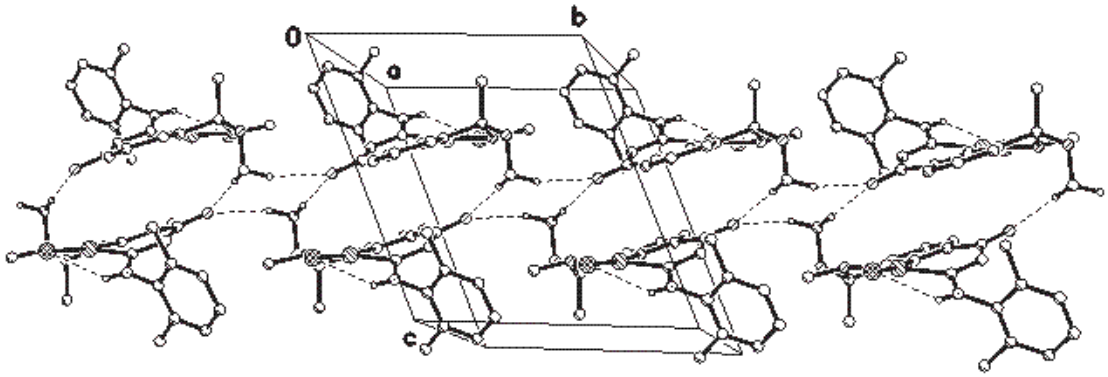


Figure 9. Packing diagram showing the hydrogen bonds in complex **7a**.

The structures of complexes **5b** and 7**a** show that Pd and the Xy group are mutually trans as shown in Schemes 3 and 4. Although a complete X-ray crystallographic study was not possible for **5a**, the same geometry around the PdC–NHXy bond was established with certainty, which was also observed in other *β*-ketoenamine complexes previously described by us.[6] In addition, both have a high degree of electron delocalization over the OCCCN group as shown in Scheme 5 because (1) it is almost planar (mean deviation of the five atoms from the mean plane 0.034°, 0.020° (for the two molecules of **5b**) and 0.051° (7**a**), respectively), (2) the C–O bond distance is longer (**5b**: 1.293(4), 1.289(4) Å; 7**a**: 1.242(2) Å) than in **1** (1.217(3) Å) or **6a** (1.2205(18) Å), (2) the C(1)–C(2) distances (**5b**: 1.412(4) Å, 1.408(4); 7**a**: 1.379(3) Å) and C(2)–C(3) (**5b**: 1.386(4), 1.389(4) Å; 7**a**: 1.418(2) Å) are intermediate between that of a single (O)*C*–*C*=C (1.464 Å) and a double (O)C–*C*=*C* bond (1.340 Å)[28] and (3) the C–N bond distances (**5b**: 1.324(4), 1.326(4) Å; 7**a**: 1.351(2) Å) are intermediate between that of a single R_2N–CH_2Pd bond (mean value, 1.450 Å)[29] and a double XyNH=C(Me)Pd bond (ca. 1.30 Å).[30]

The Pd–CH_2 bond distance is longer in **6a** (2.0558 (14) Å) than in **1** (2.000(2) Å), showing the greater trans influence of the Cl ligand than the O-donor ligand. The Pd–N bond distances decrease in the series **6a** (2.1169(12) Å), 7**a** (2.0257(15) Å), **1** (1.9752(19) Å), because the angle between the coordination and pyridine planes decreases (44.3°, 18.4°, 5.8°), thus favoring the Pd to pyridine π-back bonding, and also becuase of the greater trans influence of the XyNC than the Cl ligand. The Pd–Cl bond distances in complexes **1** and 7**a** (2.3040(5) and 2.3022(5) Å) are shorter than those in **5b** (2.3846(8), 2.3956(7) Å) and **6a** (2.4001(4) Å), attributable to the lower trans influence of a N-donor ligand than a C-donor ligand.

Spectroscopic Properties. The ^{1}H and $^{13}C\{^1H\}$ NMR spectra of all compounds are in agreement with the structures shown in Schemes 2–6, except for the MeO protons and the corresponding carbons, which appear as only one resonance corresponding to the six protons or the two carbons, respectively, in the range *δ* 3.08–3.47 and 49–52.2 ppm, respectively. The exchange of these MeO groups cannot be slowed down enough at – 60 °C to see the expected two resonances in their spectra but they coalesce at this temperature in complex **1**. The ^{1}H and $^{13}C\{^1H\}$ NMR methyl resonances of the *Me*C(OMe)$_2$ group appear as singlets in the ranges *δ* 1.48–2.03 and 23–26.3 ppm, respectively.

The ketonyl complexes (**1**, **4**, **6**, **9-11**) show the CH_2 protons as singlets in the range *δ*

3.73–3.35. In the case of **6**, the equivalence of the CH_2 protons can be explained assuming a fast equilibrium with the cationic [Pd(O^1,N^1,C^1-L)(CNR)]Cl. These protons are less shielded than the CH_2 of the acetonyl palladium complexes [$Pd_2\{CH_2C(O)Me\}_2(\mu\text{-}Cl)_2(CNR)_2$], *trans*-[$Pd\{CH_2C(O)Me\}Cl(CNR)_2$] and [$Pd\{CH_2C(O)Me\}(CNR)_3$]TfO (R = XyNC, ^{t}BuNC; range δ 3.18–2.61),[6] caused by the pyridine group. As expected, for isocyanide complexes **4** and **6**, the CH_2 protons are more shielded for ^{t}BuNC (**4b**: 3.35; **6b**: 3.27) than XyNC (**4a**: 3.73; **6a**: 3.44) complexes. The NH proton in L_R palladacyclic complexes **5** and 7 appears as a broad resonance in the range 6.00–8.65 ppm, shielded with respect to that in the monocoordinate L_R ligands (**8a**: 13.68; **8b**: 12.96), which supports the proposal of an intramolecular hydrogen bond in the latter (Scheme 4). Again, the NH proton is more shielded for R = ^{t}Bu (7**b**: 7.63; **8b**: 12.96) than for Xy (7**a**: 8.65; **8a**: 13.68). The C*H*C(O) proton is weakly coupled with the NH proton for **5a** or **5b** (6.45 or 5.86 ppm, J = 1 Hz) but it appears as a singlet for 7**a**, **8a**, or **8b** (4.67, 7.22, or 6.86 ppm) or a broad signal for 7**b** (5.17 ppm).

In the ^{1}H NMR spectrum of **9** at room temperature, the Me acac protons appear as a broad resonance but at –40 °C this resolves into two signals, which could be associated with an equilibrium between [Pd(N^1,C^1-L)(*O*,*O*-acac)] and [Pd(O^1,N^1,C^1-L)(*C*-acac)]. However, in the $^{13}C\{^1H\}$ NMR spectrum, the two Me acac carbon nuclei resonate as two broad singlets at room temperature.

The IR spectra of chloro complexes show a band assignable to ν(PdCl) at various wavenumbers depending on the nature of the ligands in trans position. Thus, complexes with chloro trans to a N-donor ligand (**1**, 7, **10**, **11**) show ν(PdCl) absortion in the range 337–321 cm^{-1}, while in complexes with chloro trans to a C-donor ligand (**4**, **6**, **8**, **12**, **13**) the absorption is observed in the range 290–280 cm^{-1}, in agreement with the stronger trans influence of a C-donor ligand with respect to a N-donor ligand.

The ketonyl complexes **1**, **4**, **9-11** show the ν(C=O) absortion in the range 1684-1608, cm^{-1} while in complexes **5**, 7 and **8** the ν(C=O) appears at lower frequency, 1590-1538 cm^{-1}, showing the reduction of the C–O bond order, consistent with the results of the X-ray diffraction study of complexes **5b** and 7**a**, and attributable to the electron delocalization over the OCCCNC group of the β-ketoenamine ligand.

The IR spectra of complexes with the ligand XyNC show the ν(N≡C) band in the region 2192–2175 cm^{-1} and those with ^{t}BuNC in the narrow range 2211–2208 cm^{-1} showing, as usual, an increase with respect to ν(CN) in the free ligands (2109 and 2134 cm^{-1}, respectively).

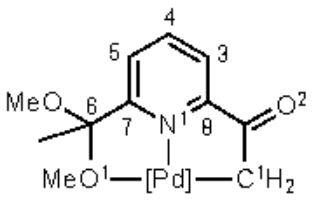
CONCLUSIONS

2,6-Diacetylpyridine can be palladated using $PdCl_2$ in methanol via its transformation into its dimethylketal. The resulting complex, which contains the monoanionic pincer ligand resulting from the deprotonation of the acetyl methyl group of the monoketal of dap, reacts with isocyanides, giving complexes resulting from coordination or/and insertion of the isocyanide followed by a tautomerization process from *β*-ketoimine to *β*-ketoenamine. The reaction pathway has been studied at different molar ratios and temperatures.

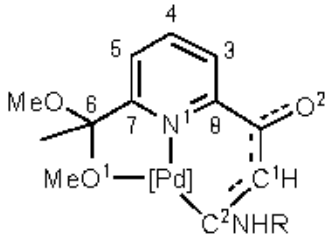
EXPERIMENAL SECTION

General Procedures

The reactions were carried out without precautions to exclude light or atmospheric oxygen or moisture. Melting points were determined on a Reicher apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on a Bruker AC 200, or Avance 300 or 400 spectrometer at room temperature. Chemical shifts were referred to TMS (^{1}H, ^{13}C) or H_3PO_4 (^{31}P). When needed, NMR assignments were performed with the help of APT, HMQC and HMBC techniques. Chart 1 shows the atom numbering used to name the ligands in the NMR assignments. The R groups (Xy, ^{t}Bu) of inserted and coordinated isocyanides are distinguished by using the notation Xy^i, $^tBu^i$ and $^tBu^c$, Xy^c, respectively.



[Pd](O^1,N^1,C^1-L)



[Pd](O^1,N^1,C^2-L_R)

Chart 1

Synthesis

Synthesis of [Pd(O^I,N^I,C^I-L)Cl] (**1**) *and* ($C_5H_3NH\{C(OMe)_2Me\}$-2,6)$_2$[{$PdCl_2(\mu$-Cl)}]$_2$ (**2**). To a suspension of $PdCl_2$ (390.6 mg, 2.20 mmol) in MeOH (20 mL) was added 2,6-diacetylpyridine (359.3 mg, 2.20 mmol) and NEt_3 (57 μL, 0.40 mmol). The suspension was refluxed for 95 min and then filtered through Celite. The orange filtrate was concentrated (2 mL) and Et_2O (1 mL) was added. The resulting precipitate was filtered off and air-dried. The solid was extracted with $CHCl_3$ (4x5 mL) giving a solution A (used to prepare **1**) and a solid, which was air-dried giving orange **2**. Yield 92.4 mg, 18% (based on the stoichiometry shown in Scheme 2). Mp: 131–132 °C. IR (cm^{-1}): *ν*(NH) 3248, 3217, *ν*(CN) 1617, *ν*(PdCl) 346, 334. ^{1}H NMR (300 MHz, MeCN-d_3): *δ* 12.55 (br, NH), 8.75 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.13 (d, 2 H, H3,5, $^3J_{HH}$ = 8 Hz), 3.30 (s, 12H, OMe), 1.71 (s, 6H, Me). ^{13}C{^{1}H} NMR (75.4 MHz, MeCN-d_3): *δ* 150.4 (C4), 126.1 (C3,5), 100.2 (C6), 50.8 (MeO), 24.7 (Me). Anal. Calcd for $C_{26}H_{44}N_2O_8Cl_6Pd_2$: C, 33.29; H, 4.72; N, 2.98. Found: C, 33.08; H, 4.92; N, 2.90. Single crystals of **2** were obtained by slow evaporation of a MeOH solution of **2**.

Solution A was concentrated (1 mL) and column chromatographed on silica gel using $CHCl_3$ as eluent. The first collected fraction was concentrated (1 mL). Addition of Et_2O (4 mL) and *n*-pentane (4 mL) gave a suspension that was filtered off to give complex **1** as a yellow solid. Yield: 267.1 mg, 69% (based on the stoichiometry shown in Scheme 2). Mp: 137–138 °C. IR (cm^{-1}): *ν*(C=O) 1684, *ν*(CN) 1603, *ν*(PdCl) 321. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.14 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.80 (dd, 1 H, H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.63 (dd, 1 H, H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 3.52 (s, 2 H, CH_2), 3.42 (s, 6 H, OMe), 1.77 (s, 3 H, Me). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): *δ* 203.7 (CO), 158.5 (C7), 152.7 (C8), 139.8 (C4), 126.4 (C5), 123.6 (C3), 106.9 (C6), 51.5 (MeO), 30.7 (C1), 25.0 (Me). Anal. Calcd for $C_{11}H_{14}NO_3ClPd$: C, 37.74; H, 4.03; N, 4.00. Found: C, 37.63; H, 3.97; N, 3.95. Single crystals of **1** were obtained by slow evaporation of a MeOH solution of **1**.

Synthesis of $C_5H_3N\{C(OMe)_2Me\}_2$ (**3**)**.** To a suspension of **2** (2466.9 mg, 2.63 mmol) in MeOH (30 mL) was added NEt_3 (733 μL, 5.26 mmol). The reaction mixture was stirred for 24 h and then concentrated to dryness. The residue was extracted with *n*-pentane (2x20 mL) and the solution was concentrated to dryness to give **3** as a colorless solid. Yield: 1246.0 mg, 93%. Mp: 103-104 °C. IR (cm^{-1}): *ν*(CN) 1582. ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 7.71-7.57 (m, 3H,

py), 3.19 (s, 12H, MeO), 1.66 (s, 6H, Me). $^{13}C\{^1H\}$ NMR (50.30 MHz, $CDCl_3$): δ 159.7 (*o*-C), 136.2 (*p*-C), 120.4 (*m*-C), 101.8 (*C*Me), 49.1 (OMe), 23.6 (Me). Anal. Calcd for $C_{13}H_{21}NO_4$: C, 61.16; H, 8.29; N, 5.49. Found: C, 61.05; H, 8.57; N, 5.58.

Synthesis of trans-[Pd(C^1-L)Cl(CNXy)$_2$]·0.5H_2O (**4a**). To a cooled (0 °C) solution of **1** (23.3 mg, 0.07 mmol) in $CHCl_3$ (5 mL), XyNC (20.2 mg, 0.15 mmol) was added. After 5 min the solution was concentrated to dryness. The residue was vigorously stirred in a cooled (0 °C) mixture of Et_2O (2 mL) and *n*-pentane (6 mL). The resulting suspension was filtered off, the solid washed with *n*-pentane and air-dried to give **4a** as a pale yellow solid. Yield: 37.4 mg, 90%. Mp: 134-135 °C. IR (cm^{-1}): ν(N≡C) 2192, ν(C=O) 1647, ν(C=N) 1579, ν(PdCl) 280. ^1H NMR (400 MHz, $CDCl_3$): δ 7.92-7.90 (m, 1 H, ABC system), 7.77-7.72 (m, 2H, ABC system), 7.27-7.11 (m, 6H, Xy), 3.73 (s, 2H, CH_2), 3.08 (s, 6H, OMe), 2.49 (s, 12H, Me, Xy), 1.48 (s, 3H, Me). $^{13}C\{^1H\}$ NMR spectrum could not be registered because **4a** transforms quickly to **5a**. Anal. Calcd for $C_{29}H_{33}N_3O_{3.5}ClPd$: C, 56.05; H, 5.35; N, 6.76. Found: C, 55.91; H, 5.29; N, 6.81.

Synthesis of trans-[Pd(C^1-L)Cl(CN^{t}Bu)$_2$] (**4b**). To a cooled (0 °C) solution of **1** (18.7 mg, 0.05 mmol) in CH_2Cl_2 (6 mL), ^{t}BuNC (11.1 mg, 0.13 mmol) was added and the mixture was stirred for 20 min. Concentration to dryness, addition of *n*-pentane (6 mL) and vigorous stirring led to a suspension. The solid was filtered off, washed with Et_2O and air-dried to give **4b** as a colorless solid. Yield: 26.2 mg, 96%. Mp: 124-125 °C. IR (cm^{-1}): ν(N≡C) 2211, ν(C=O) 1651, ν(C=N) 1579, ν(PdCl) 289. ^1H NMR (200 MHz, $CDCl_3$): δ 7.95-7.70 (m, 3H, ABC system), 3.35 (s, 2H, CH_2), 3.22 (s, 6H, OMe), 1.72 (s, 3H, Me), 1.52 (s, 18H, ^{t}Bu). $^{13}C\{^1H\}$ NMR spectrum could not be registered because **4b** decomposes quickly to **5b**. Anal. Calcd for $C_{21}H_{32}N_3O_3ClPd$: C, 48.85; H, 6.25; N, 8.14. Found: C, 48.53; H, 6.58; N, 8.07.

Synthesis of [Pd(O^2,C^2-L_{Xy})Cl(CNXy)] (**5a**). To a cooled solution (0 °C) of **7a** (22.9 mg, 0.05 mmol) in CH_2Cl_2 (8 mL) was added XyNC (6.3 mg, 0.05 mmol) and the mixture stirred for 10 min. Concentration (1 mL) and addition of *n*-pentane (9 mL) gave a suspension; the solid was filtered off, washed with *n*-pentane and air-dried to give a mixture (26.2 mg) of **5a**, **7a** and **8a** (81:15:4) with traces of XyNC. ^1H NMR (300 MHz, $CDCl_3$) of **5a**: δ 8.20 (dd, 1 H,

H3 or 5, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.2 Hz), 7.75 (t, 1 H, H4, $^3J_{HH}$ = 7.5 Hz), 7.67 (dd, 1 H, H5 or 3, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.2 Hz), 7.30-7.20 (m, 6H, Xy), 5.86 (d, 1 H, H1, J = 1 Hz), 3.12 (s, 6 H, MeO), 2.52 (s, 6 H, Me, Xy^o), 2.28 (s, 6 H, Me, Xy^i), 1.51 (s, 3 H, Me).

Synthesis of [Pd(O^2,C^2-L_{Bu})Cl(CN^{t}Bu)] (**5b**). To a solution of **1** (129.4 mg, 0.37 mmol) in $CHCl_3$ (15 mL), ^{t}BuNC (3.43 mL, 226.2 mM solution, 0.78 mmol) was added. The solution was stirred for 4.5 days at room temperature and then concentrated to dryness. The resulting residue was purified by preparative TLC chromatography on silica gel (70–200 μm) using CH_2Cl_2/Et_2O (1:2) as eluent. The first fraction (R_f = 0.50) was collected and extracted with acetone (3x15 mL) to give a solution that was concentrated to dryness. The residue was dissolved in CH_2Cl_2 and anhydrous $MgSO_4$ was added. The resulting suspension was stirred and filtered. The filtrate was concentrated to dryness and the resulting residue was recrystallized from Et_2O/*n*-pentane, to give **5b** as a yellow solid. Yield: 150.9 mg, 79%. Mp: 240 °C dec. IR (cm^{-1}): ν(C≡N) 2211, ν(C=O) 1590, ν(C=N) 1513, ν(PdCl) 281. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz), 7.75 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.69 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz, 6.45 (d, 1 H, H1, J = 1 Hz), 6.00 (br, 1 H, NH), 3.19 (s, 6H, MeO), 1.66 (s, 3H, Me), 1.61 (br, 9H, Me, ^{t}Bu^i), 1.48 (s, 9H, Me, ^{t}Bu^o). ^{13}C{^{1}H} NMR (100.81 MHz, $CDCl_3$): δ 196.6 (CO), 190.5 (C2), 159.1 (C7), 151.9 (C8), 136.5 (C4), 127.5 (t, *C*N^{t}Bu, $^1J_{CN}$ = 20 Hz), 123.4 (C5), 121.7 (C3), 105.1 (C1), 101.6 (C6), 59.3 (br, *C*Me$_3^o$), 56.5 (*C*Me$_3^i$), 49.2 (OMe), 30.2 (Me, ^{t}Bu^o), 29.4 (Me, ^{t}Bu^i), 23.0 (Me). Anal. Calcd for $C_{21}H_{32}N_3O_3ClPd$: C, 48.85; H, 6.25; N, 8.14. Found: C, 48.56; H, 6.25; N, 8.15. Single crystals were obtained by slow diffusion of a mixture Et_2O/*n*-hexane into a toluene solution of **5b** (1:1:1).

Synthesis of [Pd(N^1,C^1-L)Cl(CNXy)] (**6a**). To a cooled (0 °C) solution of **1** (44.5 mg, 0.13 mmol) in $CHCl_3$ (3 mL) was added XyNC (16.7 mg, 0.13 mmol) and the resulting pale yellow solution was stirred for 30 min and concentrated (1 mL). Addition of *n*-pentane (4 mL) gave a suspension; the solid was filtered off, washed with *n*-pentane and air-dried to give a mixture (56.2 mg) of **6a**, **1**, **4a** (85 : 9 : 6) with traces of XyNC that could not be separated. ^{1}H NMR (400 MHz, $CDCl_3$) of **6a**: δ 8.06 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.94 (dd, 1 H, H3 or 5, $^3J_{HH}$ = 8 Hz,

$^4J_{HH}$ = 1.2 Hz), 7.73 (dd, 1 H, H5 or 3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.26-7.11 (m, 3 H, Xy), 3.44 (s, 2 H, CH_2), 3.27 (s, 6 H, OMe), 2.49 (s, 6 H, Me, Xy), 2.03 (s, 3 H, Me).

Synthesis of [Pd(N^1,C^1-L)Cl(CN^{t}Bu)] **(6b).** To a cooled (0 °C) solution of **1** (30.2 mg, 0.09 mmol) in $CHCl_3$ (4 mL) was added ^{t}BuNC (400 μL of a 226.2 mM $CHCl_3$ solution, 0.09 mmol). The resulting pale yellow solution was stirred for 20 min and concentrated (1 mL). Addition of *n*-pentane (4 mL) gave a suspension; the solid was filtered off, washed with *n*-pentane and air-dried to give a mixture (32.1 mg) of **6b**, **1** and **4b** (84 : 7 : 9) with traces of ^{t}BuNC that could not be separated. ^{1}H NMR (400 MHz, $CDCl_3$) of **6b**: δ 8.02 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.90 (dd, 1 H, H3 or 5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.70 (dd, 1 H, H5 or 3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 3.27 (s, 2 H, CH_2), 3.24 (s, 6 H, OMe), 1.99 (s, 3 H, Me), 1.55 (s, 9 H, ^{t}Bu).

Synthesis of [Pd(O^1,N^1,C^2-L$_{Xy}$)Cl] (7**a**)**.** To a solution of **1** (104.6 mg, 0.30 mmol) in $CHCl_3$ (15 mL) was added XyNC (47.1 mg, 0.36 mmol). The pale yellow solution was stirred for 10 days to give a orange solution that was concentrated to dryness. The resulting solid was purified by preparative TLC chromatography using silica gel (70–200 mm) with CH_2Cl_2/Et_2O (7:1) as eluent. The yellow fraction at R_f = 0.26 was collected and extracted with acetone (3 x 20 mL) to give a solution, which was concentrated to dryness. The residue was stirred with Et_2O (2 mL) and *n*-pentane (8 mL). The suspension was filtered, the solid washed with *n*-pentane and air-dried to give 7**a** as an orange solid. Yield: 98.3 mg, 68%. Mp: 180 °C dec. IR (cm^{-1}): ν(NH) 3321, ν(C=N, py) 1609, ν(C=O) 1566, ν(C=NH) 1504, ν(PdCl) 334. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.69 (dd, 1 H, H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 8.65 (br, 1 H, NH), 8.15 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.59 (dd, 1 H, H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.13-7.03 (m, ABC system, 3 H, Xy), 4.67 (s, 1 H, H1), 3.47 (s, 6H, MeO), 2.25 (s, 6H, Me, Xy) 1.92 (s, 3H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, $CDCl_3$): δ 181.9 (CO), 164.9 (C2), 158.2 (C7), 150.5 (C8), 140.0 (C4), 138.2 (C–N, Xy), 135.0 (*o*-*C*(Xy)), 128.3 (*m*-*C*(Xy)), 127.5 (*p*-*C*(Xy)), 126.2 (C3), 124.7 (C5), 108.5 (C6), 93.5 (C1), 52.2 (MeO), 26.3 (Me), 18.3 (Me, Xy). Anal. Calcd for $C_{20}H_{23}O_3N_2ClPd$: C, 49.91; H, 4.82; N, 5.82. Found: C, 49.91; H, 5.03; N, 5.74. Single crystals of 7**a** were obtained by slow diffusion of *n*-pentane into a $CHCl_3$ solution of 7**a**.

Synthesis of [Pd(O^1,N^1,C^2-L_{Bu})Cl] (**7b**). To a solution of **1** (69.6 mg, 0.20 mmol) in $CHCl_3$ (15 mL) was added ^{t}BuNC (924 μL, 226.2 mM $CHCl_3$ solution, 0.21 mmol). The yellow solution was refluxed for 16 h and the resulting solution was concentrated to dryness. The resulting solid was purified by means of silica gel (70–200 mm) preparative TLC chromatography using CH_2Cl_2/Et_2O (3:1) as eluent. The yellow fraction at R_f = 0.14 was collected and extracted with acetone (3 x 20 mL) and the solution was concentrated to dryness. The residue was stirred with Et_2O (2 mL) and *n*-pentane (8 mL). The suspension was filtered, the solid washed with *n*-pentane and air-dried to give **7b** as a yellow solid. Yield: 79.8 mg, 89%. Mp: 172-173 °C. IR (cm^{-1}): ν(NH) 3334, ν(C=N, py) 1607, ν(C=O) 1560, ν(C=NH) 1534, ν(PdCl) 321. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz), 8.13 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.63 (br, 1 H, NH), 7.55 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.2 Hz), 5.17 (br, 1 H, H1), 3.41 (s, 6H, MeO), 1.88 (s, 3H, Me), 1.42 (s, 9H, ^{t}Bu). ^{13}C{^{1}H} NMR (100.81 MHz, $CDCl_3$): δ 180.8 (br, CO), 164.8 (br, C2), 158.0 (C7), 150.6 (C8), 139.9 (C4), 126.0 (C3), 124.5 (C5), 108.0 (C6), 94.2 (C1), 55.6 (*C*Me$_3$), 52.1 (MeO), 29.1 (C*Me*$_3$), 26.1 (Me). Anal. Calcd for $C_{16}H_{25}O_4N_2ClPd$: C, 42.59; H, 5.58; N, 6.20. Found:C, 42.70; H, 5.35; N, 6.35.

Synthesis of trans-[Pd(C^2-L_{Xy})Cl(CNXy)$_2$]·1/4$CHCl_3$ (**8a**). To a cooled (0 °C) solution of **7a** (50.7 mg, 0.11 mmol) in $CHCl_3$ (7 mL) was added XyNC (29.0 mg, 0.22 mmol). The solution was stirred for 5 min and concentrated to dryness. The resulting residue was dissolved in Et_2O and *n*-pentane was added. The suspension was filtered, the solid washed with *n*-pentane and air-dried to give **8a** as a pale yellow solid. Yield: 69.2 mg, 85%. Mp: 125-126 °C. IR (cm^{-1}): ν(N≡C) 2175, ν(C=O) 1567, ν(PdCl) 285. ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.68 (br, 1 H, NH), 8.12 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz), 7.80 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.72 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz), 7.22 (s, 1 H, H1), 7.25-6.95 (m, 9H, Xy), 3.19 (s, 6H, MeO), 2.37 (s, 6H, Me, Xy^j), 2.32 (s, 12H, Me, Xy^o), 1.71 (s, 3H, Me). ^{13}C{^{1}H} NMR (100.81 MHz, $CDCl_3$): δ 180.1 (C2), 178.5 (CO), 158.9 (C7), 155.5 (C8), 141.4 (br, C≡N), 141.5 (C_{ipso}, Xy^j), 136.6 (C4), 136.2 (*o*-C, Xy^o), 134.7 (*o*-C, Xy^j), 130.3 (*p*-C, Xy^o), 128.4 (*m*-C, Xy^j), 128.0 (*m*-C, Xy^o), 126.7 (*p*-C, Xy^j), 122.3 (C5), 120.9 (C3), 102.5 (C1), 101.8 (C6), 49.0 (OMe), 23.2 (Me), 19.3 (Me, Xy^j), 18.7 (Me, Xy^o). Anal. Calcd for $C_{38.25}H_{41.25}N_4O_3Cl_{1.75}Pd$: C, 59.40; H, 5.38; N, 7.24. Found: C, 59.44; H, 5.13; N, 7.50.

Synthesis of trans-[Pd(C^2-L_{Xy})Cl(CN^tBu)$_2$]· 1/4$CHCl_3$ (**8b**). To a cooled (0 °C) solution of **7b** (24.8 mg, 0.06 mmol) in $CHCl_3$ (6 mL) was added ^{t}BuNC (531 μL, 226.2 mM, 0.12 mmol). The solution was stirred for 5 min at 0 °C and concentrated to dryness. The resulting residue was dissolved in Et_2O and *n*-pentane was added. The suspension was filtered, the solid washed with *n*-pentane and air-dried to give **8b** as a pale yellow solid. Yield: 32.6 mg, 91%. Mp: 127-128 °C. IR (cm^{-1}): ν(N≡C) 2208, ν(C=O) 1538, ν(PdCl) 290. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.96 (br, 1 H, NH), 8.02 (dd, 1 H, H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz,), 7.75 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.65 (dd, 1 H, H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 6.86 (s, 1 H, H1), 3.21 (s, 6H, MeO), 1.75 (s, 3H, Me), 1.64 (s, 9H, ^{t}Bu^j), 1.45 (s, 18H, ^{t}Bu^c). ^{13}C{^{1}H} NMR (100.81 MHz, $CDCl_3$): δ 178.3 (CO), 176.0 (C2), 158.6 (C7), 156.3 (C8), 136.4 (C4), 130 (m, C≡N), 121.8 (C3), 120.5 (C5), 101.9 (C6), 99.1 (C1), 58.5 (CNH), 53.0 (CMe_3^c), 49.1 (MeO), 31.3 (Me, ^{t}Bu^j), 29.8 (Me, ^{t}Bu^c), 23.3 (Me). Anal. Calcd for $C_{26.25}H_{41.25}N_4O_3Cl_{1.75}Pd$: C, 50.10; H, 6.61; N, 8.90. Found: C, 49.89; H, 6.57; N, 9.19.

Synthesis of [Pd(N^l,C^l-L)(O,O-acac)] (**9**)**.** To a solution of **1** (39.7 mg, 0.11 mmol) in $CHCl_3$ (8 mL), Tl(acac)[19] (34.3 mg; 0.11 mmol) was added. The suspension was filtered through Celite, and the filtrate was concentrated to dryness. The residue was crystallized from Et_2O (2 mL) and *n*-pentane (7 mL). The crystals were filtered off, washed with *n*-pentane and air-dried to give **9** as a yellow solid. Yield: 44.6 mg, 96%. Mp: 159-160 °C. IR (cm^{-1}): ν(C=O) 1673, ν(CO, acac) 1579, 1515. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.96 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.75 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.6 Hz), 7.64 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.6 Hz), 5.28 (s, 1 H, CH, acac), 3.43 (s, 2 H, H1), 3.25 (s, 6 H, OMe), 1.92 (s, 6H, Me, acac), 1.84 (s, 3 H, Me). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 192.9 (br, CO), 186.8 (br, CO, acac), 185.3 (br, CO, acac), 163.3 (C7), 160.3 (C8), 139.4 (C4), 124.8 (C5), 120.2 (C3), 101.2 (C6), 99.6 (CH, acac), 49.3 (OMe), 40.5 (C1), 27.2 (br, Me, acac), 26.7 (br, Me, acac), 24.4 (Me). Anal. Calcd for $C_{16}H_{21}NO_5Pd$: C, 46.44; H, 5.12; N, 3.39. Found: C, 46.32; H, 5.01; N, 3.44.

Synthesis of [Pd(C^l-L)Cl(bpy)] (**10**)**.** To a solution of **1** (17.9 mg, 0.05 mmol) in acetone (4 mL), bpy (8.0 mg, 0.05 mmol) was added. After stirring for 20 min, the suspension was

filtered and the resulting yellow solid was washed with acetone and air-dried to give **10**. Yield: 21.2 mg, 82%. Mp: 224-225 °C. IR (cm^{-1}): ν(C=O) 1608, ν(CN) 1580, ν(PdCl) 336. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 9.58 (d, 1 H, bpy, $^3J_{HH}$= 5 Hz), 9.14 (d, 1 H, bpy, $^3J_{HH}$= 5 Hz), 8.05 (m, 3 H, bpy + 1 H, py), 7.94 (d, 1 H, py, $^3J_{HH}$= 8 Hz), 7.76 (t, 1 H, H4, $^3J_{HH}$= 8 Hz), 7.70 (m, 2 H, bpy), 7.52 (t, 1 H, bpy, $^3J_{HH}$= 5 Hz), 3.59 (s, 2 H, CH_2), 3.15 (s, 6 H, MeO), 1.63 (s, 3 H, Me). Anal. Calcd for $C_{21}H_{22}N_3O_3ClPd$: C, 49.82; H, 4.38; N, 8.30. Found: C, 49.94; H, 4.41; N, 8.23.

Synthesis of [Pd(C^1-L)Cl(dbbpy)] 1/2H$_2$O (**11**)**.** To a solution of **1** (61.8 mg, 0.18 mmol) in CH_2Cl_2 (6 mL), dbbpy (4,4'-di-tert-butyl-2,2'-bipyridine, 47.5 mg, 0.18 mmol) was added. The resulting solution was stirred (5 min) and concentrated (1 mL). Addition of *n*-pentane (8 mL) gave a suspension that was cooled in the fridge (–4 °C) for 30 min, and filtered. The solid was washed with *n*-pentane and air-dried to give **11** as a pale yellow solid. Yield: 104.1 mg, 94%. Mp: 218-219 °C. IR (cm^{-1}): ν(C=O) 1642, ν(CN) 1614, 1583, 1545, ν(PdCl) 337. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (d, 1 H, dbbpy, $^3J_{HH}$= 6 Hz), 9.04 (d, 1 H, dbbpy, $^3J_{HH}$= 6 Hz), 7.99 (dd, 1 H, H5, $^3J_{HH}$= 8 Hz, $^4J_{HH}$= 2 Hz), 7.90 (d, 1 H, dbbpy, $^4J_{HH}$= 2 Hz), 7.87 (d, 1 H, dbbpy, $^4J_{HH}$= 2 Hz), 7.73 (t, 1 H, H4, $^3J_{HH}$= 8 Hz, $^4J_{HH}$= 2 Hz), 7.69 (dd, 1 H, H3, $^3J_{HH}$= 8 Hz, $^4J_{HH}$= 2 Hz), 7.66 (dd, 1 H, dbbpy, $^3J_{HH}$= 6 Hz, $^4J_{HH}$= 2 Hz), 7.43 (dd, 1 H, dbbpy, $^3J_{HH}$= 6 Hz, $^4J_{HH}$= 2 Hz), 3.69 (s, 2H, CH_2), 3.21 (s, 6H, MeO), 1.72 (s, 3H, Me), 1.45 (s, 9H, ^{t}Bu), 1.39 (s, 9H, ^{t}Bu). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$): δ 205.8 (CO), 163.6 (C, dbbpy), 163.2 (C, dbbpy), 158.7 (C7), 157.1 (C8), 156.3 (C, dbbpy), 153.9 (C, dbbpy), 151.9 (CH, dbbpy), 149.2 (CH, dbbpy), 136.4 (C4), 124.2 (CH, dbbpy), 123.2 (CH, dbbpy), 122.8 (C3), 121.3 (C5), 118.4 (CH, dbbpy), 117.6 (CH, dbbpy), 101.9 (C6), 49.2 (MeO), 35.4 (*C*Me$_3$), 30.3 (C*Me$_3$*), 30.2 (C*Me$_3$*), 23.7 (Me), 21.3 (C1). Anal. Calcd for $C_{29}H_{39}N_3O_{3.5}ClPd$: C, 55.51; H, 6.26; N, 6.70. Found: C, 55.68; H, 6.26; N, 6.63.

Synthesis of [Pd(N^1,C^1-L)Cl(PPh$_3$)] (**12**). To a cooled solution (0 °C) of **1** (35.4 mg, 0.10 mmol) in CH_2Cl_2 (5 mL) was added PPh_3 (26.5 mg, 0.10 mmol). The resulting yellow solution was stirred for 20 min and concentrated (1 mL). Addition of Et_2O (5 mL) gave a suspension; the solid was filtered off, washed with Et_2O and air-dried to give a mixture (60.9 mg) of **12**, **1** and **13** (90 : 5 : 5) that could not be separated. NMR data of **12**: ^{1}H (300 MHz, $CDCl_3$): δ 7.95

(t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.86 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.76-7.41 (m, 16 H, H5 or H3 + PPh_3), 3.30 (br, 6 H, OMe), 2.89 (br, 2 H, H1), 2.03 (s, 3 H, Me). $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ 36.8 (s).

Synthesis of trans-[Pd(C^1-L)Cl(PPh$_3$)$_2$] (**13**). To a cooled solution (0 °C) of **1** (59.3 mg, 0.17 mmol) in CH_2Cl_2 (8 mL) was added PPh_3 (90.6 mg, 0.35 mmol). The resulting yellow solution was stirred for 10 min and concentrated (1 mL). Addition of Et_2O (2 mL) and *n*-pentane (8 mL) gave a suspension; the solid was filtered off, washed with *n*-pentane and air-dried to give **13** (140.3 mg) contamined with a product containing PPh_3 that we could not remove. NMR data of **13:** ^1H (300 MHz, $CDCl_3$), δ 7.94 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.82 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.80-7.40 (m, 16 H, H5 or H3 + PPh_3), 3.45 (br, 2 H, H1), 3.20 (br, 6 H, OMe), 1.68 (s, 3 H, Me); $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$), δ 23.8 (s).

Synthesis of C$_5$H$_3$N{C(O)Me-2}{C(OMe)$_2$Me-6} (**14**). To a solution of **1** (15.2 mg, 0.04 mmol) in $CDCl_3$ (0.8 mL) in a NMR tube PPh_3 (57.7 mg, 0.22 mmol) was added. After 5 min at room temperature, a ^1H NMR spectrum was recorded showing signals that we assign to **14**. In addition, $^{31}P\{^1H\}$ NMR showed resonances due to $[Pd(PPh_3)_4]$ and its dissociation products $[Pd(PPh_3)_3]$ and PPh_3. **14** could not be purified by recrystallization becuase of the excess of PPh_3; TLC chromatography in silica gel led to hydrolysis to give dap. ^1H NMR (400 MHz, $CDCl_3$) of **14**: δ 7.94 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1 Hz), 7.85 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1 Hz), 7.80 (t, 1 H, H4, $^3J_{HH}$ = 7.4 Hz), 3.21 (s, 6 H, OMe), 2.75 (s, 3H, Me), 1.71 (s, 3 H, Me).

X-ray Structure Determinations. Complexes **2**, **5a**, **6a** and 7**a** were measured on a Bruker Smart APEX diffractometer and **1** on an Oxford Diffraction Nova O diffractometer. Data were collected in ω scan mode using monochromated Mo *K*α radiation for **2**, **5a**, **6a** and 7**a** and mirror-focussed Cu *K*α radiation (α = 1.54184 Å) for **1**. Absorption corrections were applied on the basis of multiscans (program SADABS for **2**, **5a**, **6a** and 7**a** and CrysAlis RED for **1**). All structures were refined anisotropically on F^2 using the program SHELXL-97.[20] NH

hydrogens were refined freely, but with a DFIX restraint to the NH distance in **5b**. The ordered methyl groups were refined as rigid groups (AFIX 137), and the other hydrogens were refined using a riding model. *Special features and exceptions*: for complex **5b** the absolute structure parameter is -0.006(16).[21] The $C(OMe)_2Me$ group of one of the molecules is disordered over two positions, (*ca* 67:33%).

Table 1. Crystal data and structure refinement of complexes 1, 2, 5b, 6a and 7a.

Complex	**1**	**2**	**5b**	**6a**	**7a**
formula	$C_{11}H_{14}ClNO_3Pd$	$C_{13}H_{22}Cl_3NO_4Pd$	$C_{21}H_{32}ClN_3O_3Pd$	$C_{20}H_{23}ClN_2O_3Pd$	$C_{20}H_{23}ClN_2O_3Pd$
Fw	350.08	469.07	516.35	481.25	481.25
Temp (K)	103(2)	100(2)	100(2)	100(2)	100(2)
Crystal system	*P2√c*	*P -1*	*P c a 2₁*	*P2√n*	*P -1*
Space group	monoclinic	triclinic	orthorhombic	monoclinic	triclinic
a (Å)	9.6781(3)	9.6256(11)	17.7339(13)	8.9235(8)	9.5126(8)
b (Å)	9.8431(3)	9.9998(11)	16.8224(12)	13.3711(9)	9.9473(8)
c (Å)	13.6170(4)	11.0056(12)	16.5342(12)	17.1832(9)	11.0615(8)
α (deg)	90	101.138(2)	90	90	85.846(2)
β (deg)	107.968(2)	99.345(2)	90	104.841(2)	84.091(2)
γ (deg)	90	115.648(2)	90	90	84.091(2)
Volume (Å^3)	1233.92(6)	900.00(17)	4932.6(6)	1981.9(2)	95.55(13)
Z	4	2	8	4	2
ρ_{calcd}(Mg m^{-3})	1.884	1.731	1.391	1.613	1.674
μ (mm^{-1})	14.109(Cu*K*α)	1.490 (Mo *K*α)	0.885 (Mo *K*α)	1.094 (Mo *K*α)	1.135 (Mo *K*α)
F(000)	696	472	2128	976	488
crystal size (mm)	0.18x0.15x 0.10	0.18x0.07x0.05	0.27x0.14x0.08	0.25x0.19x0.13	0.25x0.17x0.10
θ range (deg)	5.65 to 71.17	1.96 to 28.17	1.67 to 28.61	1.96 to 28.15	2.01 to 28.19
no. of rflns coll	17199	10399	57505	22209	10968
no. of indep rflns /R_{int}	2255/0.0195	4013/0.0202	11843/0.0289	4564/0.00190	4257/0.0146
Transmissn	1.000 - 0.5095	0.9292 - 0.7752	0.9326 - 0.8175	0.8709 - 0.8181	0.8949 - 0.7613
restrs/parmters	0 / 157	0 / 209	13 / 541	0 / 249	0 / 253
Goodness-of-fit on F^2	1.108	1.074	1.135	1.055	1.074
*R*1 ($I>2\sigma(I)$)	0.0194	0.0254	0.0317	0.0197	0.0215
*wR*2 (all reflns)	0.0502	0.0553	0.0716	0.0527	0.0538
L.diff.Peak/hole (e. Å^{-3})	0.852/-0.750	0.536/-0.750	0.836/-0.475	0.422/-0.595	1.236/-0.480

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Section II.2: Synthesis and Hydrolysis of Cationic 2,6-Diacetylpyridine Dimethylketal Palladium(II) Complexes. The Cyclopalladation of 2,6-Diacetylpyridine. Palladium-Catalyzed Synthesis of a 1,5-Benzodiazepine

ABSTRACT

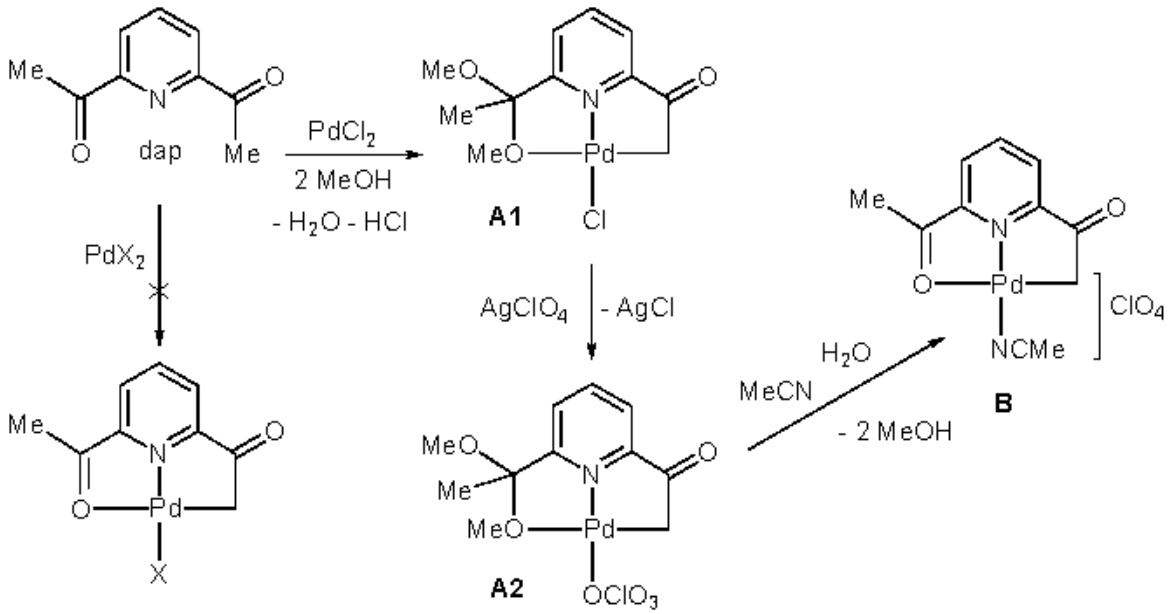
The complex [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)($OClO_3$)] (L = monoanionic ligand resulting from deprotonation of the acetyl group of the dimethylmonoketal of 2,6-diacetylpyridine) reacts (1) with phosphines to give [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)(PPh_3)]ClO_4, [Pd($N^{\prime}$,$C^{\prime}$-L)(dppm)]ClO_4 (dppm = bis(diphenylphosphino)methane), [Pd_2($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)$_2$(μ-dppm)]$(ClO_4)_2$; (2) with N-donor ligands to afford [Pd($N^{\prime}$,$C^{\prime}$-L)(dbbpy)]ClO_4 (dbbpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine), [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)(NCMe)]ClO_4, [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)($NH_2CH_2C_6H_4$OMe-4)]ClO_4, [Pd($N^{\prime}$,$C^{\prime}$-L)(*N*,*N*-$NH_2C_6H_4NH_2$-2)]ClO_4·0.5H_2O, which in acetone gives the benzodiazepine complex [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)(Bzdiaz)]ClO_4 (Bzdiaz = 2',2',4'-trimethyl-2',3'-dihydro-1-H-1',5'-benzodiazepine); (3) with CO to give [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)(CO)]ClO_4 and (4) with RNC to afford [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)(CNR)]ClO_4 (R = ^{t}Bu, Xy), *cis*-[Pd($N^{\prime}$,$C^{\prime}$-L)(CN^tBu)$_2$]ClO_4 or [Pd($C^{\prime}$-L)$(CNR)_3$]ClO_4. The ligand L of some of the above complexes hydrolyzes to give their homologues, for example, [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L')(PPh_3)]ClO_4 (L' = monoanionic ligand resulting from the deprotonation of one acetyl group of 2,6-diacetylpyridine), [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L')(NCMe)]ClO_4 (**B**) and [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L')(CN^tBu)]ClO_4. The 2,6-diacetylpyridium perchlorate, (Hdap)ClO_4, reacts with one equiv of $Pd(OAc)_2$ in MeCN or THF to afford **B** or [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L')(OH_2)]ClO_4, respectively. The crystal structures of **B** and [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)(CNXy)]ClO_4 have been determined.

INTRODUCTION

Pd(II) ketonyl compounds of the type [Pd]$CH_2C(O)R$,[1-3] are interesting because of their stability, reactivity, and role as intermediates in organic synthesis.[4] We have reported the synthesis and/or reactivity of ketonyl derivatives of other metals, as Pt,[2, 5] Au,[6] Hg[3, 5] and Tl.[7] In this context, we have recently described our attempts to prepare ketonyl Pd(II) complexes derived from 2,6-diacetylpyridine (dap; Scheme 1);[8] however, as a result of the low nuclephilicity of this ligand, owing to the electronwithdrawing nature of the two acetyl groups, all attempts were unsuccessful. It was only after the ketalization of one these groups that the metalation of the other could be observed. Both processes occurred when the reaction was carried out between $PdCl_2$ and dap in refluxing MeOH, which allowed to isolate the pincer complex [Pd($O^{\prime}$,$N^{\prime}$,$C^{\prime}$-L)Cl] (**A1**; Scheme 1),[8] where L is the monoanionic ligand resulting from deprotonation of the acetyl methyl group of the monoketal of 2,6-diacetylpyridine. Complex **A1** has allowed us to isolate some homologues[8] and the first family of Pd(IV) pincer

complexes [Pd($O^{\wedge}$,$N^{\wedge}$,$C^{\wedge}$-L)X_3] (X = Cl, Br,[9] I[10]). Recently, we have reported the first oxidative addition of an aryl halide to a palladium(II) complex, which led to the synthesis of the Pd(IV) complex [Pd($O^{\wedge}$,$N^{\wedge}$,$C^{\wedge}$-L)(C,O-$C_6H_4CO_2$-2)I].[11] The latter and the Pd(II) derivatives [Pd($O^{\wedge}$,$N^{\wedge}$,$C^{\wedge}$-L)(OAc)],[11] [Pd($O^{\wedge}$,$N^{\wedge}$,$C^{\wedge}$-L)($OClO_3$)] (**A2**; Scheme 1) and [Pd($O^{\wedge}$,$N^{\wedge}$,$C^{\wedge}$-L')(NCMe)]ClO_4 (**B**; L' = monoanionic ligand resulting from the deprotonation of one acetyl group of 2,6-diacetylpyridine; Scheme 1) were shown to be precatalysts for some room temperature Heck-type reactions.[12] In the study of these reactions, we provided the first clear evidences of a Pd(II)/Pd(IV) catalytic cycle,[11, 12] kinetic data proving that **B** was the best precatalyst and a method for the isolation of complex **B** from the catalytic mixture. This surprised us because we unfruitfuly attempted to prepare homologues of B directly from palladium salts and dap (Scheme 1).

The above results recognized the great interest of the pincer complexes containing the ligands L and L' and, at the same time, the need for further work to prepare and study the reactivity of **A** and **B** derivatives. In particular, we set out to find a more direct synthesis of **B**, from which derivatives could easily be prepared by replacing MeCN. In this paper, we report (1) the preparation of a family of cationic derivatives of **A2**, some of which hydrolyze to give **B** and some of its derivatives, and (2) a rationale synthesis of **B**, from dap and $Pd(OAc)_2$, as well as its X-ray crystal structure.



Scheme 1

RESULTS AND DISCUSSION

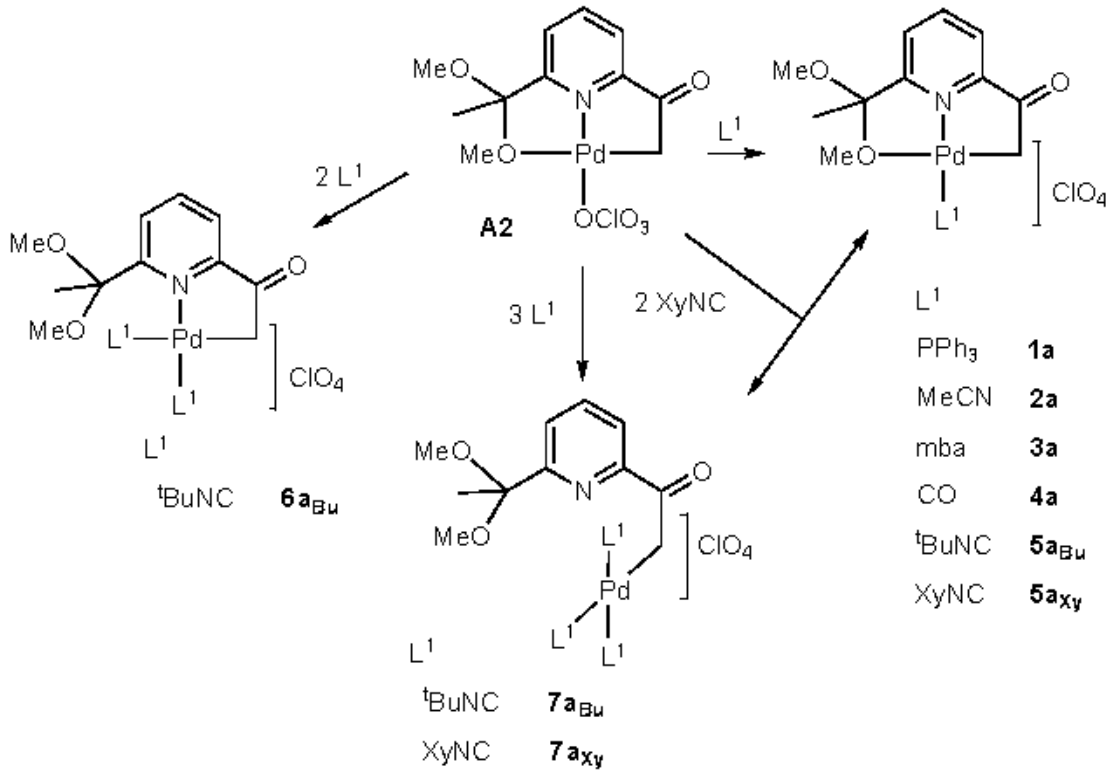
Synthesis of Cationic Complexes from [Pd(O^1,N^1,C^1-L)($OClO_3$)] (A2). In the course of the study of the Heck olefination of 2-iodobenzoic acid in acetone using **A2** as precatalyst,[12] we observed the formation of the cationic solvento complex [Pd(*O,N,C*-L)(S)]ClO_4 (S = acetone) and its slow hydrolysis to give MeOH and [Pd(*O,N,C*-L')(S)]ClO_4 (L' = monoanionic ligand resulting from the deprotonation of one acetyl group of 2,6-diacetylpyridine). From the mixture resulting after the catalytic reaction, containing [Pd(*O,N,C*-L')(S)]ClO_4, we isolated [Pd(*O,N,C*-L')(NCMe)]ClO_4 (**B**) after addition of MeCN. As we did not observe this hydrolysis in solutions of the complex [Pd(O^1,N^1,C^1-L)Cl] (**A1**; Scheme 1) and its neutral homologues,[8] we concluded that the hydrolysis of [Pd(*O,N,C*-L)(S)]ClO_4 in acetone ocurred because of its cationic nature, *i.e.* the increase in the acidic character of the metal center favored the hydrolysis. This explains that our previous attempts to prepare cationic complexes from **A1** gave products that decomposed very easily at room temperature.

Therefore, to prepare the desired cationic complexes, we reacted P-, N- or C-donor neutral ligands with $CHCl_3$ or CH_2Cl_2 solutions of **A2** at short reaction times and temperatures around 0° C, in order to slow down the hydrolysis. In the case of the reaction with primary amines ($H_2NCH_2C_6H_4OMe$-6 = mba; *o*-phenylendiamine = pda) or with one equiv of XyNC, the greater stability of the resulting cationic complex allowed to carried it out at room temperature.

Monodentate ligands L^l reacted with **A2** affording complexes [Pd(O^l,N^l,C^l-L)L^l]ClO_4 (L^l = PPh_3 (**1a**), MeCN (**2a**), mba (**3a**), CO (**4a**), ^{t}BuNC (**5a$_{Bu}$**), XyNC (**5a$_{Xy}$**; Xy = $C_6H_3Me_2$-2,6); Scheme 2). One equiv of L^l was used to prepare **1a**, **3a**, **5a$_{Bu}$** or **5a$_{Xy}$**. Dissolution of solid **A2** in MeCN or bubbling CO during 15 min through a $CHCl_3$ solution of **A2**, sufficed to prepare **2a** or **4a**, respectively.

The reaction of **A2** with two equiv of RNC afforded [Pd(N^l,C^l-L)(CN^{t}Bu)$_2$]ClO_4 (**6a$_{Bu}$**) or equimolecular amounts of **5a$_{Xy}$** and [Pd(C^l-L)(CNXy)$_3$]ClO_4 (**7a$_{Xy}$**); however, using three equiv of RNC, only the complex [Pd(C^l-L)(CNR)$_3$]ClO_4 (R = ^{t}Bu (**7a$_{Bu}$**), Xy (**7a$_{Xy}$**)) was obtained. We have reported that **A1** reacts with isocyanides giving, at low temperature, neutral complexes resulting from coordination and insertion of RNC into the Pd–C bond. When the temperature was raised, a tautomerization process from *β*-ketoimine to *β*-ketoenamine took place.[8] This represents a significant difference with respect to the reactions with cationic **A2**

that we attribute to a reinforcement of the Pd–C bond in the cationic complexes that prevents the insertion reaction. Recently, a similar behavior has been reported in the migratory insertion of allyl groups across the Pd–C bond in Pd(II) isocyanide complexes.[13]

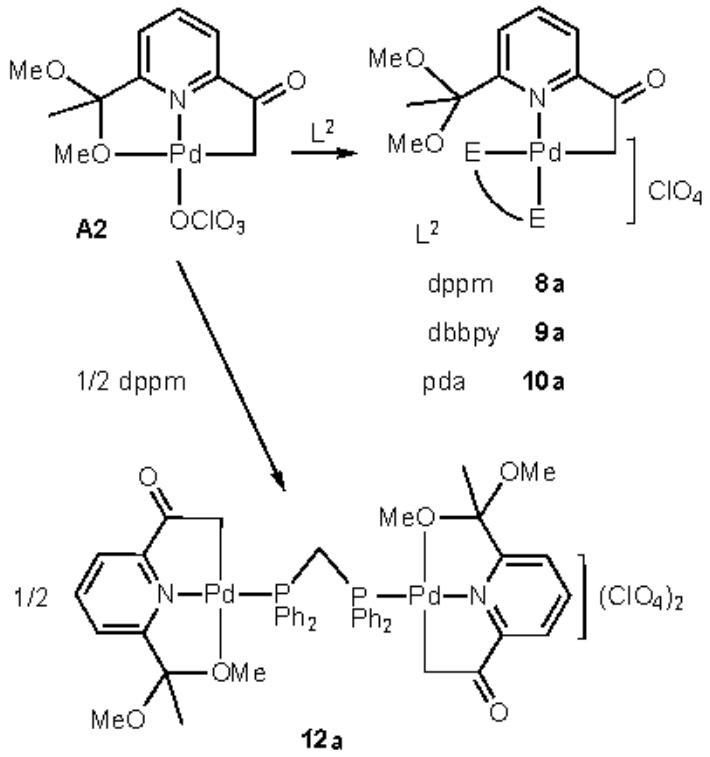


Scheme 2

One equiv of a bidentate ligand L^2 gave complexes $[Pd(N^1,C^1\text{-}L)L^2]ClO_4$ (L^2 = bis(diphenylphosphino)methane = dppm (**8a**), 4,4'-di-*tert*-buty-2,2'-bipyridine = dbbpy (**9a**), *o*-phenylendiamine = pda (**10a**); Scheme 3]. When a 2:1 molar ratio between **A2** and dppm was used, the dinuclear complex $[Pd_2(O^1,N^1,C^1\text{-}L)_2(\mu\text{-dppm})](ClO_4)_2$ (**12a**) was obtained.

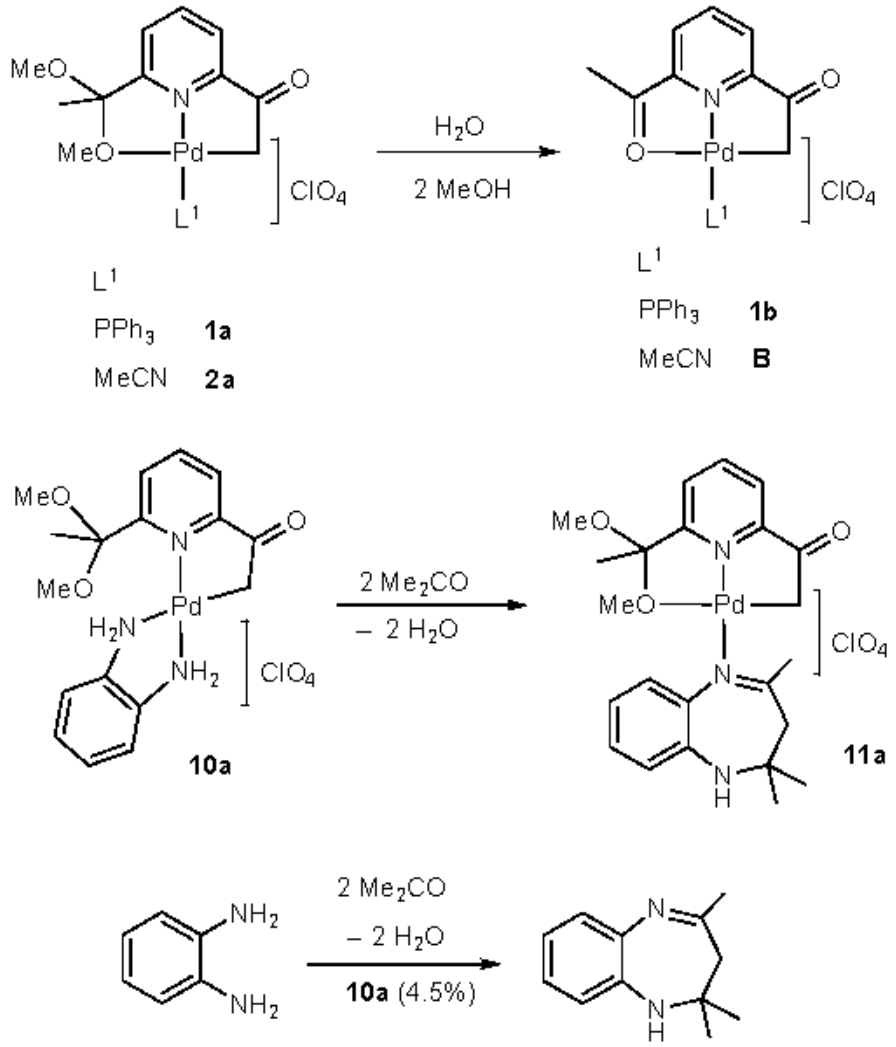
Reactivity of Cationic Complexes. Most of these cationic complexes are stable at room temperature in the solid state (exceptions are complexes $7a_{Bu}$, $7a_{Xy}$ and **4a** that have to be stored at approx. -30 °C) but, with the exception of **3a** and **10a**, hydrolyze in open-to-air solutions. In most cases this hydrolytic process affords an irresolvable mixture of products but in the rest, a clean and slow hydrolysis of the cationic complex was observed. Thus, when a solution of **1a** in $CHCl_3$ was stirred for 24 h at room temperature, $[Pd(O^1,N^1,C^1\text{-}L')(PPh_3)]ClO_4$ (**1b**; Scheme 4) was quantitatively isolated as a stable compound in the solid state and in

solution. Similarly, a solution of **2a** in $CHCl_3$ led after 15 days at room temperature to **B** (95% yield). In solution, the carbonyl complex **4a** hydrolyzes, loses CO and decomposes giving Pd metal. The hydrolysis of $\mathbf{5a_{Bu}}$ was followed by ^{1}H NMR in $CDCl_3$. After 3 days, only $\mathbf{5b_{Bu}}$ was observed but it could not be isolated analytically pure from this solution.



Scheme 3

Complex **10a** is insoluble in $CHCl_2$ or $CHCl_3$. When a solution of **10a** in acetone was stirred for 4 days at room temperature, the condensation of the amine ligand with the solvent occurred to give in good yield (85%) the complex [Pd(O^1,N^4,C^4-L)(Bzdiaz)]ClO_4 (**11a**; Bzdiaz = 2',2',4'-trimethyl-2',3'-dihydro-1-H-1',5'-benzodiazepine coordinated through N5'; Scheme 4) which is stable in the solid state and does not hydrolyze in open-to-air solutions . As far as we know, only a few 1,5-benzodiazepine complexes have been reported,[14-16] some of which have been used as catalysts in ethylene oligomerization and polymerization.[16] Only one is a palladium complex[14] and all have been obtained by reacting a metal complex with Bzdiaz. Therefore, **11a** represents the first example of a 1,5-benzodiazepine complex obtained by attack of a ketone to the coordinated diamine.



Scheme 4

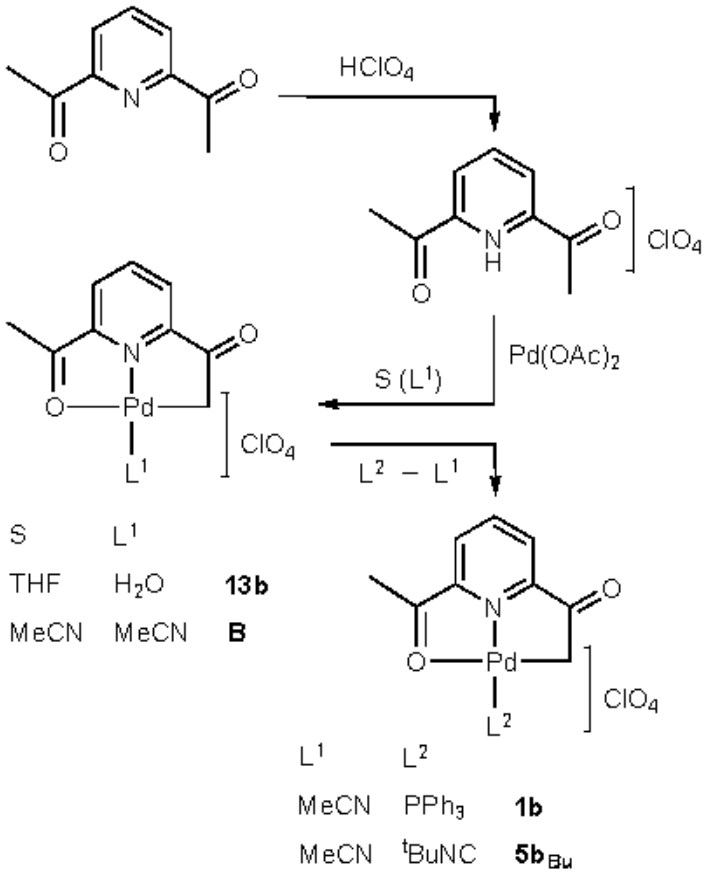
We have studied complex **10a** as a catalyst for the reaction between pda and acetone. Thus, an acetone solution of *o*-phenylidenediamine, in the presence of 4.5% of **10a**, gave quantitatively Bzdiaz, after 5 days at room temperature (Scheme 4). In the absence of the catalyst, the reaction afforded only traces of Bzdiaz after 24 h and a mixture, which major component was Bzdiaz, after 10 days. The most general method for the synthesis of 1,5-benzodiazepines involves the condensation of *o*-pheneylenediamine with α,β-unsaturated carbonyl compounds, β-haloketones or ketones. Many catalysts have been reported in the literature for this reaction.[17] Antineuroinflammatory effects, anxiolytic activity and cytotoxic activity against human cancer have been reported.[18]

We have described the synthesis of stable neutral complexes containing the [Pd](O^I,N^I,C^I-L), [Pd](N^I,C^I-L), [Pd](C^I-L) moieties.[8] However, all attempts to isolate the

corresponding complexes with the hydrolyzed L' ligand by reaction the stable $O^{\prime},N^{\prime},C^{\prime}$-L' complexes with neutral ligands were unfruitfull. Thus, the reaction of a $CDCl_3$ solution of **5b**$_{Bu}$ with one equiv of ^{t}BuNC did not afford **6b**$_{Bu}$ but metallic palladium and a complex mixture of products in which non coordinated 2,6-diacetylpyridine was identified. The same result was observed when **B** was reacted with one equiv of bpy (2,2'-bipyridine) or dbbpy or two equiv of ^{t}BuNC (to prepare 7**b**$_{Bu}$). We have attempted to find an explanation for this behavior using DFT calculations and find that **6b**$_{Bu}$ and 7**b**$_{Bu}$ were stable complexes. Therefore, the decomposition of some of these species must afford even more stables compounds, which must be responsible for their decomposition. Unfortunately, the unknown nature of the decomposition products prevented us from completing the calculation of the entire process.

The Palladation of dap. Synthesis of B and Related Complexes. Once we realized that complexes **B** and **1b**, obtained by hydrolysis from the cationic ketal derivatives, were stable and isolable complexes, we planned to retry the palladation of dap. As we were aware that the low nucleophilicity of dap prevents it to coordinate to Pd, which is essential to assist the palladation, we decided to try the reaction between 2,6-diacetylpyridininium perchlorate, $(dapH)ClO_4$, with $Pd(OAc)_2$ in a weakly coordinating solvent, S. In this way, we generated dap and a highly electrophilic palladium compound potentially able to coordinate dap ("$Pd(OAc)(ClO_4)(S)_n$"), which, in addition, has a basic ligand (OAc) to deprotonate it. Thus, the reaction of a THF suspension of $(dapH)ClO_4$ with one equiv of $Pd(OAc)_2$ gave $[Pd(O^{\prime},N^{\prime},C^{\prime}$-L')$(OH_2)]ClO_4$ (**13b**; Scheme 5) in almost quantitative yield (98%), which decomposes at room temperature in the solid state or in acetone solution but can be stored in the solid state without decomposition at 4 °C, under N_2. When this reaction was carried out in MeCN, **B** was isolated in 94% yield. The same synthetic strategy has been recently applied to prepare orthopalladated primary and sencondary amines, which had been previously obtained by more complex methods or in lower yields.[19]

Complex **B**, which is stable in the solid state and in solution, is the best starting material for the synthesis of other palladated derivatives of 2,6-diacetylpyridine. Thus, the best way to prepare **1b**, which was first prepared from **1a** (Scheme 4), is the reaction of **B** with PPh_3 (Scheme 5). In some case, this is the only way, for example, although solutions of complex **5a**$_{Bu}$ lose spontaneously MeOH at room temperature, it was not possible isolate pure complex **5b**$_{Bu}$; however, it can be prepared, with 89% yield, by reacting **B** with one equiv of ^{t}BuNC.



Scheme 5

Crystal Structures. The crystal structures of complexes **B** (Figure 1), and $\mathbf{5a_{Xy}}$ (Figure 2) have been determined by X-ray diffraction (Table 1). Both show a nearly square-planar coordination around the palladium atom (mean deviation from the coordination plane: 0.0313 and 0.0292 Å for **B** and $\mathbf{5a_{Xy}}$, respectively). In complex **B**, the py ring and the palladacycles PdNCCO and PdNCCC are almost coplanar (the angles between the mean planes are 2.9° and 5.0°, respectively) suggesting some electronic delocalization involving the pyC(Me)CO groups. The molecules are connected by Pd···Pd (3.2179(3) Å) contacts (van der Waals radii of Pd: 2.05 Å)[20] giving dimers with an inversion center. These dimers are connected through C(11)–H(11A)···O(1) interactions giving chains along the *c* axis. Anions and cations are connected by two non-classical hydrogen bonds C–H···O giving all together a complex 3D network. Both C–O distances are significantly different (1.207(3) and 1.232(2) Å), being longer the one corresponding to the carbonyl group bonded to palladium. The electronic delocalization involving the pyC(Me)CO group forces the Pd–O bond distance (2.2711(14) Å) being longer than in $\mathbf{5a_{Xy}}$ (2.2028(14) Å), in which, as expected, the PdNCCO ring is not planar (Figure 2),

being the O(1) atom –0.3286 Å and C(8) +0.2157 Å out of the plane formed by the pyridyl ring and the palladium atom (mean deviation 0.0385 Å). In $\mathbf{5a}_{Xy}$, the XyNC ligand is almost coplanar with the pyridine ring (the angle between both planes is 11.3°). Anions and cations are connected by two non-classical C–H···O_4 hydrogen bonds, giving centro-symmetric dimers. The cations are also connected between them by a non clasical C(9)–H(9A)···O(3) hydrogen bond giving another centro-symmetric dimer. All these non-clasical hydrogen bonds produce a double chain. The Pd–N(1) bond distance is longer in $\mathbf{5a}_{Xy}$ (1.9939 (17) Å) than in **B** (1.9705(16) Å), showing the greater trans influence of the C- than the N-donor ligand.

Spectroscopic Properties. The low stability of some complexes in solution prevented from recording their $^{13}C\{^1H\}$ spectra. The protons of CH_2 and MeO groups in those complexes in which the ketal group is coordinated, **1a–5a**, **11a** and **12a**, are equivalent at room temperature because of a fast exchange between both MeO groups.[8-11] This equivalence is maintained in the other complexes in which the ketal group is not coordinated because a swinging motion of the group must confer to the molecule a symmetry plane. The isocyanides in complexes $\mathbf{6a}_{Bu}$ and **7a** are equivalents probably because the neutral ligands are involved in dissociation/reassociation processes such as shown in Scheme 6.

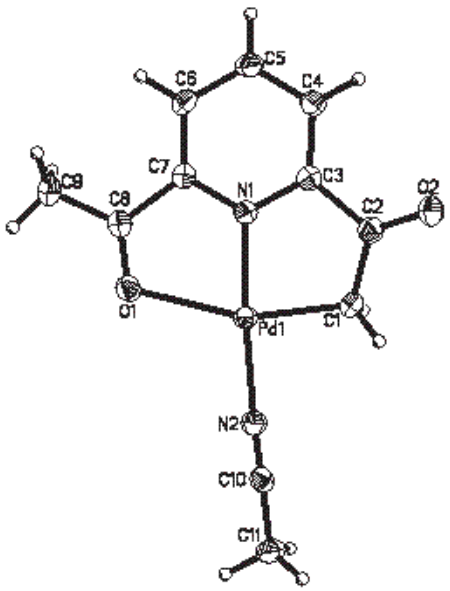


Figure 1. Ellipsoid representation of **B** (50% probability). Selected bond lengths (Å) and angles (deg): Pd(1)-N(1) 1.9705(16), Pd(1)-N(2) 2.0072(17), Pd(1)-C(1) 2.012(2), Pd(1)-O(1) 2.2711(14), Pd(1)-Pd(1)#1 3.2179(3), N(1)-C(7) 1.343(2), C(7)-C(8) 1.501(3), O(1)-C(8) 1.232(2), O(2)-C(2) 1.207(3), N(1)-Pd(1)-C(1) 83.25(7), N(2)-Pd(1)-C(1) 91.95(8), N(1)-Pd(1)-O(1) 76.08(6), N(2)-Pd(1)-O(1)

108.39(6), C(8)-O(1)-Pd(1) 111.55(12), O(1)-C(8)-C(7) 118.22(17), N(1)-C(7)-C(8) 113.47(17), C(7)-N(1)-Pd(1) 120.35(13).

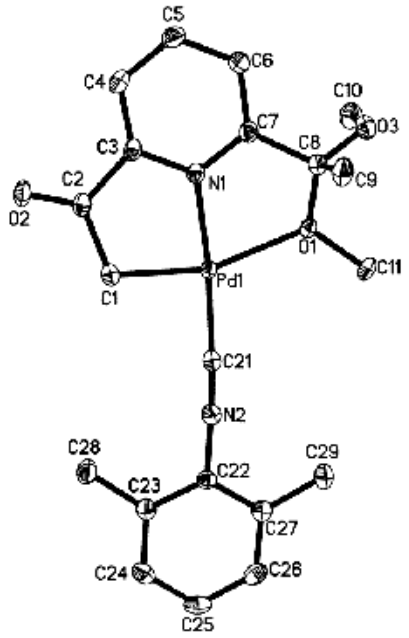
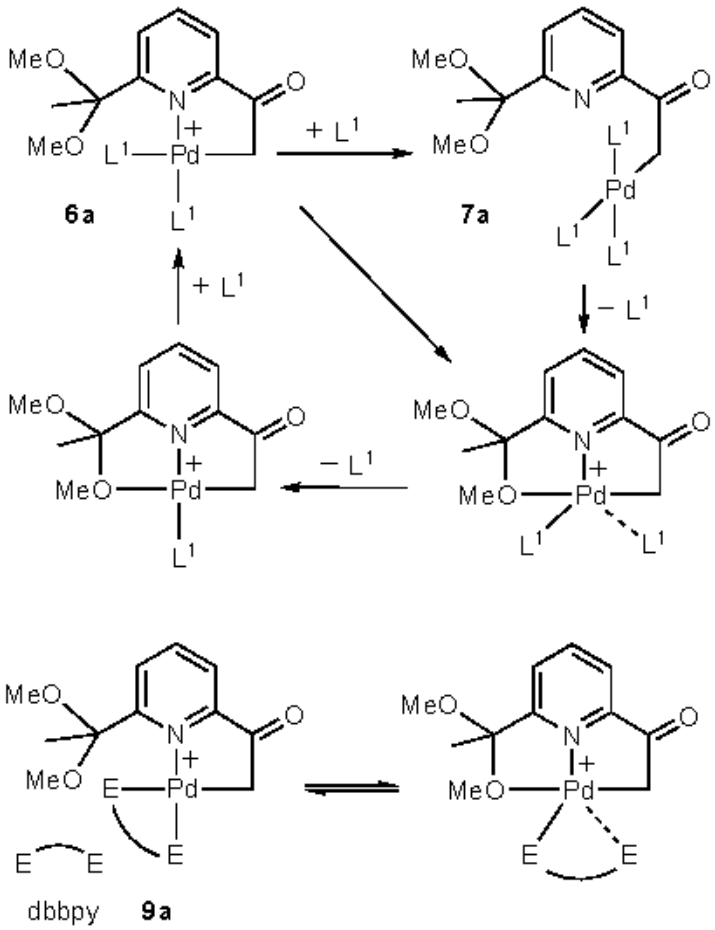


Figure 2. Ellipsoid representation of $\mathbf{5a_{Xy}}$ (50% probability). Selected bond lengths (Å) and angles (deg): Pd(1)-C(21) 1.937(2), Pd(1)-N(1) 1.9939(17), Pd(1)-C(1) 2.016(2), Pd(1)-O(1) 2.2028(14), N(1)-C(7) 1.336(3), C(7)-C(8) 1.527(3), O(1)-C(8) 1.461(2), O(2)-C(2) 1.213(2), C(21)-Pd(1)-C(1) 91.24(8), N(1)-Pd(1)-C(1) 83.42(8), N(1)-Pd(1)-O(1) 76.22(6), C(21)-Pd(1)-O(1) 109.18(7), C(8)-O(1)-Pd(1) 112.24(11), O(1)-C(8)-C(7) 105.21(16), N(1)-C(7)-C(8) 116.37(18), C(7)-N(1)-Pd(1) 120.76(14).

The exchange of RNC ligands can be slowed down at –60 °C to see two types of isocyanides in the expected 1:1 ($\mathbf{6a_{Bu}}$) or 2:1 molar ratio (7a). A this temperature, $\mathbf{6a_{Bu}}$ gives two broad MeO resonances and a singlet for the CH_2 protons, $\mathbf{7a_{Bu}}$ a broad resonance including MeO and CH_2 protons and $\mathbf{7a_{Xy}}$ shows a singlet for MeO and another for CH_2 protons. Similarly, in the ^{1}H NMR spectrum of 9a at room temperature, the CH_2 group gives a broad resonance and each of the ^{t}Bu and MeO protons, a singlet, which suggests the existence of the fast equilibrium shown in Scheme 6. At –60 °C they resolve into two doublets (CH_2) and two pairs of singlets (^{t}Bu and MeO).

The IR spectra of all complexes show an absorption in the region 1652–1723 cm^{-1} corresponding to ν(CO) of the L or L' ligands. Complexes with L' ligands show also a band at lower frequency (range 1636–1705 cm^{-1}) assignable to ν(CO) of the coordinated carbonyl group; these data are in agreement with those obtained in the X-ray diffraction study of B (see above). The band due to ν(C≡O) in the carbonyl complex 4a appears at 2136 cm^{-1}, only

slightly lower than that in free CO (2143 cm^{-1}), which is a consequence of the cationic nature of this complex, that decreases the π-donor ability of the palladium atom.[21]



Scheme 6

CONCLUSIONS

Solutions of the complex [Pd($O^{\wedge}$,$N^{\wedge}$,$C^{\wedge}$-L)($OClO_3$)], where L is the monoanionic ligand resulting from deprotonation of the acetyl group of the dimethylmonoketal of 2,6-diacetylpyridine, have been used as starting material for the synthesis of cationic dimethylketal complexes with the L ligand acting as pincer, chelate ($N^{\wedge}$,$C^{\wedge}$-L) or terminal ($C^{\wedge}$-L). Complex [Pd($N^{\wedge}$,$C^{\wedge}$-L)(*N*,*N*-$NH_2C_6H_4NH_2$-2)]ClO_4, which reacts with acetone to afford the 1,5-benzodiazepine complex resulting from the condensation of *o*-phenylenediamine with two molecules of acetone, is a catalyst for the synthesis of such 1,5-benzodiazepine from *o*-phenylenediamine in acetone. Some of these complexes hydrolyze spontaneously to give

MeOH and the corresponding complexes with the pincer O^1,N^1,C^1-L' ligand (L' = monoanionic ligand resulting from deprotonation of one acetyl group of 2,6-diacetylpyridine). The complex [Pd(O^1,N^1,C^1-L')(NCMe)]ClO_4, which can also be prepared by metalation of 2,6-diacetylpyridine provides another way to prepare other complexes with the L' ligand.

EXPERIMENTAL SECTION

General Procedures.

Unless otherwise stated, the reactions were carried out without precautions to exclude light or atmospheric oxygen or moisture. Melting points were determined on a Reicher apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on a Bruker AC 200, or Avance 300 or 400 spectrometers. Chemical shifts were referred to TMS (^{1}H, ^{13}C) or H_3PO_4 (^{31}P). When needed, NMR assignments were performed with the help of APT, HMQC and HMBC techniques. Chart 1 shows the atom numbering used to name the ligands in NMR assignments. Complex [Pd(O^1,N^1,C^1-L)Cl] (**A1**) was prepared as reported previously.[8] $CHCl_3$ or CH_2Cl_2 solutions of [Pd(O^1,N^1,C^1-L)($OClO_3$)] (**A2**)[12] were obtained by reacting **A1** with excess of $AgClO_4$ and removing AgCl and the excess of $AgClO_4$.

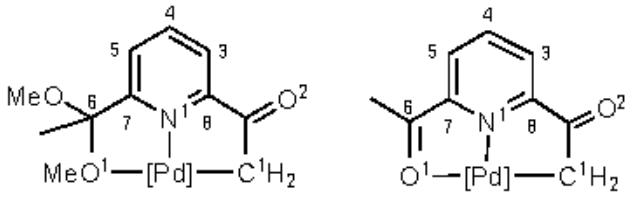


Chart 1

Synthesis

Synthesis of (Hdap)ClO_4. To a solution of 2,6-diacetylpyridine (1.95 g, 11.95 mmol) in Et_2O (40 mL) was slowly added $HClO_4$ (70%, 1.54 mL, 17.92 mmol). When the mixture reached room temperature it was filtered off. The resulting solid was washed with Et_2O and then recrystallized in acetone (6 mL)/Et_2O (30 mL) to give (Hdap)ClO_4 as a colorless solid.

Yield: 97%. Mp: 121-122 °C. IR (cm^{-1}): ν(C=O) 1723, ν(C=N) 1617, ν(N–H) 3234, 3205, 3186, ν(Cl–O) 1081. ^{1}H NMR (400 MHz, acetone-d_6): δ 9.10 (m, 1H, *p*-H), 8.95 (m, 2H, *m*-H), 2.93 (s, 6H, 2 Me). ^{1}H NMR (300 MHz, MeCN-d_3): δ 11.15 (br, 1H, NH), 9.14 (t, 1H, *p*-H, $^2J_{HH}$ = 7.8 Hz), 8.83 (d, 2H, *m*-H, $^2J_{HH}$ = 7.8 Hz), 2.87 (s, 6H, Me). ^{13}C NMR (75.45 MHz, MeCN-d_3): δ 190.9 (s, CO), 153.5 (s, *p*-C), 143.2 (s, *o*-C), 131.3 (s, *m*-C), 26.6 (s, Me). Anal. Calcd for $C_9H_{10}NO_6Cl$: C, 41.00; H, 3.82; N, 5.31. Found: C, 41.07; H, 3.96; N, 5.67.

Synthesis of [Pd(O^I,N^I,C^I-L')(NCMe)]ClO_4 (**B**). *Method a*. To a solution of (Hdap)ClO_4 (894.2 mg, 3.39 mmol) in MeCN (40 mL) was added $Pd(OAc)_2$ (761.5 mg; 3.39 mmol). The resulting solution was stirred for 40 min and then concentrated to dryness. The resulting oil was dissolved in acetone (20 mL) and then concentrated to dryness; this process was carried out twice. The resulting solid was stirred in Et_2O (2 x 40 mL) in a cooled (0 °C) bath until gave a suspension that was filtered off under N_2. The resulting solid was washed with Et_2O and dried under a N_2 stream giving an orange solid that was recrystallized in MeCN/Et_2O to give **B** as a spectroscopically pure solid.[12] Yield: 94%.

Method b. A solution of **2a** (19.9 mg; 0.04 mmol) in $CHCl_3$ (3 mL) was stirred for 15 days to give a suspension that was filtered off. The resulting solid was washed with Et_2O and air-dried to give **B** as an orange solid. Yield: 95%.

Synthesis of [Pd(O^I,N^I,C^I-L)(PPh_3)]ClO_4 (**1a**). A cooled (0 °C) solution of **A2** (from 0.05 mmol of **A1** and 0.16 mmol of $AgClO_4$ in 5 mL of $CHCl_3$) was stirred with PPh_3 (13.9 mg; 0.05 mmol) for 40 min and then concentrated (1 mL). Addition of Et_2O (5 mL) gave a suspension that was filtered off, and the solid washed with Et_2O and air-dried to give **1a** as a pale yellow solid. Yield: 89%. Mp: 115-116 °C. IR (cm^{-1}): ν(C=O) 1699, ν(C=N) 1600, ν(Cl-O) 1094. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.94 (m, 1 H, H3), 7.84 (m, 1 H, H5), 7.78-7.68 (m, 6 H, PPh_3), 7.62-7.50 (m, 9 H, PPh_3), 3.19 (d, 2 H, CH_2, $^3J_{HP}$ = 4 Hz), 3.05 (s, 6 H, OMe), 1.88 (s, 3 H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, $CDCl_3$): δ 200.8 (s, CO), 157.1 (s, C7), 150.8 (d, $^3J_{CP}$ = 2 Hz, C8), 142.5 (s, C4), 134.0 (d, $^2J_{CP}$ = 13 Hz, *o*-*C*H, PPh_3), 132.1 (d, $^4J_{CP}$ = 3 Hz, *p*-*C*H, PPh_3), 129.5 (d, $^3J_{CP}$ = 11 Hz, *m*-*C*H, PPh_3), 127.5 (d, $^1J_{CP}$ = 51.5 Hz, C_{ipso}), 127.3 (d, $^4J_{CP}$ = 3 Hz, C5), 124.2 (s, C3), 109.2 (s, C6), 52.5 (s, OMe), 41.1

(d, $^{2}J_{CP,\,cis}$ = 5.3 Hz, CH_2), 25.2 (s, Me). $^{31}P\{^{1}H\}$ NMR (162.29 MHz, $CDCl_3$): δ 30.85. Anal. Calcd for $C_{29}H_{29}NO_7ClPPd$: C, 51.50; H, 4.32; N, 2.07. Found: C, 51.15; H, 4.45; N, 2.36.

Synthesis of [Pd(O^{I},N^{II},C^{I}-L')(PPh$_3$)]ClO$_4$·H$_2$O **(1b).** *Method a.* To a solution of [Pd(dap)(NCMe)]ClO_4 (**B**) (61.2 mg; 0.15 mmol) in acetone (12 mL) was added PPh_3 (39.3 mg; 0.15 mmol). The solution was stirred for 15 min and then concentrated (2 mL). Addition of Et_2O (10 mL) gave a suspension that was stirred in cool bath (0 °C) for 10 min. The resulting suspension was filtered off, the solid washed with Et_2O and air-dried to give **1b** as an orange solid. Yield: 83%.

Method b. A solution of **1a** (10.0 mg; 0.02 mmol) in $CHCl_3$ (2 mL) was stirred for 24 h and then concentrated (1 mL). Addition of Et_2O (4 mL) gave a suspension that was stirred in cool bath (0 °C) for 10 min. The resulting suspension was filtered off, the solid washed with Et_2O and air-dried to give **1b** as an orange solid. Yield: 93%. Mp: 161-162 °C. IR (cm^{-1}): ν(C=O) 1708, 1636, ν(C=N) 1595, ν(Cl-O) 1095. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (m, 1 H, H5), 8.52 (t, 1 H, H4, $^{3}J_{HH}$ = 8 Hz), 8.12 (m, 1 H, H3), 7.65-7.49 (m, 15H, PPh_3), 3.17 (d, 2 H, CH_2, $^{3}J_{HP}$ = 3.6 Hz), 3.07 (s, 3H, Me), 1.78 (s, 2 H, H_2O). $^{13}C\{^{1}H\}$ NMR (100.81 MHz, $CDCl_3$): δ 206.5 (s, C6), 200.5 (s, C2), 151.0 (d, C8, $^{3}J_{CP}$ = 2 Hz), 150.8 (d, C7, $^{3}J_{CP}$ = 2 Hz), 143.4 (s, C4), 133.9 (d, *o*-*C*H, PPh_3, $^{2}J_{CP}$ = 12.7 Hz), 132.4 (s, C3), 131.9 (d, *p*-*C*H, PPh_3, $^{4}J_{CP}$ = 2.4 Hz), 129.4 (d, *m*-*C*H, PPh_3, $^{3}J_{CP}$ = 11.4 Hz), 128.3 (d, C_{ipso}, PPh_3, $^{1}J_{CP}$ = 52.2 Hz), 127.9 (s, C5), 40.6 (d, CH_2, $^{2}J_{CP,\,cis}$ = 4.8 Hz), 26.6 (s, Me). $^{31}P\{^{1}H\}$ NMR (162.29 MHz, $CDCl_3$): δ 29.92 (s, PPh_3). Anal. Calcd for $C_{27}H_{23}NO_6ClPPd{\cdot}H_2O$: C, 50.02; H, 3.89; N, 2.16. Found: C, 50.04; H, 3.60; N, 2.29.

Synthesis of [Pd(O^{I},N^{II},C^{II}-L)(NCMe)]ClO$_4$ **(2a).** A solution of **A2** (from 0.08 mmol of **A1** and 0.31 mmol of $AgClO_4$ in 4 mL of $CHCl_3$) was concentrated to dryness and the resulting solid was dissolved in MeCN (1 mL). After 5 min of stirring the solution was concentrated to dryness. The residue was vigorously stirred in Et_2O (5 mL), the resulting suspension was filtered off, and the solid washed with Et_2O and air-dried to give **2a** as a pale yellow solid. Yield: 88%. Mp: 126-127 °C. IR (cm^{-1}): ν(C≡N) 2295, ν(C=O) 1703, ν(C=N) 1600, ν(Cl–O) 1091. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.35 (t, 1 H, H4, $^{3}J_{HH}$ = 7.8 Hz), 7.86 (dd, 1 H, H5, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ =1.2 Hz), 7.77 (dd, 1 H, H3, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ =1.2 Hz), 3.58 (s, 2 H, CH_2),

3.49 (s, 6 H, OMe), 2.54 (br, 3 H, MeCN), 1.82 (s, 3H, Me). ^{13}C NMR (50.30 MHz, $CDCl_3$): δ 200.9 (s, CO), 158.6 (s, C7), 151.8 (s, C8), 142.6 (s, C4), 127.7 (s, C5), 124.4 (s, C3), 123.3 (br, Me*C*N), 107.9 (s, C6), 52.8 (s, OMe), 35.7 (s, CH_2), 25.0 (s, Me), 3.5 (s, NC*C*H$_3$). Anal. Calcd for $C_{13}H_{17}N_2O_7ClPd$: C, 34.30; H, 3.76; N, 6.15. Found: C, 34.22; H, 3.80; N, 6.05.

Synthesis of [Pd(O^I,N^I,C^I-L)(NH$_2$CH$_2$C$_6$H$_4$OMe-4)]ClO$_4$ (**3a**). To a solution of **A2** (from 0.26 mmol of **A1** and 0.51 mmol of $AgClO_4$ in 10 mL of CH_2Cl_2) was added *p*-metoxibenzylamine (33.4 μL; 0.26 mmol) to give an orange solution that was stirred for 30 min. Concentration (2 mL) and addition of Et_2O (15 mL) gave a suspension; the solid was filtered off, washed with Et_2O, and air dried to give **3a** as a pale orange solid. Yield: 138.1 mg, 97%. Mp: 125-126 °C. IR (cm^{-1}): ν(N–H) 3247, ν(C=O) 1694, ν(C=N) 1610, ν(Cl-O) 1030. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.80 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 7.61 (m, 3 H), 6.90 (m, 2 H), 3.87 (m, 2 H, NH_2), 3.78 (s, 3 H, MeO), 3.69 (m, 2 H, CH_2), 3.38 (s, 2 H, CH_2Pd), 3.18 (s, 6 H, OMe), 1.65 (s, 3 H, Me). ^{1}H NMR (200 MHz, acetone-d_6): δ 8.42 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.91 (dd, 1 H, H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 7.86 (dd, 1 H, H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 7.70 (m, 2 H, *o*-amine), 6.98 (m, 2 H, *m*-amine), 4.31 (br, 2 H, NH_2), 3.96 (m, 2 H, CH_2), 3.79 (s, 3 H, MeO), 3.45 (s, 2 H, CH_2Pd), 3.27 (s, 6 H, OMe), 1.72 (s, 3 H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, acetone-d_6): δ 202.7 (C2), 160.8 (*C*OMe), 159.0 (C7), 153.2 (C8), 142.8 (C4), 131.9 (*o*-CH), 131.6 (*C*–CH_2), 128.3 (C3), 124.4 (C5), 115.0 (*m*-CH), 108.8 (C6), 55.7 (*p*-OMe), 52.5 (OMe), 49.4 (CH_2NH_2), 34.0 (CH_2Pd), 25.1 (Me). Anal. Calcd for $C_{19}H_{25}N_2O_8ClPd$: C, 41.39; H, 4.57; N, 5.08. Found: C, 41.45; H, 4.64; N, 5.06.

Synthesis of [Pd(O^I,N^I,C^I-L)(CO)]ClO$_4$ (**4a**). A stream of CO was bubbled into a solution of **A2** (from 0.18 mmol of **A1** and 0.55 mmol of $AgClO_4$ in 3 mL of $CHCl_3$) during 15 min at atmospheric pressure and colorless needles crystallized. The solid was filtered off, washed with $CHCl_3$ and air-dried to give **4a**. Yield: 78%. Mp: 119-120 °C. IR (cm^{-1}): ν(C≡O) 2136, ν(C=O) 1709, ν(C=N) 1599. ^{1}H NMR (200 MHz, acetone-d_6): δ 8.62 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.14 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 8.10 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 4.04 (s, 2H, CH_2), 3.65 (s, 6H, OMe), 1.90 (s, 3H, Me). Anal. Calcd for $C_{12}H_{14}NO_8ClPd$: C, 32.60; H, 3.19; N, 3.17. Found: C, 32.41; H, 3.05; N, 3.20.

Synthesis of [Pd(O^I,N^I,C^I-L)(CN^{t}Bu)]ClO_4 (**5a$_{Bu}$**). To a cooled (0 °C) solution of **A2** (from 0.15 mmol of **A1** and 0.58 mmol of $AgClO_4$ in 5 mL of $CHCl_3$) was added ^{t}BuNC (645 µL, 226,2 mM solution, 0.15 mmol). The solution was stirred for 20 min at 0 °C and then concentrated to dryness. The residue was stirred in Et_2O (10 mL) at 0 °C for 15 min and then filtrated off. The resulting solid was washed with Et_2O and air-dried to give **5a$_{Bu}$** as a pale yellow solid. Yield: 89%. Mp: 114-115 °C. IR (cm^{-1}): ν(C≡N) 2213, ν(C=O) 1705, ν(C=N) 1600, ν(Cl-O) 1093. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.94 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.2 Hz), 7.83 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.2 Hz), 3.55 (s, 2 H, CH_2), 3.52 (s, 6 H, OMe), 1.84 (s, 3 H, Me), 1.62 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{16}H_{23}N_2O_7ClPd$: C, 38.65; H, 4.66; N, 5.63. Found: C, 38.97; H, 4.61; N, 5.61.

Synthesis of [Pd(O^I,N^I,C^I-L)(CNXy)]ClO_4 (**5a$_{Xy}$**). To a solution of **A2** (from 0.01 mmol of **A1** and 0.3 mmol of $AgClO_4$ in 3 mL of $CHCl_3$) a solution of XyNC (13.0 mg, 0.01 mmol) in $CHCl_3$ (1 mL) was added. The reaction mixture was stirred for 2 h and then concentrated (2 mL). The resulting solid was washed with $CHCl_3$ and air-dried to give **5a$_{Xy}$** as a colorless solid. Yield: 88%. Mp: 210-211 °C. IR (cm^{-1}): ν(C≡N) 2194, ν(C=O) 1703, ν(C=N) 1601, ν(Cl-O) 1080. ^{1}H NMR (400 MHz, acetone-d_6): δ 8.59 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.12 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 8.08 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.44 (m, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.29 (m, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 3.78 (s, 2 H, CH_2), 3.66 (s, 6 H, OMe), 2.52 (s, 6 H, Me, Xy), 1.93 (s, 3 H, Me). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.41 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.02 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.87 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.35 (m, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.24 (m, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 3.73 (s, 2 H, CH_2), 3.56 (s, 6 H, OMe), 2.48 (s, 6 H, Me, Xy), 1.88 (s, 3 H, Me). ^{1}H NMR (200 MHz, MeCN-d_3): δ 8.37 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.97 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.89 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.40 (m, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.28 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 3.65 (s, 2 H, CH_2), 3.50 (s, 6 H, OMe), 2.48 (s, 6 H, Me, Xy), 1.80 (s, 3 H, Me). Anal. Calcd for $C_{20}H_{23}N_2O_7ClPd$: C, 44.05; H, 4.25; N, 5.14. Found: C, 44.02; H, 4.21; N, 5.15. Single crystals were obtained by slow concentration of a solution of **5a$_{Xy}$** in CD_2Cl_2.

Synthesis of [Pd(O^1,N^4,C^1-L')(CN^tBu)]ClO_4 (**5b$_{Bu}$**). To a solution of [Pd(O^1,N^4,C^1-L')(NCMe)]ClO_4 (**B**) (338.0 mg; 0.83 mmol) in MeCN (10 mL) was added ^{t}BuNC (93.4 μL; 0.83 mmol) and then was stirred for 15 min and concentrated to dryness. The residue was dissolved in dichloromethane (4 mL) and Et_2O (8 mL) was added. The resulting suspension was stirred at 0 °C for 30 min and then filtered off, to give a solid that was washed with Et_2O and air-dried. The resulting solid was dissolved in CH_2Cl_2 (10 mL) and filtered off through Celite. The filtrate was concentrated (2 mL) and Et_2O (10 mL) was added. The resulting suspension was filtered and the solid was washed with Et_2O and air dried to give **5b$_{Bu}$** as a yellow solid. Yield: 332.4 mg, 89%. Mp: 206 °C dec. IR (cm^{-1}): ν(C≡N) 2218, ν(C=O) 1703, 1635, ν(C=N) 1596, ν(Cl–O) 1086. ^{1}H NMR (400 MHz, acetone-d_6): δ 8.86 (dd, 1 H, H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz), 8.74 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 8.28 (dd, 1 H, H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz), 3.69 (s, 2 H, CH_2), 3.09 (s, 3H, Me), 1.67 (br, 9H, ^{t}Bu). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.67 (dd, 1 H, H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 8.53 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 8.12 (dd, 1 H, H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 3.61 (s, 2 H, CH_2), 3.04 (s, 3H, Me), 1.61 (br, 9H, ^{t}Bu). ^{13}C{^{1}H} NMR (75.45 MHz, acetone-d_6): δ 200.4 (s, C6), 152.9 (s, C8), 152.5 (s, C7), 144.6 (s, C4), 132.7 (s, C3), 128.6 (s, C5), 35.0 (s, CH_2), 29.9 (s, C(CH_3)$_3$) 26.5 (s, Me). Anal. Calcd for $C_{14}H_{17}N_2O_6ClPd$: C, 37.27; H, 3.80; N, 6.21. Found: C, 37.00; H, 3.84; N, 6.22.

Synthesis of cis-[Pd(N^4,C^1-L)(CN^tBu)$_2$]ClO_4 (**6a$_{Bu}$**). To a cooled solution (0 °C) of **A2** (from 0.23 mmol of **A1** and 0.92 mmol of $AgClO_4$ in 7 mL of CH_2Cl_2) ^{t}BuNC (2 mL, 226.2 mM, 0.46 mmol) was added. The resulting solution was concentrated 0 °C (2 mL) and Et_2O (7 mL) was added. The resulting mixture was vigorously stirred in the cold bath for 15 min, filtered off, washed with Et_2O and dried under N_2 to give **6a$_{Bu}$** as a colorless solid. Yield: 98%. Mp: 95–96 °C. IR (cm^{-1}): ν(C≡N) 2242, 2214, ν(C=O) 1677, ν(C=N) 1602, ν(Cl–O) 1093. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.30 (br, 1 H, H4), 7.96 (d, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz), 7.88 (d, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz), 3.00-3.80 (br, 8 H, CH_2 + 2 MeO), 1.78 (br, 3 H, Me), 1.61 (br, 18 H, 2 ^{t}Bu). ^{1}H NMR (400 MHz, $CDCl_3$, –60 °C): δ 8.38 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.08 (d, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz), 8.00 (d, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz), 3.39 (br, 3 H, MeO), 3.28 (br, 3 H, MeO), 3.21 (s, 2 H, CH_2), 1.73 (s, 3 H, Me), 1.70 (s, 9 H, ^{t}Bu), 1.65 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{21}H_{32}N_3O_7ClPd$: C, 43.46; H, 5.56; N, 7.24. Found: C, 43.21; H, 5.88; N, 7.31.

Synthesis of [Pd(C^I-L)(CN^tBu)$_3$]ClO$_4$ (**7a$_{Bu}$**). To a cooled (0 °C) solution of **A2** (from 0.14 mmol of **A1** and 0.55 mmol of $AgClO_4$ in 6 mL of $CHCl_3$) ^{t}BuNC (36.8 mg, 0.44 mmol) was added, the resulting solution was stirred for 20 min and then concentrated to dryness. The residue was crystallized in CH_2Cl_2/*n*-pentane and then filtered off. The resulting solid was washed with *n*-pentane and air-dried to give **7a$_{Bu}$** as a colorless solid. Yield: 94%. Mp: 104-105 °C. IR (cm^{-1}): ν(C≡N) 2222, ν(C=O) 1659, ν(C=N) 1581, ν(Cl–O) 1092. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.00-7.80 (m, 3 H, H3 + H4 + H5), 3.20 (s, 6 H, OMe), 3.14 (s, 2 H, CH_2), 1.70 (s, 3 H, Me), 1.59 (s, 27 H, ^{t}Bu). ^{1}H NMR (400 MHz, $CDCl_3$, -60 °C): δ 8.04-7.86 (m, 3 H, H3 + H4 + H5), 3.21 (br, 8 H, OMe + CH_2), 1.73 (s, 3 H, Me), 1.63 (s, 18 H, ^{t}Bu), 1.62 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{26}H_{41}N_4O_7ClPd$: C, 47.07; H, 6.23; N, 8.44. Found: C, 46.97; H, 6.27; N, 8.47.

Synthesis of [Pd(C^I-L)(CNXy)$_3$]ClO$_4$·H$_2$O (**7a$_{Xy}$**). To a cooled (0 °C) solution of **A2** (from 0.06 mmol of **A1** and 0.19 mmol of $AgClO_4$ in 3 mL of $CHCl_3$) was added a cold (0 °C) solution of XyNC (25.2 mg, 0.19 mmol) in $CHCl_3$ (1 mL). The resulting solution was stirred for 20 min, then concentrated to dryness at 0 °C and the resulting solid was dissolved in CH_2Cl_2 (1 mL). Addition of Et_2O (5 mL) gave a suspension that was stored at –33 °C for 2 h. The solid was filtered off, washed with Et_2O and air-dried to give **7a$_{Xy}$** as a pale yellow solid. Yield: 95%. Mp: 75-76 °C. IR (cm^{-1}): ν(C≡N) 2196, 2184 (sh), ν(C=O) 1660, ν(C=N) 1581, ν(Cl–O) 1091. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.81 (m, 3 H, H3 + H4 + H5), 7.35 (t, 1 H, *p*-H, Xy, $^3J_{HH}$= 7.6 Hz), 7.20 (d, 2 H, *m*-H, Xy, $^3J_{HH}$= 7.6 Hz), 3.64 (s, 2 H, CH_2), 3.08 (s, 6 H, OMe), 2.46 (s, 18 H, Me, Xy), 1.65 (br, 1 H, H_2O), 1.55 (s, 3 H, Me). ^{1}H NMR (400 MHz, $CDCl_3$, -60 °C): δ 7.98 (d, 1 H, H5 or H3, $^3J_{HH}$= 7.6 Hz), 7.93 (t, 1 H, H4, $^3J_{HH}$= 7.6 Hz), 7.88 (d, 1 H, H3 or H5, $^3J_{HH}$= 7.6 Hz), 7.44-7.41 (m, 3 H, *p*-H, Xy), 7.30-7.22 (m, 6 H, *m*-H, Xy), 3.66 (s, 2 H, CH_2), 3.06 (s, 6 H, OMe), 2.50 (s, 12 H, Me, Xy), 2.49 (s, 6 H, Me, Xy), 1.51 (s, 3 H, Me). Anal. Calcd for $C_{38}H_{41}N_4O_7ClPd·H_2O$: C, 55.28; H, 5.25; N, 6.79. Found: C, 55.20; H, 5.15; N, 6.70.

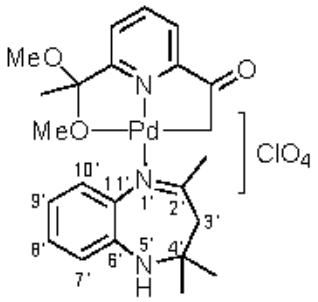
Synthesis of [Pd(N^I,C^I-L)(dppm)]ClO$_4$·0.75H$_2$O (**8a**). A mixture of a cooled (0 °C) solution of **A2** (from 0.10 mmol of **A1** and 0.31 mmol of $AgClO_4$ in 6 mL of CH_2Cl_2) and

dppm (39.4 mg; 0.10 mmol) was stirred for 30 min and then concentrated (1 mL). Addition of Et_2O (5 mL) led to a suspension that was filtered off. The solid was washed with Et_2O and air-dried to give **8a** as a pale orange solid. Yield: 89%. Mp: 172-173 °C. IR (cm^{-1}): ν(C=O) 1652, ν(C=N) 1599, ν(Cl-O) 1094. ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.05–7.98 (m, 2 H, H5 + H3), 7.70-7.35 (m, 20 H, dppm), 4.43 (dd, 2 H, CH_2, dppm, $^2J_{HP}$ = 12.4 Hz, $^2J_{HP}$ = 7.2 Hz), 3.32 (dd, 2 H, CH_2, $^3J_{HP,cis}$ = 1.6 Hz, $^3J_{HP,trans}$ = 12 Hz), 2.81 (s, 6 H, OMe), 1.58 (s, 1.5 H, H_2O), 1.39 (s, 3 H, Me). $^{31}P\{^1H\}$ NMR (162.29 MHz, $CDCl_3$): δ - 2.83 (d, $^2J_{PP}$ = 206.4 Hz), -27.65 (d, $^2J_{PP}$ = 206.4 Hz). Anal. Calcd for $C_{36}H_{36}NO_7ClPPd\cdot 0.75H_2O$: C, 53.25; H, 4.65; N, 1.72. Found: C, 53.11; H, 4.66; N, 1.64.

Synthesis of [Pd(N^I,C^I-L)(dbbpy)]ClO₄·0.5H₂O (**9a**). To a solution of **A2** (from 0.08 mmol of **A1** and 0.30 mmol of $AgClO_4$ in 8 mL of $CHCl_3$) was added dbbpy (4,4'-di-*tert*-buty-2,2'-bipyridine, 20.1 mg, 0.08 mmol). The resulting solution was stirred at 0 °C for 30 min and then concentrated (1 mL). Addition of Et_2O (3 mL) and *n*-pentane (5 mL) gave a suspension; the solid was filtered off, washed with *n*-pentane and air-dried to give **9a** as a yellow solid. Yield: 85%. Mp: 258 °C dec. IR (cm^{-1}): ν(C=O) 1673, ν(C=N) 1614, 1547, ν(Cl–O) 1081. ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (br, 2 H, ^{t}bpy), 8.23 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.17 (br, 2 H, ^{t}bpy), 7.90 (br, 2 H, H3 + H5), 7.62 (dd, 2 H, ^{t}bpy, $^3J_{HH}$ = 5.6 Hz, $^4J_{HH}$ =1.6 Hz), 3.70 (br, 2 H, CH_2), 3.16 (s, 6 H, OMe), 1.82 (s, 3 H, Me), 1.59 (br, 1 H, H_2O), 1.46 (s, 18 H, ^{t}Bu). ^1H NMR (400 MHz, $CDCl_3$, –60 °C): δ 8.58 (d, 1H, ^{t}bpy, $^3J_{HH}$ = 5 Hz), 8.37 (t, 1H, H4, $^3J_{HH}$ = 8 Hz), 8.22 (br, 1 H, ^{t}bpy), 8.17 (br, 1 H, ^{t}bpy), 8.08 (d, 1 H, ^{t}bpy, $^3J_{HH}$ = 5 Hz), 7.98 (d, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz), 7.95 (d, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz), 7.68 (m, 2 H, ^{t}bpy), 4.36 (d, 1 H, CH_2, $^1J_{HH}$ = 6.4 Hz), 3.36 (s, 3 H, MeO), 3.08 (d, 1 H, CH_2, $^1J_{HH}$ = 6.4 Hz), 3.07 (s, 3 H, MeO), 1.81 (s, 3 H, Me), 1.51 (s, 9 H, ^{t}Bu), 1.46 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{29}H_{38}N_3O_7ClPd\cdot 0.5H_2O$: C, 50.37; H, 5.68; N, 6.08. Found: C, 50.12; H, 5.85; N, 5.88.

Synthesis of [Pd(N^I,C^I-L)(N,N-NH₂C₆H₄NH₂-2)]ClO₄·0.5H₂O (**10a**). A solution of **A2** (from 0.39 mmol of **A1** and 0.80 mmol of $AgClO_4$ in 10 mL of CH_2Cl_2) was stirred with *o*-phenylidenediamine (42.3 mg; 0.39 mmol) for 5 min, then concentrated (2 mL) and Et_2O (8 mL) added. The resulting suspension was filtered off, washed with Et_2O and air dried to give **10a** as a pale yellow solid. Yield: 201.7 mg, 97%. Mp: 175 °C dec. IR (cm^{-1}): ν(N–H) 3302,

ν(C=O) 1654, ν(C=N) 1601, ν(Cl-O) 1076. ^{1}H NMR (400 MHz, acetone-d_6): δ 8.34 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 8.13 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.91 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.49 (m, 2 H), 7.32-7.30 (m, 2 H), 6.67 (br, 2 H, NH_2), 5.81 (br, 2 H, NH_2), 3.38 (s, 6 H, OMe), 3.29 (s, 2 H, CH_2), 2.84 (s, 1 H, H_2O), 2.13 (s, 3 H, Me). Anal. Calcd for $C_{17}H_{22}N_3O_7ClPd\cdot 0.5H_2O$: C, 38.43; H, 4.36; N, 7.91. Found: C, 38.50; H, 4.33; N, 7.91.



11a

Synthesis of [Pd(O^1,N^1,C^1-L)(Bzdiaz)]ClO_4 (**11a**). A suspension of **10a** (164.0 mg, 0.31 mmol) in acetone (25 mL) was stirred for 4 days and then concentrated to dryness. The residue was dissolved in CH_2Cl_2 (2 mL) and Et_2O (10 mL) was added. The resulting suspension was filtered off, washed with Et_2O and air-dried to give **11a** as a yellow solid. Yield: 160.3 mg, 85%. Mp: 134-135 °C. IR (cm^{-1}): ν(N–H) 3322, ν(C=O) 1698, ν(C=N) 1621, 1599, ν(Cl-O) 1079. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.90 (dd, 1 H, H10', $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.2 Hz), 7.84 (dd, 1 H, H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.74 (dd, 1 H, H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 7.25-7.15 (m, 2 H, H8' + H9'), 6.98 (dd, 1 H, H7', $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.2 Hz), 3.51 (br, 1 H, NH), 3.44 (s, 2 H, CH_2), 3.23 (s, 6 H, MeO), 3.10 (s, 3 H, *Me*C2'), 2.44 (s, 2 H, H3'), 1.75 (s, 3 H, Me), 1.40 (s, 6 H, *Me*C4'). ^{13}C{^{1}H} NMR (100.81 MHz, $CDCl_3$): δ 201.7 (C2), 186.1 (C2'), 158.2 (C7), 152.1 (C8), 142.0 (C4), 139.3 (C11'), 138.9 (C6'), 129.1 (C9'), 127.3 (C5), 127.0 (C10'), 124.0 (C3), 123.7 (C7'), 123.2 (C8'), 108.1 (C6), 70.5 (C4'), 52.4 (OMe), 46.0 (C3'), 33.7 (CH_2), 32.6 (N=C*Me*), 30.0 (C*Me*$_2$), 25.0 (Me). Anal. Calcd for $C_{23}H_{30}N_3O_7ClPd$: C, 45.86; H, 5.02; N, 6.98. Found: C, 45.41; H, 5.39; N, 6.94.

Pd-Catalyzed Synthesis of the 2',2',4'-trimethyl-2',3'-dihydro-1H-1',5'-benzodiazepine. To a solution of complex **10a** (17.5 mg, 0.03 mmol) in acetone (15 mL), *o*-phenylenediamine

(72.5 mg, 0.67 mmol) was added and the mixture was stirred at room temperature. After 5 days, the solvent was evaporated and Et_2O was added (10 mL). The mixture was filtered through a celite plug and the filtrate was concentrated to dryness obtaining a colorless solid corresponding to the spectroscopically pure 1,5-benzodiazepine.

Synthesis of $[Pd_2(O^I,N^I,C^I\text{-}L)_2(\mu\text{-}dppm)](ClO_4)_2$ (**12a**). To a solution of **A2** (from 0.24 mmol of **A1** and 0.52 mmol of $AgClO_4$ in 5 mL of CH_2Cl_2) was added dppm (46.7 mg; 0.12 mmol). The mixture was stirred for 4 h and then concentrated (1 mL). Addition of Et_2O (6 mL) gave an oil that was vigorously stirred in a cooled bath (0 °C). The resulting suspension was filtered off, washed with Et_2O, and air-dried to give **12a** as an orange solid. Yield: 98%. Mp: 167-168 °C. IR (cm^{-1}): ν(C=O) 1698, ν(C=N) 1600, ν(Cl-O) 1094. ^1H NMR (400 MHz, $CDCl_3$): δ 8.26 (t, 2 H, H4, $^3J_{HH}$ = 8 Hz), 7.90-7.80 (m, 10 H, H5 or H3 and 8 H, dppm), 7.75 (dd, 2 H, H3 or H5, $^3J_{HH}$ = 8 Hz), 7.42-7.35 (m, 12 H, dppm), 3.96 (t, 2 H, CH_2, dppm, $^2J_{HP}$ = 10.8 Hz), 3.34 (d, 4 H, CH_2, $^3J_{HP}$ = 3.6 Hz), 3.05 (s, 12 H, OMe), 1.82 (s, 6 H, Me). $^{31}P\{^1H\}$ NMR (162.29 MHz, $CDCl_3$): δ 19.46(s). Anal. Calcd for $C_{47}H_{50}N_2O_{14}Cl_2P_2Pd_2$: C, 46.55; H, 4.16; N, 2.31. Found: C, 46.17; H, 4.56; N, 2.47.

Synthesis of $[Pd(O^I,N^I,C^I\text{-}L')(OH_2)]ClO_4$ (**13b**). To a suspension of $(Hdap)ClO_4$ (610.3 mg; 2.31 mmol) in THF (18 mL) was added $Pd(OAc)_2$ (519.7 mg; 2.31 mmol). The reaction mixture was stirred for 30 min and then decanted, to give a suspension of **A1** and an oil. The oil was vigorously stirred with Et_2O (3 x 20 mL) for 20 min, the resulting suspension was filtered off and the solid was dried under a N_2 stream giving orange **13b**. The suspension **A1** was concentrated to dryness and the residue was stirred with acetone (20 mL) and concentrated to dryness. The resulting residue was grinded with Et_2O (20 mL) for 10 min and filtered off under N_2 to get a second crop of **13b**. Yield: 98%. Mp: 260 °C dec. IR (cm^{-1}): $\nu(H_2O)$ 3371, ν(C=O) 1721 (sh), 1705, ν(C=N) 1570, ν(Cl–O) 1089. ^1H NMR (200 MHz, acetone-d_6): δ 8.82 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz), 8.68 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 8.15 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.4 Hz), 3.66 (s, 2 H, CH_2), 3.07 (s, 3 H, Me), 3.05 (br, 2 H, H_2O). Anal. Calcd for $C_9H_{10}NO_7ClPd$: C, 28.00; H, 2.61; N, 3.63. Found: 27.76; H, 2.75; N, 3.56.

X-ray Structure Determinations. Complexes **B** and **5a**$_{Xy}$ were measured on a Bruker Smart APEX machine. Data were collected using monochromated Mo-Kα radiation in ω-scan. The structures were solved by direct methods. All of the non-hydrogen atoms were refined anisotropically on F^2. The methyl groups were refined using rigid groups and the other hydrogens a riding mode.

Table 1. Crystal Data for **B** and **5a**$_{Xy}$.

	B	**5a**$_{Xy}$
formula	C_{11} H_{11} Cl N_2 O_6 Pd	C_{20} H_{23} Cl N_2 O_7 Pd
cryst size (mm^3)	0.23 x 0.23 x 0.11	0.27 x 0.14 x 0.07
cryst syst	Monoclinic	Triclinic
space group	P 2(1)/n	P -1
a (Å)	7.6698(4)	8.6119(6)
b (Å)	23.7216(12)	8.7766(6)
c (Å)	7.8644(4)	14.8426(12)
α (deg)	90	82.108(2)
β (deg)	104.965(2)	78.096(2)
γ (deg)	90	78.395(2)
V ($Å^3$)	1382.32(12	1069.90(14)
Z	4	2
λ (Å)	0.71073	0.71073
ρ(calc) (Mg m^{-3})	1.564	1.693
F(000)	808	552
T (K)	100	100
μ (mm^{-1})	1.564	1.037
Transmissions	0.8468 and 0.771	0.9309 and 0.7754
θrange (deg)	2.82 to 28.13	2.38 to 28.16
index ranges	-10 ≤ h 10	-11 ≤ h ≤ 11
	-31 ≤ k<=31	-11 ≤ h ≤11
	-10 ≤ l ≤ 10	-19 ≤ h ≤ 19
reflns collected	15633	12439
independent reflns	3197	4803
R_{int}	0.0168	0.019
abs. corr	semi-empirical from equivalents	semi-empirical from equivalents
refinement method	full-matrix least-squares on F^2	full-matrix least-squares on F^2
data/restraints/params	3197 / 0 / 192	4803 / 0 / 285
GOF on F^2	1.102	1.058
R1[a]	0.0225	0.0253
wR2[b]	0.0565	0.0624
largest diff peak (e $Å^{-3}$)	0.613and -0.583	0.962 and -0.346

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and *a* and *b* are constants set by the program.

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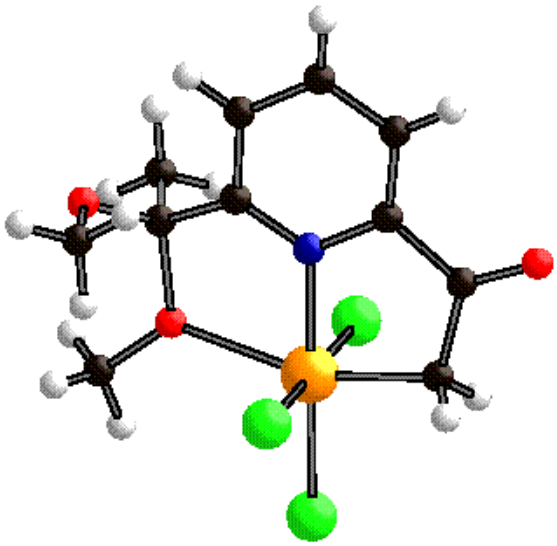
CHAPTER III

Organometallic Trihalopalladium(IV) Complexes. Reductive Elimination Reactions



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SUMMARY CHAPTER III

In the context of our investigation regarding Pd(II) complexes derived from 2,6-diacetylpyridine, we wanted to give one more step studying oxidation reactions in order to isolate the corresponding Pd(IV) derivatives.

Although the chemistry of Pd(0), Pd(I) and Pd(II) is well established, Pd(IV) complexes are less known. In the last few years, there is an increasing interest in preparing this kind of complexes, because of their participation in many palladium-catalyzed C–C bond formation and C–H bond activation. A deep understanding of the behaviour of Pd(IV) complexes could lead to the design and development of novel catalytic reactions that could not be accessed by the traditional Pd(0)/Pd(II) chemistry.

This challenging aim became even more interesting to us when we realized that pincer-type Pd(IV) complexes had not been previously isolated at all. In spite of the great number of fully characterized pincer-type Pd(II) complexes, their Pd(IV) homologues have been described as especially unstable species. In **Chapter III** are presented the oxidation reaction of some Pd(II) we prepared, with halogens (Cl_2, Br_2, I_2), affording trihalo organopalladium(IV) complexes.

The chloro and bromo pincer-type Pd(II) complexes reacted with chlorine or bromine at low temperature to give the corresponding Pd(IV) derivatives, as showed in **Section III.1**. These first members of the family of isolated pincer-type Pd(IV) complexes were fully characterized, even by X-Ray diffraction. At room temperature or heating, such complexes underwent reductive elimination reactions giving the corresponding halogenated ligands produced through C–X (X = Cl, Br) coupling and the palladium dihalide.

In the **Section III.2**, the synthesis of the triiodo organopalladium(IV) complex is presented. This compound, which was prepared starting from the Pd(II) derivative and iodine, deserves special mention because it contains three reducing iodo ligands coordinated to a strongly oxidizing Pd(IV) metal centre. Moreover, the X-ray crystal structure could be determined. It is the most iodated organopalladium(IV) complex reported.

In addition, the oxidation reaction leading to this product wasn't complete and an equilibrium formed in solution at low temperature. This allowed us to calculate the thermodynamic parameters of the oxidation using the van't Hoff equation. In the same way of

the other trihalo organopalladium(IV) complexes, the iodo Pd(IV) derivative decomposes through a reductive elimination coupling reaction affording the corresponding iodated ligand.

Section III.1: Quantitative Synthesis and Full Characterization of the First Isolated and Stable Pincer Palladium(IV) Complexes. Quantitative and Regioselective Synthesis of the C–X (X = Cl, Br) Reductive Elimination Products

ABSTRACT

The pincer complexes [Pd(O^I,N^I,C^I-L)X], where X = Cl, Br and L is the monoanionic ligand resulting from deprotonation of the acetyl methyl group of the monoketal of 2,6-diacetylpyridine (dap), react with excess of Cl_2 or Br_2 affording, quantitatively, the Pd(IV) complexes [Pd(O^I,N^I,C^I-L)X_3], which have been characterized by X-ray diffraction, and their decomposition that quantitatively affords the reductive elimination products L-X has been studied.

INTRODUCTION

Pd(IV) is usually described as a comparatively rare oxidation state. However, three very recent reviews show the extraordinary current activity in the synthesis of organometallic Pd(IV) complexes and the study of processes involving Pd(II)/Pd(IV) catalysis and C–H activation chemistry.[1] These organometallics,[2] can be classified in three categories: (1) those detected *in situ* or mainly characterized by NMR spectroscopy,[3-7] (2) complexes isolated but not characterized by X-ray diffraction (XRD)[6-9] and (3) those fully characterized, including XRD studies. In this group there are (3a) trimethyl,[10, 11] scorpionate[12, 13] or trimethyl(scorpionate)[7, 10, 14] complexes, (3b) alkyl[15-17] or aryl[18] complexes with a N^N chelating ligand, (3c) C^O[19] or C^N[20-22] metallacyclic complexes, or (3d) a few having Si–Pd bonds.[23] In this paper we report two Pd(IV) complexes that do not belong to any of these types.

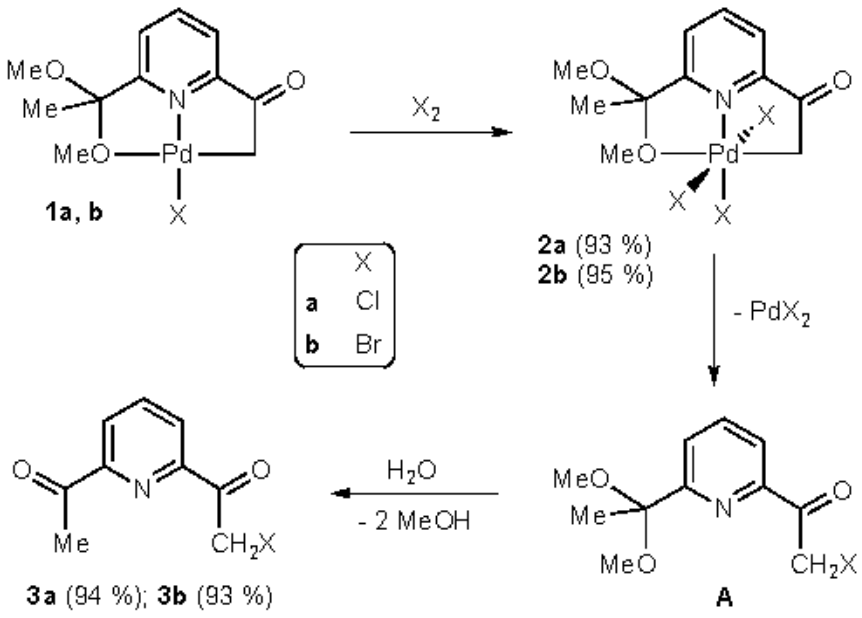
In spite of the great number and the interest of the Pd(II) pincer complexes,[24] their Pd(IV) homologues are too unstable to be isolated and characterized[5, 6, 25] or even detected.[26] It has been proposed that there is intermediacy of Pd(IV) complexes with a P^C^P pincer ligand in Pd(II)/Pd(IV) redox cycle based Heck-type catalysis, although attempts to detect or isolate them were not carried out.[27] We report here that it is possible to isolate and characterize remarkably stable Pd(IV) complexes containing a pincer ligand instead of the bidentate chelating or scorpionate ligands that stabilize all previously reported organometallic Pd(IV) complexes.

Although some halo-complexes are among the most stable Pd(IV) complexes, the number of those being also organometallics are very limited. Thus, in the above mentioned group of fully characterized Pd(IV) organometallics, several monohalo[7, 10, 13, 15, 17, 21] and only three dihalo derivatives are included: [$PdCl_2$(C^N)(C^O)],[28] [PdF_2(C^N)(N^N)],[22] and

$[PdF_2(FHF)(C_6H_4F\text{-}4)(N\text{^}N)]$[18]. We report here the first synthesis and full characterization of very stable trihalo Pd(IV) organo-complexes, of which there are examples among those not fully characterized, $[PdCl_3(C_6F_5)(N\text{^}N)]$ (N^N = bpy, phen, tmeda)[9] and those very unstable and only characterized in solution by NMR spectroscopy.[4-6] As far as we are aware, not trihalo non-organometallic Pd(IV) complexes have been reported either.

RESULTS AND DISCUSSION

We have recently reported that the reaction of $PdCl_2$ with 2,6-diacetylpyridine (dap) in refluxing MeOH affords [Pd(*O,N,C*-L)Cl] (Scheme 1, **1a**);[29] its homologous bromo derivative **1b** was obtained (98% yield) by reacting **1a** with NaBr. The reaction at 0°C during 5 min of a CH_2Cl_2 solution of **1a** with excess of Cl_2 or of **1b** with Br_2 afforded quantitatively **2a** or **2b**, respectively. The reaction of **1a** with XeF_2 did not lead to any Pd(IV) complex. Complexes **2** are the first ketonyl Pd(IV) compounds obtained from a ketonyl Pd(II) derivative. There exist only a few obtained by oxidative addition of $BrCH_2C(O)Ar$ (Ar = Ph, C_6H_4Br-2) to $[PdMe_2L_2]$ (L_2 = bpy, phen).[17]



Scheme 1

Crystaline **2a** or **2b** or amorphous solid **2a** can be stored without decomposition at 20, 4 or 4 °C, respectively. The amorphous solid **2a** shows < 6% decomposition after 30 day at

20 °C. The ^{1}H NMR spectra of $CDCl_3$ solutions of **2b** showed, after 24 h at room temperature, full decomposition to the coupling product **3b** (Scheme 1). During this period, formation of an intermediate, for which resonances were consistent with the diketal **A** (X = Br), was observed. Attempts to isolate **A** were unfruitful because it hydrolyzed very easily. $CDCl_3$ solutions of complex **2a** showed only a 5% decomposition after four days, but the corresponding diketal intermediate was not observed.

The remarkable stability of complexes **2a**, greater than that of the three dihalo Pd(IV) mentioned above,[18,22,28] can only be attributed to the pincer ligand. However, because other Pd(IV) pincer complexes could only be characterized in solution,[5, 6, 25] the stability of **2** must be related with the nature and/or mutual disposition of the functional groups in our pincer ligand. Further studies are being carried out in order to prepare other Pd(IV) complexes with the same or related pincer ligands.

Complexes **2** in MeCN solutions or when **2a** was reacted with 4,4'-di-t-butyl-2,2'-bypiridine (^{t}Bubpy) and $NaClO_4$ (also without this salt) led to the quantitative and regioselective synthesis of the monohalogenated dap **3** (Scheme 1). The bromination of dap has been reported to give the symmetric dihalogenated dap.[30] It is reasonable to assume that both MeCN and ^{t}Bubpy cleave the Pd–O bond giving adducts (not detected by ^{1}H NMR spectroscopy) that decompose through a C–X coupling process due to the steric hindrance between the entering ligand and the $CMe(OMe)_2$ group. It is well-known that palladium organometallics [Pd]–R react with halogens X_2 to give [Pd]–X and R–X.[31, 32] However, only a few works report the detection of the Pd(IV) intermediates in these reactions[32] or the formation of R–X directly from an isolated Pd(IV) complex, such as **2**.[18, 21, 22] Complexes of Fe(II) and Co(II) with bis(imino) derivatives of dap are highly active catalysts for polymerization and oligomerization of olefins.[33] Compounds **3** and their derivatives could be used to prepare new catalysts with unsymmetrical dap ligands.[34]

The ^{1}H NMR spectra of complexes **1** show a fast exchange between the MeO groups, that even at –60 °C causes their equivalence and that of the CH_2 protons. However, in **2** two separate (broad at room temperature and sharp at –55 °C) resonances are observed for MeO and CH_2 protons, in keeping with the expected strenghthening of the Pd–OMe bond in **2** with respect to **1**. The high oxidation of the metal center in **2** also explains the high deshielding of the CH_2 protons (~6 ppm) with respect to those in the **1** precursors (~3.5 ppm).

Complexes **1b** (Fig. 1; CCDC 784548), **2a** (Fig. 2; CCDC 784549) and **2b** (Fig. 3; 784550) were analyzed by X-ray diffraction. The structure of **1b** is similar to that of **1a**.[29] When the bond distances in Pd(II) complexes **1** are compared with those of **2**, the main difference is that the Pd–N, Pd–C and Pd–O bond distances are longer in **2** (X = Cl: 2.0058(15), 2.0245(18), 2.2755(12) Å; Br: 2.0207(15), 2.0319(19), 2.2833(13) Å, respectively) than in **1** (X = Cl: 1.9752(19), 2.000(2), 2.2149(16) Å; Br: 1.9806(16), 1.999(2), 2.2169(14) Å, respectively) in keeping with the increase in coordination number. The same was observed when distances in homologous Pt^{IV} and Pt^{II} complexes are compared.[26]

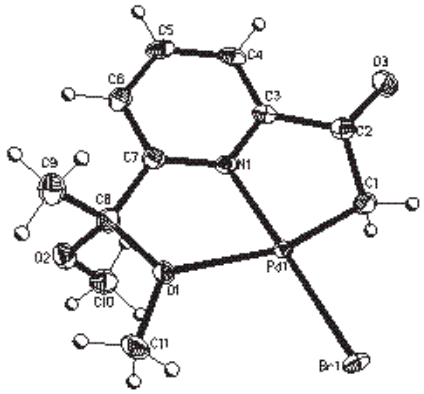


Figure 1. Ellipsoid representation of **1b** (50% probability).

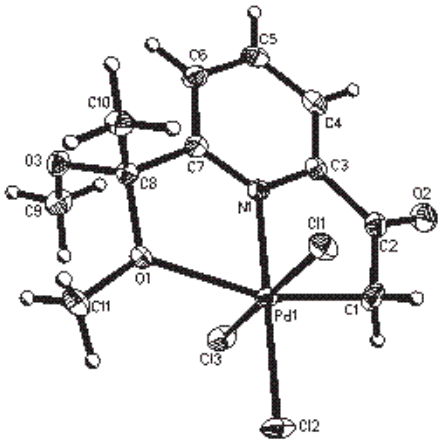


Figure 2. Ellipsoid representation of **2a** (50% probability).

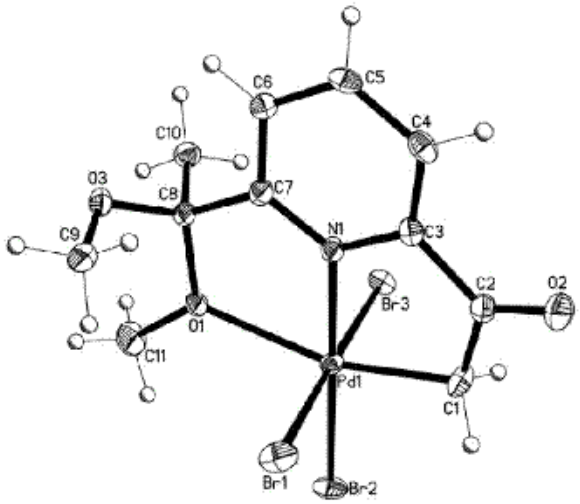


Figure 3. Ellipsoid representation of **2b** (50% probability).

CONCLUSIONS

In conclusion, this communication reports the quantitative synthesis of (1) the first fully characterized and highly stable Pd(IV) complexes containing a pincer ligand or having three halo ligands and (2) their C–X reductive elimination products. The great stability of these complexes is due to the specific pincer ligand used in this work. The C–X coupling products could be useful for the synthesis of catalysts for polymerization or oligomerization of olefins or as oxidative addition reagents. As a whole, the yields of Pd(IV) complexes **2** and their reductive elimination products **3** as well as the stability of complexes **2** are better than those of analogous Pd(IV).[35] These results prove that Pd(IV) complexes with pincer ligands can be stable if their arms are adequately chosen, which opens an interesting new field of research.

EXPERIMENTAL SECTION

General Procedures

The reactions were carried out without precautions to exclude light, atmospheric oxygen or moisture. Melting points were determined on a Reicher apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on a Bruker AC 200, or Avance 300 or 400

spectrometers. Chemical shifts were referred to TMS (^{1}H, ^{13}C). When needed, NMR assignments were performed with the help of APT, HMQC and HMBC techniques. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS; the exact masses have been calculated for the combination of the most abundant isotopes. Complex [Pd(*O,N,C*-L)Cl] was prepared as reported previously.[29] Chart 1 shows the atom numbering used for NMR assignments.

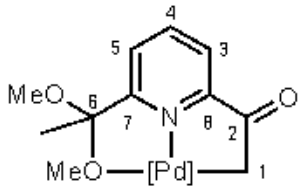


Chart 1

Synthesis

Synthesis of [Pd(O^1,N^1,C^1-L)Br] **(1b).** To a solution of [Pd(*O*^{1},*N*^{1},*C*^{1}-L)Cl][29] (225.2 mg; 0.643 mmol) in acetone (27 mL), NaBr (265.4 mg; 2.58 mmol) was added. The reaction mixture was stirred for 45 min, concentrated to dryness and extracted with CH_2Cl_2 (20 mL). The solution was concentrated (1 mL) and Et_2O (3 mL) and *n*-pentane (15 mL) were added. The resulting suspension was filtered and the solid washed with *n*-pentane and air-dried to give **1b** as a yellow solid. Yield: 248.3 mg, 98%. Mp: 198–199 °C. IR (cm^{-1}): ν(C=O) 1686; ν(C=N) 1601. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 7.82 (dd, 1 H, H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.64 (dd, 1 H, H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ =1.2 Hz), 3.50 (s, 2 H, CH_2), 3.43 (s, 6 H, OMe), 1.77 (s, 3 H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, $CDCl_3$): δ 204.0 (CO), 158.3 (C7), 152.2 (C8), 139.3 (C4), 126.5 (C5), 123.6 (C3), 107.0 (C6), 51.6 (MeO), 29.6 (C1), 25.0 (Me). Anal. Calcd for $C_{11}H_{14}NO_3BrPd$: C, 33.49 ; H, 3.58 ; N, 3.55. Found: C, 33.42 ; H, 3.38 ; N, 3.82. Single crystals were obtained by slow diffusion of *n*-pentane into a $CHCl_3$ solution of **1b**.

Synthesis of mer-[Pd(O^1,N^1,C^1-L)Cl$_3$] **(2a).** To a cooled (0 °C) solution of [Pd(*O*^{1},*N*^{1},*C*^{1}-L)Cl] (**1a**) (48.7 mg, 0.14 mmol) in CH_2Cl_2 (1 mL) was added a saturated solution of Cl_2 in CCl_4 (1 mL). The resulting suspension was stirred for 5 min, and Et_2O (6 mL) was added. The suspension was filtered, and the solid was washed with Et_2O, and air-dried, to give **2a** as a

yellow solid. Yield: 54.6 mg, 93 %. Mp: 107–108 °C. IR (cm^{-1}): ν(C=O) 1723, ν(Pd–Cl) 355. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 8.14 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz), 7.92 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ =1.2 Hz), 6.04 (br, 2 H, CH_2), 3.89 (br, 3 H, OMe), 3.28 (br, 3 H, OMe), 1.95 (s, 3 H, Me). ^{1}H NMR (400 MHz, $CDCl_3$, -50 °C): δ 8.50 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 8.24 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz), 8.05 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz), 6.20 (d, 1 H, CH_2, $^1J_{HH}$= 12.4 Hz), 5.97 (d, 1 H, CH_2, $^1J_{HH}$= 12.4 Hz), 3.94 (s, 3 H, OMe), 3.28 (s, 3 H, OMe), 1.99 (s, 3 H, Me). Anal. Calcd for $C_{11}H_{14}NO_3Cl_3Pd$: C, 31.38 ; H, 3.35; N, 3.33. Found: C, 31.07 ; H, 3.11 ; N, 3.19. Single crystals were obtained by slow diffusion of Et_2O into a CH_2Cl_2 solution of **2a** at 4 °C.

Synthesis of mer-[Pd(O^1,N^1,C^1-L)Br_3] (**2b**). To a cooled (0 °C) solution of **1b** (45.0 mg, 0.11 mmol) in CH_2Cl_2 (1 mL) was added Br_2 (20 μL, 0.39 mmol). The mixture was stirred for 2 min, and Et_2O (6 mL) was added. The suspension was filtered, and the solid was washed with Et_2O, and dried under N_2, to give **2b** as a dark red crystals. Yield: 59.9 mg, 95 %. Mp: 110–111 °C. IR (cm^{-1}): ν(C=O) 1718, ν(C=N) 1570, ν(Pd–Br) 275. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.30 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 8.13 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.4 Hz), 7.87 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.4 Hz), 6.06 (br, 2 H, CH_2), 3.83 (br, 3 H, OMe), 3.32 (br, 3 H, OMe), 1.96 (s, 3 H, Me). ^{1}H NMR (400 MHz, $CDCl_3$, -55 °C): δ 8.46 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 8.24 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.4 Hz), 8.01 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.4 Hz), 6.20 (d, 1 H, CH_2, $^1J_{HH}$= 13 Hz), 5.96 (d, 1 H, CH_2, $^1J_{HH}$= 13 Hz), 3.88 (s, 3 H, OMe), 3.31 (s, 3 H, OMe), 2.00 (s, 3 H, Me). Anal. Calcd for $C_{11}H_{14}NO_3Cl_3Pd$: C, 23.83 ; H, 2.55; N, 2.53. Found: C, 23.65 ; H, 2.33 ; N, 2.35. Single crystals were obtained at 4 °C by slow diffusion of Et_2O into a CH_2Cl_2 solution of **2b.**

Synthesis of 2-{C(O)Me}-6-{C(O)CH_2Cl}C_5H_3N (**3a**). ***Method a.*** A mixture of **2a** (181.4 mg, 0.43 mmol) and no destilated NCMe (30 mL) was stirred until **2a** disolved (1 h) and then was concentrated to dryness. The resulting residue was vigorously stirred in *n*-pentane (30 mL) for 30 min to give a suspension, which was filtered, and the solid washed with *n*-pentane and air-dried to give [$PdCl_2$(NCMe)$_2$] as a yellow solid. The filtrate was concentrated to dryness to give **3a** as a colorless solid. Yield: 80.2 mg, 94%. Mp: 115-116 °C. IR (cm^{-1}): ν(C=O) 1721, 1694; ν(C=N) 1579. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (m, 2H), 8.05 (m, 1H), 5.16 (s, 2H,

CH_2), 2.77 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (100.81 MHz, $CDCl_3$): δ 198.7 (s, *C*(O)Me), 191.5 (s, *C*(O)CH_2Cl), 152.7 (s, *C*C(O)Me), 150.7 (s, *C*C(O)Cl), 138.5 (s, CH, *p*-C), 125.7 (s, CH, *m*-C), 125.6 (s, CH, *m*-C), 46.9 (s, CH_2), 25.6 (s, Me). HRMS calc for $C_9H_8O_2ClN$ $[M+H]^+$ *m/z* 197.024, found *m/z* 197.025. Anal. Calcd for $C_9H_8O_2ClN$: C, 54.70 ; H, 4.08; N, 7.09. Found: C, 55.05 ; H, 4.19 ; N, 6.96.

Method b. To a cooled (0 °C) solution of **2a** (36.6 mg, 0.09 mmol) in CH_2Cl_2 (6 mL) was added 4,4'-^{t}Bu-bipyridine (^{t}bpy, 23.3 mg, 0.09 mmol) and $NaClO_4$ (21.3 mg, 0.17 mmol). After 10 min the solution was filtered through Celite and concentrated (1 mL). Addition of Et_2O (8 mL) gave a suspension that was filtered off. The resulting solid was identified as [$PdCl_2$(^{t}bpy)]. The filtrate was concentrated to dryness to give **3a** as a colorless solid. Yield:15.8 mg, 92 %.

Synthesis of 2-{C(O)Me}-6-{C(O)CH$_2$Br}C$_5$H$_3$N (**3b**). A mixture of **2b** (216.0 mg, 0.46 mmol) and no destilated NCMe (40 mL) was stirred (3 h) and then was concentrated to dryness. The resulting residue was vigorously stirred in *n*-pentane (40 mL) for 30 min to give a suspension, which was filtered to give ([$PdBr_2(NCMe)_2$]). The filtrate was concentrated to dryness to give **3b** as a colorless solid. Yield: 101.9 mg, 93%. Mp: 93-94 °C. IR (cm^{-1}): ν(C=O) 1721, 1694; ν(C=N) 1578. ^1H NMR (200 MHz, $CDCl_3$): δ 8.31-8.24 (m, 2H), 8.05 (m, 1H), 4.88 (s, 2H, CH_2), 2.79 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (50.30 MHz, $CDCl_3$): δ 198.8 (s, *C*(O)Me), 191.8 (s, *C*(O)CH_2Br), 152.7 (s, *C*C(O)Me), 150.3 (s, *C*C(O)Br), 138.4 (s, CH, *p*-C), 125.8 (s, CH, *m*-C), 125.5 (s, CH, *m*-C), 31.4 (s, CH_2), 25.6 (s, Me). HRMS calc for $C_9H_8O_2BrN$ $[M+H]^+$ *m/z* 241.9811, found *m/z* 241.9812. Anal. Calcd for $C_9H_8O_2BrN$: C, 44.66 ; H, 3.33; N, 5.79. Found: C, 44.62; H, 3.29 ; N, 5.89.

Table 1. **Crystal Data for Complexes 1b, 2a and 2b.**

	1b	**2a**	**2b**
formula	$C_{11}H_{14}BrNO_3Pd$	$C_{11}H_{14}Cl_3NO_3Pd$	$C_{11}H_{14}Br_3NO_3Pd$
Mr	394.54	420.98	554.36
cryst size (mm)	0.17x0.12x0.10	0.21x0.15x0.09	0.24x0.22x0.16
cryst syst	Monoclinic	Monoclinic	Monoclinic
space group	P2(1)/c	P2(1)/n	P2(1)/n
cell constants			
a, Å	9.6687(2)	8.5235(4)	8.8728(8)
b, Å	9.9942(7)	13.5319(7)	13.3587(12)
c, Å	13.8064(11)	12.8239(7)	13.1184(12)
α, Å	90	90	90
β, Å	107.748(2)	98.407(2)	99.193(2)
γ, Å	90	90	90
volume, Å^3, Z	12070.63(16), 4	1463.20(13), 4	1534.9(2), 4
λ, Å	0.71073	0.71073	0.71073
ρ(calc) (Mgm^{-3})	2.062	1.911	2.399
T (K)	100(2)	100(2)	100(2)
μ, mm^{-1}	4.600	1.817	9.020
transmissions	0.656 – 0.568	0.854 – 0.767	0.326 – 0.212
θ, range (deg)	2.56 – 28.67	2.20 – 28.15	2.19 – 28.72
limiting indices	-13 ≤ h ≤ 12	-10 ≤ h ≤ 11	-11 ≤ h ≤ 11
	-13 ≤ k ≤ 12	-17 ≤ k ≤ 117	-17 ≤ k ≤ 17
	-17 ≤ l ≤ 18	-16 ≤ l ≤ 16	-17 ≤ l ≤ 17
no. of reflns			
measd	15327	16440	18602
indep	3089	3390	3734
R_{int}	0.021	0.0193	0.019
abs. corr	Semi-empirical	Semi-empirical	Semi-empirical
	from equivalents	from equivalents	from equivalents
refinement method	full-matrix least	full-matrix least	full-matrix least
	squares on F^2	squares on F^2	squares on F^2
no. data/rest/params	3089/0/157	3390/5/190	3734/0/190
S (F^2)	1.059	1.083	1.078
R1[a]	0.019	0.019	0.016
wR2[b]	0.046	0.049	0.040
largest diff peak (e Å^{-3})	0.764	0.422	0.434
max. Dr (e Å^{-3})	-0.593	-0.684	-0.744

[a] $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ for reflections with $I > 2\sigma(I)$. [b] $wR2 = [\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{0.5}$ for all reflections; $w^{-1} = \sigma^2(F^2) + (aP)^2 + bP$, where $P = (2F_c^2 + F_o^2)/3$ and *a* and *b* are constants set by the program.

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[35] $[PdCl_2(C^N)(C^O)]$:[28] quantitatively yield, stable in MeCN solution at -35 °C, decomposes at 33 °C to give the Pd(II) complex $[PdCl_2(ClC^N)(C^O)]$ as the major product in 75% or 46% isolated yield. $[PdF_2(C^N)(N^N)]$:[22] 88% isolated yield, stable at 23 °C in the solid state for at least a week and in chloroform solution at 50 °C for at least 2 h; heating it at 150 °C in DMSO affords FC^N in 71 % isolated yield. $[PdF_2(FHF)(C_6H_4F\text{-}4)(N^N)]$:[18] 38% yield; heating it at 80 °C in nitrobenzene afforded only traces of 1,4-$C_6H_4F_2$.

Section III.2: Synthesis, Isolation and Characterization of an Organometallic Triiodopalladium(IV) Complex. Quantitative and Regioselective Synthesis of Two C–I Reductive Elimination Products

ABSTRACT

Iodine and the pincer complex [Pd(*O,N,C*-L)I], where L is the monoanionic ligand resulting from deprotonation of the acetyl group of the dimethylmonoketal of 2,6-diacetylpyridine, are in equilibrium at low temperatures with the Pd(IV) complex [Pd(*O,N,C*-L)I_3], which can be isolated at –40 °C and characterized by ^{1}H NMR spectroscopy and X-ray diffraction studies, in spite of its great instability. When the same reaction is carried out at room temperature, a quantitative reductive elimination process occurs, giving L–I, which in the presence of water affords L'–I, resulting from hydrolysis of L–I.

INTRODUCTION

The number of fully characterized organopalladium(IV) complexes reported is increasingly growing in recent years in parallel with the interest for their use in catalytic and stoichiometric organic reactions. The difficulty of preparing, isolating and characterizing such complexes stands on their spontaneous tendency to undergo reductive elimination processes to give Pd(II) complexes and C–C or C–X (X = halogen, RCO_2) coupling products, which accounts for their applications in organic synthesis.[1-3]

Since the synthesis of the first organopalladium(IV) complexes by Usón and Forniés in the 1970s, by reacting perfluorophenylpalladium(II) complexes wth chlorine,[4] only a very recent studies devoted to obtaining Pd(IV) complexes by using dihalogens, $PhIX_2$ or XeF_2 have succeeded in giving oxidative addition products stable enough to be isolated and characterized by X-ray diffraction: [PdF_2(C^N)(N^N)] (X^Y is an *X,Y*-monoanionic chelating ligand),[5] [$PdCl_2$(C^N)(C^O)],[6] [PdF_2(FHF)(C_6H_4F-4)(N~N)] (X~Y is an *X,Y*-neutral chelating ligand),[7] [$PdBr_2$(C^N^N)(CN^{t}Bu)] (X^Y^Z is an *X,Y,Z*-monoanionic tridentate ligand),[2] [PdX_3(C^N^O)] (X = Cl, Br).[3] Neutral monohalo derivatives [PdX(C^C)(N^N^N)] (X = Cl, Br, I) are the isolated products when the halogen is reacted with some anionic complexes.[8] In the meantime, most of the reported reactions of this type in which the Pd(IV) complex has been isolated but not characterized by X-ray diffraction,[9] not isolated[10, 11] or even not detected,[12] have been used to prepare the corresponding C–X coupling products resulting from the reductive elimination process.

The above results set I_2 quite apart from the other halogens. In fact, the only reported diiodo organometallic Pd(IV) complexes are [PdI_2Me(R)L_2] (L_2 = bidentate nitrogen donor ligands, R = Me, Tol), prepared by reacting I_2 with [PdMe(R)L_2], which decomposes in

solution or upon attempted isolation.[13, 14] The sulfur ylide complex [Pd{$(CH_2)_2S(O)Me$}$_2$] reacts with I_2 to afford the unstable complex [Pd{$(CH_2)_2S(O)Me$}$_2I_2$],[15] which was characterized only by elemental analysis. Even Pd(IV) complexes with only one iodo ligand, usually obtained by the oxidative addition of alkyl iodides to alkylpalladium(II) complexes, are unstable when isolated or only detected in solution.[13, 16] At difference with dihalopalladium(IV) complexes, which decompose to give the C–X reductive elimination products, monohalopalladium(IV) complexes usually decompose through C–C coupling processes. Only one such complex, *fac*-[$PdMe_3I$(bpy)], has been characterized by X-ray diffraction.[17] When these data on Pd(IV) complexes are compared with those of the corresponding Pt(IV) complexes the great differences between both d^6 ions are evident. For example, many Pt(IV)I_n-complexes (n =1 – 6), in particular stable triiodo complexes, have been isolated.[18]

We have recently reported the synthesis of the pincer complexes [Pd(*O,N,C*-L)X],[3, 19] where X = Cl, Br and L is the monoanionic ligand resulting from deprotonation of the monoketal of 2,6-diacetylpyridine (dap), and its use to prepare Pd(IV) complexes [Pd(*O,N,C*-L)X_3] (X = Cl, Br) by reacting them with Cl_2 or Br_2.[3] Because this pincer ligand provides these complexes with a remarkable stability, we considered the synthetic challenge of completing the series by preparing the triiodopalladium(IV) complex, [Pd(*O,N,C*-L)I_3], whose stability was predicted to be very precarious considering all the above data.

RESULTS AND DISCUSSION

The reaction of [Pd(*O,N,C*-L)Cl] with NaI afforded quantitatively [Pd(*O,N,C*-L)I] (**1**; Scheme 1). The reaction at –40 °C, under N_2, between a CH_2Cl_2 solution of **1** and I_2 (1 : 1.25 molar ratio) gave a very dark solution, which upon slow diffusion of Et_2O and standing for 5 days at –33 °C, gave black single crystals of the triiodopalladium(IV) complex [Pd(*O,N,C*-L)I_3] (**2**). Although crystalline solid **2** shows no noticeable decomposition after 1 month at –33 °C, the amorphous solid decomposes immediately at 20 °C, preventing us from obtaining good elemental analyses. However, **2** has been characterized by ^{1}H NMR spectroscopy and X-ray crystallography (see below). This result contrasts with that obtained in the related reaction between [Pd(N^C^N)I] (N^C^N = 2,6-bis[(dimethylamino)methyl]phenyl)) and I_2, which affords [Pd(N^C^N)I···$(I_2)_2$] containing two molecules of I_2 interacting with the iodo ligand at distances of 3.3 Å. This complex is a possible model for the initial stage in the formation of **2**

although another with a Pd···I_2 interaction, such as has been described for the homologous Pt(II) pincer complex,[20] cannot be discarded.

The reaction of **1** with one equiv of I_2 was followed by ^{1}H NMR in CD_2Cl_2 and in $CDCl_3$ at various temperatures. At room temperature, the spectra of the reaction mixtures showed full and almost immediate decomposition of **2** to the C–I coupling product, L–I (**3**) (Scheme 1), and precipitation of a black solid, identified as PdI_2. Therefore, the room temperature reaction of a $CHCl_3$ solution of **1** with one equiv of I_2 allowed the quantitative and regioselective isolation of **3**. When this reaction was carried out in the presence of water, using MeCN as the solvent, hydrolysis of **3** took place, allowing the quantitative and regioselective isolation of compound **4**. We could not isolate the chloro and bromo homologues of **3**, from the corresponding Pd(IV) complexes, because they quickly hydrolyzed to give the corresponding homologues of **4**.[3] The only reported halogen derivative of dap is the symmetric dibromo-dap obtained by bromination.[21]

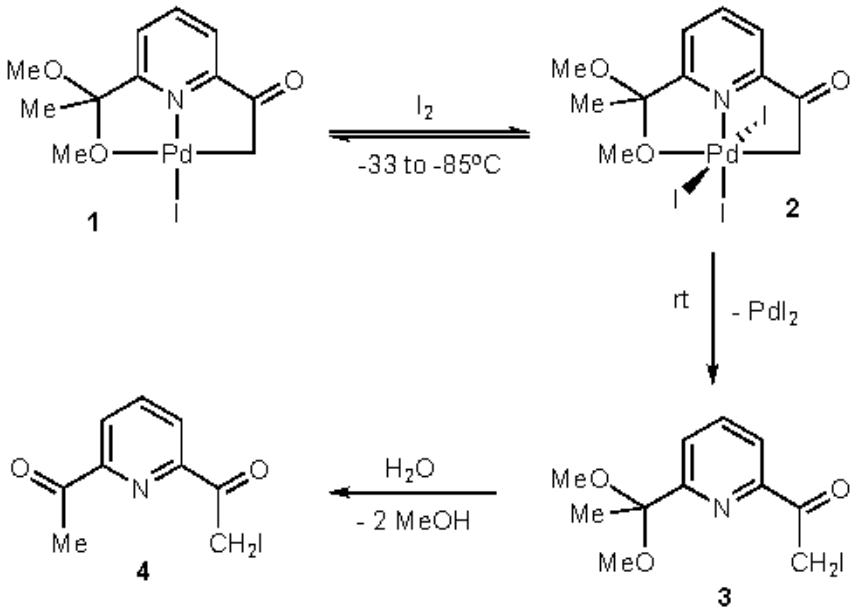
Complexes of Fe(II) and Co(II) with bis(imino) derivatives of dap are highly active catalysts for polymerization and oligomerization of olefins. Compound **4** and derivatives prepared by replacing iodine, could be used to synthesize new catalysts with unsymmetrical dap derivatives.[22]

Although Pd(IV) intermediates have been invoked in some reactions between alkyl Pd(II) complexes and I_2 affording C–I coupling products, they have not even been detected in solution.[11] The same occurs with the diiodination of some arenes using $Pd(OAc)_2$ as the catalyst and IOAc as the oxidant.[23]

At temperatures below –33 °C, the ^{1}H NMR spectra of the I_2 + **1** mixture showed only the presence of **1** and **2**. The **2**/**1** ratio increases when the temperature decreases, reaching >99% conversion of **1** into **2** at –85 °C. The temperature dependence of the equilibrium **1** + I_2 ⇆ **2** in $CDCl_3$ was investigated in the range 240 to 211 K. A van't Hoff analysis (R = 0.999) yields values of ΔH = –24 kJ mol^{-1} and ΔS = –59 J K^{-1} mol^{-1}. Values of K_{eq} at 211 and 240 K are 757 and 142, respectively ([**2**] = [I_2] = 2.88x10^{-2} mol L^{-1}). A similar study was reported for the reaction between [PdMe(C_6H_4OMe-4)(bpy)] and (4-ClC_6H_4)$_2$Se$_2$ to afford [PdMe(C_6H_4OMe-4)(SeC_6H_4Cl-4)$_2$(bpy)] (ΔH = –130 kJ mol^{-1}, ΔS = –472 J K^{-1} mol^{-1}, and K_{eq} = 759 at 248 K).[24]

The tendency of **2** to disproportionate into the reagents used to prepare it, **1** and I_2, represents an essential difference with respect to its homologues trichloro and tribromo

complexes[3] and other Pd(IV) organometallic complexes with the only exception shown above.[24] It can be considered normal for an organometallic complex of a highly oxidizing metal center, Pd(IV), bonded to three reducing ligands like I^- and is in line with our initial skepticism on the success of the synthesis of **2**.



Scheme 1

The ^{1}H NMR spectrum of complex **1** shows the equivalence of the MeO groups and that of the CH_2, protons at room temperature, while at –33 °C the corresponding signals are broad. In the chloro and bromo derivatives the equivalence of the MeO and CH_2 protons is maintained even at –60 °C, which shows that the Pd–OMe bond is stronger in the iodo complex **1** than in its halide homologues. In contrast to **1**, the MeO and CH_2 protons of **2** at –33 °C are observed as two singlets and an AB system, respectively, which reveals the stronger Pd–OMe bond in the Pd(IV) complex **2** with respect to the Pd(II) complex **1**. The CH_2 protons in complex **2** appear highly deshielded (6.29, 6.01 ppm) with respect to those in **1** (3.49 ppm), which was also observed in the chloro and bromo derivatives.

The structure of complex **2** (Figure 1)[25] is similar to those of its chloro and bromo homologues.[3] The main difference (apart from the Pd–X bond distances) is the Pd–N bond length, which is longer in **2** (2.045(3) Å) than in the other $[PdLX_3]$ complexes (X = Br (2.0207(15) Å), Cl (2.0058(15) Å)), according to the trans influence scale I > Br > Cl.[26]

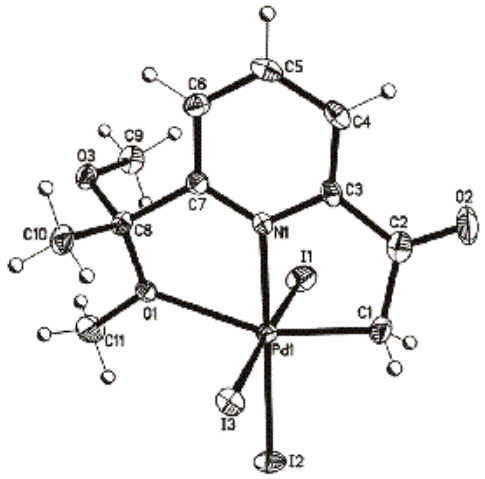


Figure 1. Ellipsoid representation of 2 (50% probability)

CONCLUSIONS

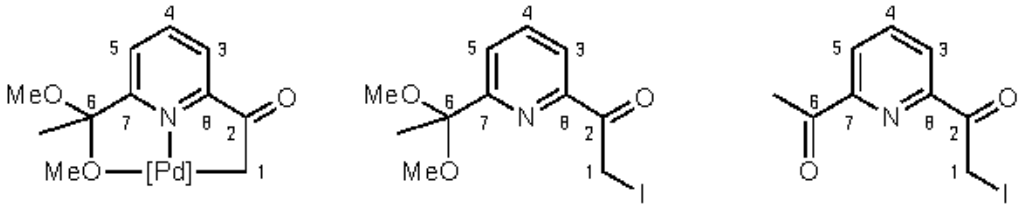
In conclusion, we have studied 1) the reaction between an organometallic Pd(II) pincer complex and I_2 being able to isolate and characterize (by NMR and X-ray diffraction) the first triodo organometallic Pd(IV) complex ever reported, in spite of its instability, 2) the first equilibrium [Pd(II)] + X_2 (halogen) ⇆ [Pd(IV)X_2], 3) the reductive elimination process that, at room temperature, affords the unreported C–I coupling product, and 4) the hydrolysis of the latter, which leads to the first monohalo derivative of dap.

EXPERIMENTAL SECTION

General Procedures

Unless otherwise stated, the reactions were carried out without precautions to exclude light, atmospheric oxygen or moisture. Melting points were determined on a Reicher apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on a Bruker AC 200, or Avance 300 or 400 spectrometers. Chemical shifts were referred to TMS (^{1}H, ^{13}C). When needed, NMR assignments were performed with the help of APT, HMQC and HMBC techniques. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS; the exact masses have been calculated for the combination of the most abundant isotopes. Complex [Pd(*O,N,C*-L)Cl] was prepared as reported previously.[3] Chart 1

shows the atom numbering used for NMR assignments.



1, 2 **3** **4**

Chart 1

Synthesis

Synthesis of [Pd(O^1,N^1,C^1-L)I] (**1**). To a solution of [Pd(*O*,*N*,*C*-L)Cl][19] (354.2 mg, 1.01 mmol) in acetone (30 mL), NaI (151.8 mg, 1.01 mmol) was added. The reaction mixture was stirred for 15 min and then filtered through Celite. The filtrate was concentrated (2 mL) and Et_2O (2 mL) and *n*-pentane (15 mL) were added. The resulting suspension was filtered off, and the solid washed with *n*-pentane and air-dried to give **1** as a yellow solid. Yield: 432.8 mg, 97%. Mp: 201 °C dec. IR (cm^{-1}): ν(C=O) 1691; ν(C=N) 1601. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.18 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.87 (dd, 1 H, H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.65 (dd, 1 H, H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 3.49 (s, 2 H, CH_2), 3.45 (s, 6 H, OMe), 1.76 (s, 3 H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, $CDCl_3$): δ 204.6 (CO), 158.0 (C7), 151.4 (C8), 140.0 (C4), 126.6 (C5), 123.5 (C3), 107.0 (C6), 52.0 (MeO), 27.0 (C1), 25.1 (Me). Anal. Calcd for $C_{11}H_{14}NO_3IPd$: C, 29.92 ; H, 3.20 ; N, 3.17. Found: C, 29.95; H, 2.96; N, 3.34.

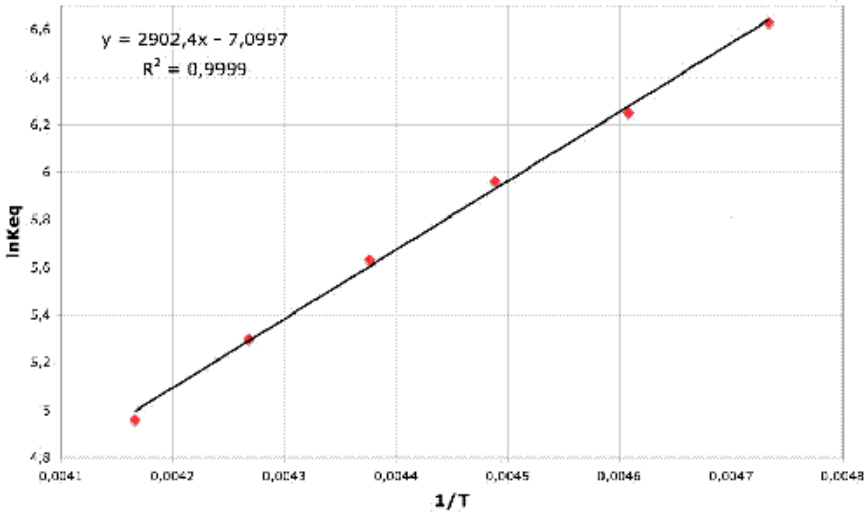
Synthesis of mer-[Pd(O^1,N^1,C^1-L)I_3] (**2**). To solid I_2 (25.5 mg, 0.10 mmol), in a test tube cooled at – 40 °C, was added a solution of **1** (34.3 mg, 0.08 mmol) in CH_2Cl_2 (1.5 mL) under N_2. The tube was manually stirred for 2 min in the cool bath and then Et_2O was slowly diffused into the solution. The tube was stored at – 33 °C for 5 days to give **2** as black single crystals. ^{1}H NMR (400 MHz, CD_2Cl_2, –85 °C): δ 8.33 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 8.18 (d, 1 H, H3 or H5, $^3J_{HH}$ = 7.6 Hz), 7.88 (d, 1 H, H5 or H3, $^3J_{HH}$ = 7.6 Hz), 6.29 (d, 1 H, CH_2, $^1J_{HH}$= 13.6 Hz), 6.01 (d, 1 H, CH_2, $^1J_{HH}$= 13.6 Hz), 3.67 (s, 3 H, OMe), 3.27 (s, 3 H, OMe), 1.92 (s, 3 H, Me).

Synthesis of L–I (**3**). To a solution of **1** (139.3 mg, 0.32 mmol) in $CHCl_3$ (15 mL) was added I_2 (80.0 mg, 0.32 mmol). The resulting suspension was stirred for 3 h and then concentrated to dryness. The resulting residue was vigorously stirred in *n*-pentane (20 mL) and filtered through Celite. The filtrate was concentrated to dryness to give **3** as a pale yellow oil. Yield: 99.1 mg, 94%. IR (cm^{-1}): ν(C=O) 1694; ν(C=N) 1585. ^1H NMR (200 MHz, $CDCl_3$): δ 8.03-7.99 (m, 2H), 7.93-7.83 (m, 1H), 4.71 (s, 2H, CH_2), 3.23 (s, 6H, OMe), 1.70 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (50.30 MHz, $CDCl_3$): δ 194.6 (CO), 160.1 (C7), 150.0 (C8), 137.4 (C4), 125.7 (C5), 121.7 (C3), 101.5 (C6), 49.3 (MeO), 23.4 (Me), 1.9 (CH_2). HRMS calc for $C_{11}H_{14}O_3IN$ (M + H+) *m/z* 336.0091, found *m/z* 336.0084.

Synthesis of L'–I (***4***). A mixture of **1** (73.3 mg, 0.17 mmol), I_2 (42.1 mg, 0.17 mmol), H_2O (50 µL, 2.78 mmol) and MeCN (10 mL) was stirred for 2 days and then was concentrated to dryness. The resulting residue was vigorously stirred in *n*-pentane (30 mL) for 10 min and then was filtered through Celite. The filtrate was concentrated to dryness to give **4** as a pale yellow oil. Yield: 45.1 mg, 94%. IR (cm^{-1}): ν(C=O) 1703, 1694; ν(C=N) 1581. ^1H NMR (200 MHz, $CDCl_3$): δ 8.29-8.23 (m, 2H), 8.09-8.01 (m, 1H), 4.69 (s, 2H, CH_2), 2.80 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (50.30 MHz, $CDCl_3$): δ 199.0 (C6), 193.5 (C2), 152.5 (C7), 149.7 (C1), 138.4 (C4), 125.9 (C3 or 5), 125.3 (C3 or 5), 25.7 (Me), 0.6 (CH_2). HRMS calc for $C_9H_8O_2IN$ (M + H+) *m/z* 289.9672, found *m/z* 289.9665.

NMR studies. Van't Hoff analysis

In a typical experiment for the determination of equilibrium constants for the formation of complex **2**, a sample of [Pd(O^1,N^1,C^1-L)I] (**1**) (10.16 mg, 0.023 mmol) and I_2 (5.84 mg, 0.023 mmol) was cooled and dissolved in cold $CDCl_3$ (800 µL). The sample was kept at the required temperature for 15 min before recording the spectrum. The concentration of **1** and **2** was determined by integration. The sample temperature was calibrated manually with a solution of MeOH 4% in Methanol-d^4.



$\Delta H = -24$ kJ mol^{-1}; $\Delta S = -59$ J K^{-1} mol^{-1}

T (K)	K_{eq}
211.2	756.98
217.0	517.12
222.8	388.66
228.5	278.78
234.3	199.68
240.0	142.40

Table 1. Crystal data and structure refinement of complex **2**.

Empirical formula	C11 H14 I3 N O3 Pd	
Formula weight	695.33	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2(1)/n	
Unit cell dimensions	a = 9.328(4) Å	α = 90°
	b = 13.261(5) Å	β = 100.154(6)°
	c = 13.698(5) Å	γ = 90°
Volume	1667.9(11) $Å^3$	
Z	4	
Density (calculated)	2.769 Mg/m^3	
Absorption coefficient	6.668 mm^{-1}	
F(000)	1264	
Crystal size	0.21 x 0.20 x 0.16 mm^3	
Theta range for data collection	2.15 to 28.62°	
Index ranges	-12<=h<=9, -14<=k<=16, -18<=l<=17	
Reflections collected	10864	
Independent reflections	3929 [R(int) = 0.0171]	
Completeness to theta = 26.50°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.4151 and 0.3278	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3929 / 5 / 190	
Goodness-of-fit on F^2	1.143	
Final R indices [I>2sigma(I)]	R1 = 0.0248, wR2 = 0.0548	
R indices (all data)	R1 = 0.0269, wR2 = 0.0557	
Largest diff. peak and hole	1.306 and -0.931 $e.Å^{-3}$	

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[25] The crystal data and experimental details of the structural refinement for **2** are provided in the Supporting Information. CCDC 813803 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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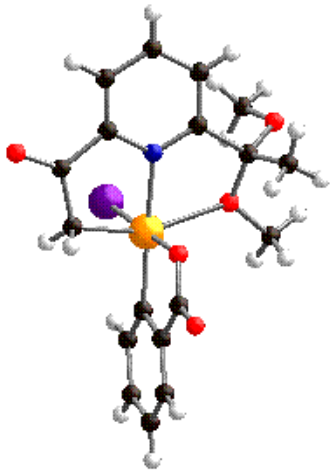
CHAPTER IV

Pd(II)/Pd(IV) Catalytic Cycle in a Heck-Type Arylation of Olefins



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F. Juliá-Hernández, A. Arcas, J. Vicente, D. Bautista *Chem. Eur. J. Submitted*

SUMMARY CHAPTER IV

Catalytic C–C coupling reactions are one of the most important processes in Organic Chemistry. This has been recognized with the award of the 2010 Nobel Prize in Chemistry. Recently, new types of catalytic or stoichiometric C–C coupling processes are being reported involving the oxidation of Pd(II) to Pd(IV) complexes. This has moved us to study new oxidation reactions of our pincer Pd(II) complexes.

The arylation of olefins catalyzed by Pd(0) complexes, i. e., the Heck reaction, changed considerably when in the nineties Pd(II) precatalysts containing chelate or pincer-type ligands allowed to achieve outstanding results in this, and also other C–C coupling reactions. Although initially, a Pd(II)/Pd(IV) catalytic cycle was proposed, it soon became clear, that the Pd(II) complex decomposed to give Pd nanoparticles that were the actual catalysts. However, an increasing number of recent publications report that in some catalytic reactions using Pd(II) precatalysts do not involve Pd nanoparticles or Pd(0) complexes, which again suggest the possibility of a Pd(II)/Pd(IV) cycle in such reactions. Nevertheless, the solution of two problems has to be addressed: the possibility of some aryl halide to add oxidatively to a Pd(II) complex and the detection of a Pd(IV) during the catalytic cycle. The results described in this **Chapter IV** attempt to resolve this controversy.

Section IV.1 is aimed at achieving an oxidation reaction of a Pd(II) complex by an haloarene. In this context, the acetate derivative of our pincer Pd(II) complex was reacted with 2-iodobenzoic acid to yield the first Pd(IV) complex synthesized by an oxidative addition of an aryl halide to a Pd(II) compound. The reaction gives the corresponding benzoate Pd(II) complex that undergoes an intramolecular oxidative addition. In addition, we detected the presence of two Pd(IV) isomers when we lower the temperature. As this reactions correspond to the first step in a Pd(II)/Pd(IV) catalytic cycle, we decided to study the catalytic properties of the Pd(IV) complexes in a Heck-type coupling reaction.

Noteworthy, methyl acrylate was coupled with 2-iodobenzoic acid in the presence of silver perchlorate and catalytic amounts of the Pd(IV) isomers at room temperature. These results suggested us on the possibility of the existence of a Pd(II)/Pd(IV) catalytic cycle in this reaction. Thus, in **Section IV.2** we carried out a complete investigation about the reaction mechanism, not only with the Pd(IV) complex as catalyst but using some of our pincer Pd(II) complexes.

Thereby, we carried out kinetic data, poisoning experiments to show if Pd nanoparticles are involved or not, the dibenzyl test to exclude or not if some Pd(0) is implicated and ESI-MS trying to detect some Pd(IV) complex during the catalytic cycle.

After performed many experiments under different conditions, we could rule out that a Pd(0)/Pd(II) cycle operates in the above catalytic reaction, which combined with the detection of a couple of Pd(IV) complexes during the catalysis by ESI-MS support a Pd(II)/Pd(IV) mechanism. We are convinced we have shed light on one of the most open problems in homogeneous catalysis.

Section IV.1: Synthesis of a Palladium(IV) Complex by Oxidative Addition of an Aryl Halide to Palladium(II) and Its Use as Precatalyst in a C–C Coupling Reaction

ABSTRACT

The complex [Pd(*O,N,C*-L)Cl] (**1**·Cl), where L is the monoanionic ligand resulting from deprotonation of the acetyl group of the dimethylmonoketal of 2,6-diacetylpyridine, reacts with one equiv of AgOAc to give [Pd(*N,C*-L)OAc] (**1**·OAc). This, in turn, reacts with 2-iodobenzoic acid at room temperature in CH_2Cl_2 to afford the very stable pair of Pd^{IV} complexes (OC-6-54)- and (OC-6-26)-[Pd(*O,N,C*-L)(*O,C*-$C_6H_4CO_2$-2)I] (**2a** and **2b**, respectively, in 1.5:1 molar ratio, respectively). Complexes **2** are precatalysts for the room temperature ortovinylation of 2-iodobenzoic acid with CH_2=$CHCO_2Me$ and $AgClO_4$. The reaction neither quenches by addition of 4000 equiv of Hg per Pd nor affords dibenzyl when benzyl chloride is added to the reaction mixture. These results, suggest that neither palladium nanoparticles nor some Pd(0) is involved in the process, leaving a Pd(II)/Pd(IV) catalytic cycle with the participation of some derivative of 2 as an reasonable alternative to the classical Pd(0)/Pd(II) cycle.

INTRODUCTION

The recent award of the 2010 Nobel Prize in Chemistry to Heck, Negishi and Suzuki for their studies on catalytic cross couplings has recognized the important role of palladium in organic synthesis.[1,2] Their methods were later improved by the use of Herrmann's palladacycles as precatalysts.[3] Most of both types of reactions involve a Pd(0)/Pd(II) catalytic cycle.[4,5] Pd(0) species are the precatalysts in the classical reactions[1] or form *in situ* from the Pd(II) precatalyst as a Pd(0) complex or as Pd nanoparticles.[6-8] However, based on various experimental data, Pd(II)/Pd(IV) catalytic cycles have been proposed as an alternative.[9,10] Some computational studies also support this proposal.[7,11,12] However, since the oxidative addition of an aryl halide to a Pd(II) complex[13] and the existence of Pd(IV) complexes in these catalytic processes[14] have not yet been conclusively demonstrated, the Pd(II)/Pd(IV) catalytic cycle has become one of the most intriguing open problems in catalysis.[15] Herein, we discuss the first of these two topics.

A few aryl palladium(IV) complexes have been isolated (or characterized in solution) from aryliodonium salts[16] or from the oxidation of corresponding aryl palladium(II) derivatives[17,18] but never from an aryl halide as required in the coupling reactions in which a Pd(II)/Pd(IV) catalytic cycle is invoked, which is one of the weaknesses of the proposal. A computational study has shown that oxidation of a N^C^N pincer Pd(II) complex with PhI is a highly endothermic reaction[19], while another study shows that not only the oxidation of

various P^C^P pincer Pd(II) complexes with PhBr but also a Pd(II)/Pd(IV) Heck-type catalytic cycle are viable.[11] Similar conclusions were drawn from a previous investigation based on a C^N chelating Pd(II) complex, thus suggesting that the presence of a weakly coordinating ligand would favor a Pd(II)/Pd(IV) mechanism.[12] Therefore, the nature of the aryl halide and the ligands around Pd(II) seem to greatly influence the viability of the crucial oxidative addition step in this alternative catalytic cycle.

RESULTS AND DISCUSSION

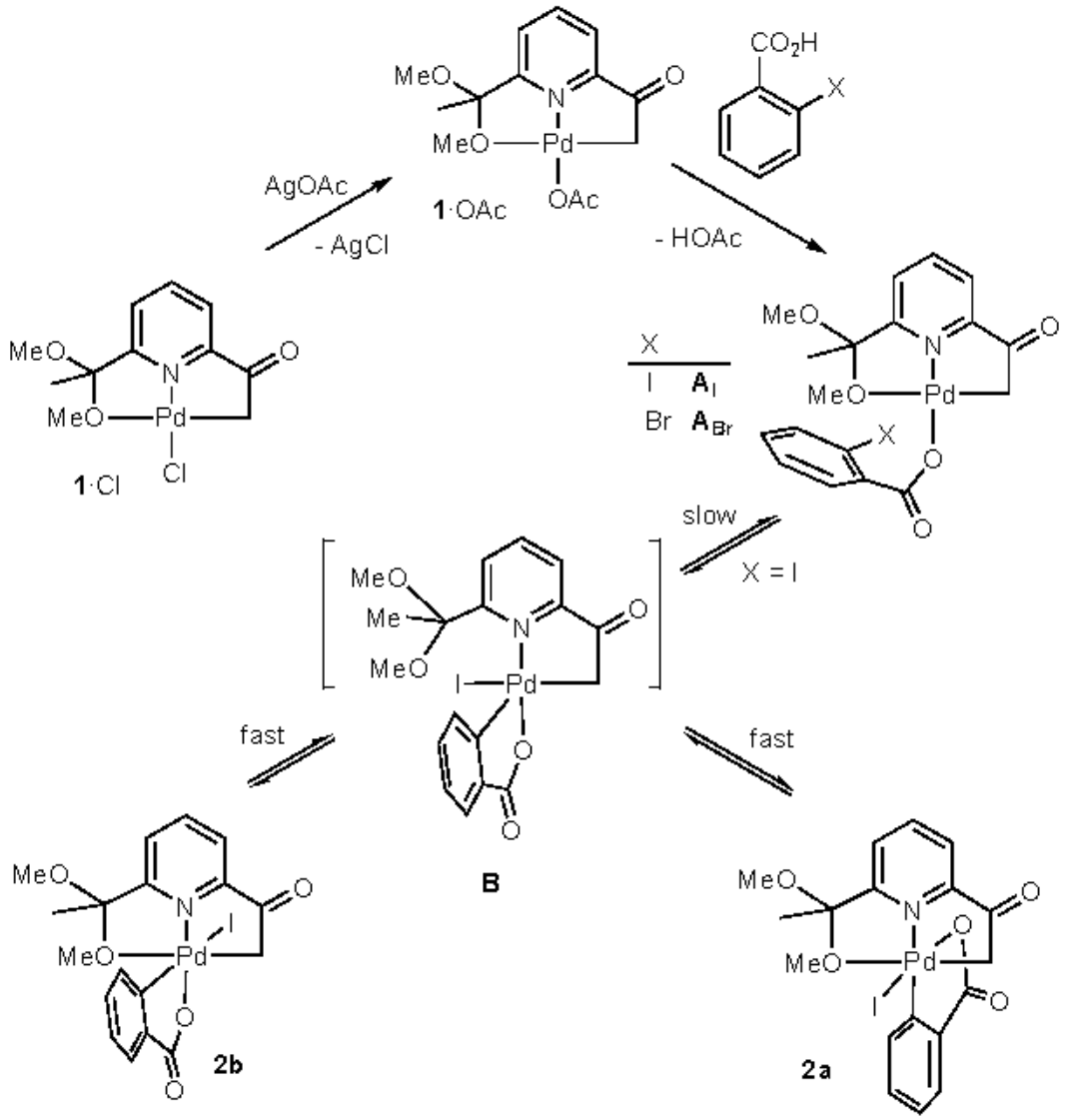
Recently, we reported the reaction of $PdCl_2$ with 2,6-diacetylpyridine in refluxing MeOH to give [Pd(*O,N,C*-L)Cl] (**1**·Cl, Scheme 1)[20] which reacts with Cl_2 or NaBr to give, respectively, the stable Pd(IV) complex [Pd(*O,N,C*-L)Cl_3] or [Pd(*O,N,C*-L)Br], which, in turn, reacts with Br_2 to afford [Pd(*O,N,C*-L)Br_3].[21] The stability of these Pd(IV) complexes (which was attributed to the pincer ligand) and the weakly coordinating ability of the MeO group in the Pd(II) complexes, (which was expected to help its oxidation to Pd(IV) (see above)) moved us to attempt the synthesis of a stable and unprecedented aryl Pd(IV) complex from an aryl iodide and a [Pd(*O,N,C*-L)X] complex. Because Pd(IV) complexes are thermally unstable, and because we also set out to use such Pd(IV) complex as a precatalyst in a C–C coupling process, we decide to prepare and test its catalytic ability at room temperature. We chose as reagents 2-iodobenzoic acid and the new complex [Pd(*O,N,C*-L)(OAc)] (**1**·OAc, Scheme 1), prepared by treating **1**·Cl[20] with AgOAc. Coordination of the benzoate moiety, after deprotonation, would bring the iodine atom close to the palladium atom, and this situation, along with the presence of the electron-withdrawing *ortho*-substituent,[4,22] would give the oxidative addition reaction a chance to occur at room temperature. Additionally, the resulting chelating phenyl benzoato ligand would increase the stability of the Pd(IV) complex. The product obtained was the expected Pd(IV) complex [Pd(*O,N,C*-L)(*O,C*-$C_6H_4CO_2$-2)I] (**2**), which is indefinitely stable in the solid state. This first Pd(II) to Pd(IV) oxidative addition using an aryl halide does not contradict studies demonstrating that other aryl halides do not oxidatively add to other Pd(II) complexes.[23]

The ^{1}H NMR spectrum of a $CDCl_3$ solution of **2** at room temperature shows the presence of traces of two non-identified decomposition products after 5 h and 24% decomposition 30 h later. Complexes **1**·OAc and **2a** were characterized by X-ray diffraction (Figure 1), NMR spectroscopy and elemental analyses. The crystal structure of **1**·OAc showed it to be a dimer

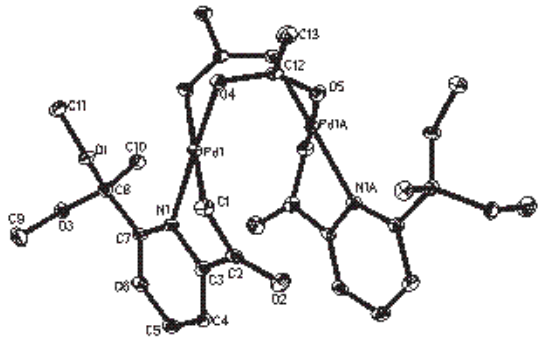
with bridging acetato ligands (Figure 1); the Pd–Pd distance 3.0315(5) Å[24] is significantly longer than the double of the Pd covalent radius (1.39 Å).[25] However, its ^{1}H and ^{13}C NMR spectra (in particular, the MeO resonances) are similar to other Pd(*O,N,C*-L) complexes and different from those containing the chelating ligand *N,C*-L[20] suggesting that in solution, its structure is that shown Scheme 1. Oxidative addition of aryl halides to Pt(II) complexes has been reported to be assisted by coordination,[26] but nothing similar had been found in the chemistry of Pd. The different nature of the assistant group in our case (anionic) with respect to those present in Pt(II) (neutral) merits to be emphasized.

During this reaction, an intermediate was detected, which remained in solution until the end. Its CH_2 protons resonate at a value (3.69 ppm) similar to those found in the other Pd(II)(*O,N,C*-L) complexes (3.73–3.27 ppm)[20,21] and lower than those in **2** (δ_A, 4.95, δ_B, 4.55 ($^{2}J_{HH}$ = 12.4 Hz)) and their homologues (6.06–6.04 ppm)[21]. Therefore, we propose that this intermediate is the Pd(II) benzoato complex [Pd(*O,N,C*-L)($O_2CC_6H_4$I-2)] (**A**$_I$, Scheme 1), which is also observed when **2** is dissolved in $CDCl_3$. An additional evidence on the nature of **A**$_I$ was obtained when, attempting to prepare the Br homologue of **2** at room temperature by treating **1**·OAc with 2-bromobenzoic acid, we isolated only the complex **A**$_{Br}$ (Scheme 1 and Figure 1), which we fully characterized, including by X-ray crystallography.

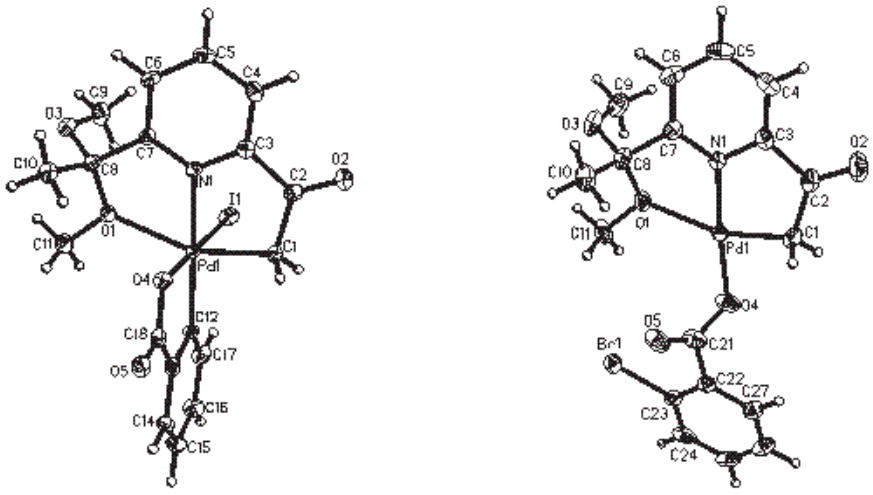
The ^{1}H NMR of **2** was studied in $CDCl_3$ between –55 and 35 °C, its upper limit of stability, a slow **2** ⇆ **A**$_I$ equilibrium in the NMR time scale was detected. The **2**:**A**$_I$ molar ratios decrease from approximately 9:1 in the range –55 to –5 °C about 2.3:1 at 25 °C and 1.9:1 at 35 °C. Furthermore, the AB system corresponding to the CH_2 protons in **2** at room temperature coalesces at –20 °C and splits into two AB systems below –35 °C, thus indicating the existence of the two possible Pd(IV) geometric isomers **2a** and **2b** in equilibrium (Scheme 1; 1.5:1 molar ratio; **2a**: δ_A, 4.84, δ_B, 4.71 ($^{2}J_{HH}$ = 12 Hz); **2b**: δ_A, 5.08, δ_B, 4.38 ($^{2}J_{HH}$ = 13.2 Hz)), which probably interconvert through the unobserved intermediate **B** (Scheme 1).[27] The isomer with the greater $\delta_A - \delta_B$ value is assigned as that bearing the iodo ligand trans to the aryl group (**2b**), which shields the nearest CH_2 proton. A line-shape analysis of the CH_2 protons resonances of the equilibrium **2a** ⇆ **2b** did not allow the determination of its activation parameters. Scheme 1 shows a proposal to account for the formation of **2a** and **2b** and their equilibrium. Oxidative addition reactions giving two Pd(IV) geometrical isomers have been reported,[18,28] those species were not in equilibrium.



Scheme 1. Synthesis of complexes **1**·OAc, $\mathbf{A_X}$ and **2** and a proposal for the equilibrium between $\mathbf{A_I}$ and the two isomers of complex **2**.



1·OAc



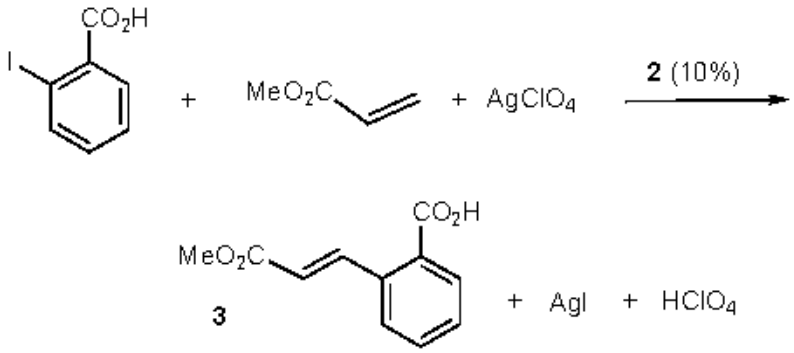
2a **A_{Br}**

Figure 1. X-ray crystal structures of complexes **1**·OAc (CCDC 807142), **2** (CCDC 807142) and A_{Br} (CCDC 807144).

Complex **2** did not react with CH_2=$CHCO_2Me$ in acetone-d_6 at room temperature, but when it was treated with two equiv CH_2=$CHCO_2Me$ in acetone-d6 in the presence of one equiv of $AgClO_4$ to remove the iodo ligand, at room temperature, the desired (*E*)-methyl 2-carboxycinnamate (**3**) was quantitatively obtained in less than 1h (Scheme 2). The Heck synthesis of **3**, using the corresponding diazonium salts instead of 2-iodobenzoic acid, has been reported.[29] Complex **2** is a precatalyst for this reaction using 10% of the stoichiometric amount (83% yield of **3** after 6h). It is clear that the interest of this result is not synthetic but associated to the use of a Pd(IV) complex as precatalyst in a C–C coupling process, the only related precedent of which is a recently reported Pd(IV)-catalyzed C–H trifluoromethylation reaction.[30] The same reaction mixture excluding **2** did not afford **3** after 4 days. The addition of a large excess of Hg (4000 equiv per Pd) to the catalytic reaction mixture did not quench the process, thus suggesting that Pd nanoparticles are not involved in the catalytic cycle,[8,9] and adding 0.5 equiv/Pd of benzyl chloride to the reaction mixture gave 80% yield of **3** after 5 h at room temperature but dibenzyl was not detected, excluding any Pd(0) complex to be involved in the catalytic cycle.[7]

The above data suggest that Pd(II)/Pd(IV) species are involved in the catalytic synthesis of **3**. Detailed studies on this reaction catalyzed by various Pd pincer complexes and attempts to detect Pd(IV) in the catalytic cycle are currently in progress. In the absence of $AgClO_4$,

complex **2** reacted with 2 equiv of CH_2=$CHCO_2Me$ in DMSO-d_6 at 140 °C giving quantitatively **3** in 1h. If 10% of the stoichiometric amount of **2** is used, 25 or 6% yield of **3** is obtained after 1 h depending on the solvent and the temperature (140 °C in DMSO-d_6 or 120 °C in DMF-d_7, respectively). However, **3** did not form when any of these high-temperature reactions were carried out in the presence of a strong excess of Hg (4900 equiv), which suggests that they are mediated by Pd nanoparticles.



Scheme 2. Catalytic synthesis of **3** using complex **2** as precatalyst.

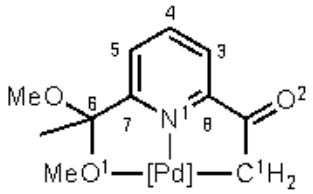
CONCLUSIONS

To sum up, we report on several *unprecedented results in the chemistry of Pd*: (1) the synthesis of a mixture of Pd(IV) complexes **2**, by oxidative addition of an aryl halide to Pd(II), (2) the intramolecular nature of the oxidative addition reaction, as suggested by the detection in solution of the precursor $\mathbf{A_I}$, (3) the isolation and full characterization of the bromine homologue $\mathbf{A_{Br}}$, (4) the anionic nature of the assistant group (benzoato) in the oxidative addition reaction, which makes a difference with the analogous reactions in Pt chemistry, assisted by neutral groups, (5) Pd(IV) complexes **2** and the precursor $\mathbf{A_I}$ are in equilibrium in solution, (6) complexes **2** react with $AgClO_4$ and 2 equiv CH_2=$CHCO_2Me$ at room temperature, to afford quantitatively **3** in less than 1h, (7) they also catalyze the same C–C coupling process, (8) experimental data suggest that this process occurs through a Pd(II)/Pd(IV) catalytic cycle and (9) in the absence of $AgClO_4$, stoichiometric or catalytic reactions of **2** and CH_2=$CHCO_2Me$ at high temperatures in DMSO or DMF afford **3** through the mediation of Pd nanoparticles.

EXPERIMENTAL SECTION

General Procedures

Unless otherwise stated, the reactions were carried out without precautions against light or atmospheric oxygen or moisture. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on Bruker Avance 200, 300 or 400 spectrometers at room temperature. Chemical shifts were referred to TMS (^{1}H, ^{13}C). NMR assignments were performed with the help of APT, HMQC and HMBC techniques. Complex **1**·Cl was prepared following a previously described procedure.[20] Chart 1 shows the atom numbering used in NMR assignments.



[Pd](*O*^{1},*N*^{1},*C*^{1}-L)

Chart 1

Synthesis

Synthesis of [Pd(O^1,N^1,C^1-L)(OAc)]·0.1 CH_2Cl_2 (**1**·OAc). To a solution of **1**·Cl[20] (46.2 mg; 0.13 mmol) in CH_2Cl_2 (6 mL), AgOAc (44.1 mg; 0.26 mmol) was added. The reaction mixture was vigorously stirred for 1.5 h and filtered through Celite. The filtrate was concentrated (2 mL) and Et_2O (2 mL) and *n*-pentane (10 mL) were added. The resulting suspension was filtered off and the solid washed with *n*-pentane and air-dried to give **1**·OAc as a yellow solid. Yield: 37.6 mg, 74%. Mp: 147-148 °C. IR (cm^{-1}): ν(C=O) 1676, 1573; ν(C=N) 1605. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.72 (dd, 1 H, H3, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz), 7.57 (dd, 1 H, H5, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz), 3.54 (s, 2 H, CH_2), 3.42 (s, 6 H, OMe), 2.02 (s, 3 H, OAc), 1.79 (s, 3 H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, $CDCl_3$) δ 203.3 (CO), 178.6 (*C*OOMe), 159.0 (C7), 153.5 (C8), 139.7 (C4), 126.1 (C5), 123.2 (C3),

106.2 (C6), 51.9 (OMe), 31.6 (C1), 24.9 (Me), 23.1 (COO*Me*). Anal. Calcd for $C_{13}H_{17}NO_5Pd \cdot 0.1\ CH_2Cl_2$: C, 41.17 ; H, 4.54 ; N, 3.66. Found: C, 41.16 ; H, 4.45 ; N, 3.56. Single crystals were obtained by slow diffusion of *n*-pentane into a CH_2Cl_2 solution of **1**·OAc.

Synthesis of [Pd(O^I,N^I,C^I-L)(O,C-$C_6H_4CO_2$-2)I] (**2**). To a solution of **1**·OAc (149.5 mg, 0.39 mmol) in CH_2Cl_2 (15 mL) was added 2-iodobenzoic acid (116.3 mg, 0.47 mmol). The resulting solution was stirred for 30 min and then concentrated to 2 mL. Addition of Et_2O (15 mL) gave a suspension which was filtered after 10 min of stirring and the solid washed with Et_2O (2x4 mL) and air-dried to give **2** as a crystalline deep orange solid. Yield: 151.8 mg, 69%. Mp: 115 °C dec. IR (cm^{-1}): ν(C=O) 1704, 1605 (br). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (dd, 1 H, Ar, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz), 8.25 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.11 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz), 7.88 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz), 7.69 (dd, 1 H, Ar, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.4 Hz), 7.40-7.20 (m, 2 H, Ar), 4.95 (d, 1 H, CH_2, $^1J_{HH}$= 12.4 Hz), 4.55 (d, 1 H, CH_2, $^1J_{HH}$= 12.4 Hz), 3.35 (s, 3 H, OMe), 3.34 (s, 3 H, OMe), 1.88 (s, 3 H, Me). ^{1}H NMR(400 MHz, acetone-d_6): δ 8.61-8.57 (m, 2 H, Ar+py), 8.25 (d, 1 H, H5 or H3, $^3J_{HH}$ = 7.6 Hz), 8.20 (d, 1 H, H5 or H3, $^3J_{HH}$ = 7.6 Hz), 7.54-7.51 (m, 1 H, Ar), 7.34-7.27 (m, 1 H, Ar), 4.77 (d, 1 H, CH_2, $^1J_{HH}$= 12 Hz), 4.64 (d, 1 H, CH_2, $^1J_{HH}$= 12 Hz), 3.31 (s, 6 H, OMe), 1.88 (s, 3 H, Me). Isomer **2a**: ^{1}H NMR (400 MHz, $CDCl_3$, -55 °C): δ 8.63 (dd, 1 H, Ar, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz), 8.38 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.18 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz), 7.99 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz), 7.71 (dd, 1 H, Ar, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.4 Hz), 7.40-7.30 (m, 2 H, Ar), 4.84 (d, 1 H, CH_2, $^1J_{HH}$= 12 Hz), 4.71 (d, 1 H, CH_2, $^1J_{HH}$= 12 Hz), 3.46 (s, 3 H, OMe), 3.29 (s, 3 H, OMe), 1.91 (s, 3 H, Me). Isomer **2b**: ^{1}H NMR (400 MHz, $CDCl_3$, -55 °C): δ 8.64 (dd, 1 H, Ar, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1 Hz), 8.38 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.19 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz), 7.99 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz), 7.71 (dd, 1 H, Ar, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 2.4 Hz), 7.40-7.30 (m, 2 H, Ar), 5.08 (d, 1 H, CH_2, $^1J_{HH}$= 13.2 Hz), 4.38 (d, 1 H, CH_2, $^1J_{HH}$= 13.2 Hz), 3.46 (s, 3 H, OMe), 3.24 (s, 3 H, OMe), 1.92 (s, 3 H, Me). Anal. Calcd for $C_{18}H_{18}NO_5IPd$: C, 38.49 ; H, 3.23; N, 2.49. Found: C, 38.51; H, 3.11; N, 2.41. Single crystals of isomer **2a** were obtained by slow diffusion of *n*-pentane into a CH_2Cl_2 solution of **2** at 4 °C.

Synthesis of [Pd(O^I,N^I,C^I-L)($OOCC_6H_4$-2-Br)] ($\mathbf{A_{Br}}$). To a solution of 1·OAc (104.8 mg, 0.27 mmol) in CH_2Cl_2 (8 mL) was added 2-bromobenzoic acid (60.5 mg, 0.30 mmol). The

reaction mixture was stirred for 10 min and then concentrated (2 mL). Addition of Et_2O (8 mL) led to a suspension that was stirred in a cool bath (0 °C) for 30 min. The solid was filtered off, washed with Et_2O and air-dried to give $\mathbf{A_{Br}}$ as a yellow solid. Yield: 129.3 mg, 92%. Mp: 117-118 °C. IR (cm^{-1}): ν(C=O) 1696, 1626. ^1H NMR (300 MHz, $CDCl_3$): δ 8.12 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.75 (dd, 1 H, H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.59 (dd, 1 H, H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.2 Hz), 7.56-7.51 (m, 2 H, Ar), 7.29-7.23 (m, 1 H, Ar), 7.16-7.11 (m, 1 H, Ar), 3.66 (s, 2 H, CH_2), 3.48 (s, 6 H, OMe), 1.82 (s, 3 H, Me). $^{13}C\{^1H\}$ NMR (75.45 MHz, $CDCl_3$) δ 203.4 (CO), 173.9 (COO), 158.9 (C7), 153.4 (C8), 139.8 (C4), 132.9 (CH, Ar), 129.5 (CH, Ar), 129.3 (CH, Ar), 126.8 (CH, Ar), 126.2 (C5), 123.4 (C3), 119.6 (C–Br, Ar), 106.6 (C6), 52.1 (OMe), 32.2 (C1), 25.0 (Me). Anal. Calcd for $C_{18}H_{18}NO_5BrPd$: C, 42.01 ; H, 3.53 ; N, 2.72. Found: C, 42.17 ; H, 3.68 ; N, 2.64. Single crystals of $\mathbf{A_{Br}}$ were obtained at 4 °C by slow diffusion of a double layer of Et_2O and *n*-hexane into a CH_2Cl_2 solution of $\mathbf{A_{Br}}$.

Synthesis of (E)-Methyl 2-carboxycinnamate (**3**) *by Heck reaction.* To a mixture of 2-iodobenzoic acid (201.3 mg, 0.81 mmol), $AgClO_4$ (167.9 mg, 0.81 mmol) and **2** (45.5 mg, 0.081 mmol) was added a solution of CH_2=$CHCO_2Me$ (145.9 μL, 1.62 mmol) in acetone (15 mL). The mixture was stirred for 6h in the dark and then filtered through Celite. The filtrate was concentrated (1 mL), and Et_2O (25 mL) was added to give a suspension that was filtered. The filtrate was washed with water (3x20 mL) and the organic phase was stirred for 20 min with anhydrous Na_2SO_4 and then filtered off. The filtrate was concentrated to dryness to give **3** as a pale yellow solid with 95% of purity by ^1H NMR. Yield: 158.7 mg, 95% of crude product. An analytically pure sample was isolated by preparative TLC (silica gel 70-200 μm, AcOEt/$CHCl_3$; 2:1). Mp: 85 °C dec. IR (cm^{-1}): ν(C=O) 1707, 1679. ^1H NMR (400 MHz, $CDCl_3$): δ 11.58 (br, 1 H, COOH), 8.56 (d, 1 H, $^3J_{HH}$ = 15.6 Hz), 8.13-8.11 (m, 1 H), 7.63-7.47 (m, 3 H), 6.34 (d, 1 H, $^3J_{HH}$ = 15.6 Hz), 3.84 (s, 3 H, Me). $^{13}C\{^1H\}$ NMR (100.81 MHz, $CDCl_3$): δ 171.9 (CO), 167.0 (CO), 144.0 (CH_{olefin}), 137.2 (Q), 133.3 (CH), 131.7 (CH), 129.5 (CH), 128.5 (Q), 128.2 (CH), 121.0 (CH_{olefin}), 51.8 (Me). HRMS calc for $C_{11}H_{11}O_4$ $[M + H]^+$ *m/z* 207.0652, found *m/z* 207.0655.

Table 1. **Crystallographic Data for Complexes 1·OAc, 2a and A_{Br}.**

	1·OAc	**2a**	**A_{Br}**
formula	$C_{26}H_{34}N_2O_{10}Pd_2$	$C_{18}H_{18}INO_5Pd$	$C_{18}H_{18}BrNO_5Pd$
M_r	747.35	561.63	514.64
cryst size (mm)	0.22x0.08x0.05	0.21x0.17x0.03	0.33x0.13x0.11
cryst syst	Monoclinic	Monoclinic	Orthorhombic
space group	C 2/c	$P2_1/n$	P b c a
cell constants			
a, Å	19.0071 (13)	9.9802(8)	12.4938(9)
b, Å	8.9477(6)	31.835(3)	13.9600(12)
c, Å	16.5127(12)	14.2603(11)	20.6225(15)
α, deg	90	90	90
β, deg	102.819(2)	106.468	90
γ, deg	90	90	90
V (Å^3)	2738.3(3)	4345.0(6)	3596.8(5)
Z	4	8	8
Wavelength (Å)	0.71073	0.71073	0.71073
ρ (calc) (Mg m^{-3})	1.813	1.717	1.901
μ mm^{-1}	1.374	2.300	3.283
F(000)	1504	2176	2032
T (K)	100(2)	100(2)	100(2)
θ_{max} (deg)	56	56	56
no. of reflns measd	16341	52882	41562
no. of indep reflns	3325	10587	4488
transmissions	0.9345, 0.7997	0.9342, 0.7204	0.7141, 0.5910
R_{int}	0.0328	0.0395	0.0226
no. rest/params	0 / 185	5 / 492	15 / 272
$R_w(F^2$, all reflns)	0.0684	0.0788	0.0542
R(F, > 4σ(F))	0.0340	0.0420	0.0266
S	1.273	1.303	1.037
Largest diff peak (e Å^{-3})	0.680 / -0.692	1.014 / -0.685	0.545 / -0.347

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Section IV.2: Providing Support in Favor of the Existence of a Pd(II)/Pd(IV) Catalytic Cycle in a Heck-Type Reaction

ABSTRACT

The complex [Pd(*O,N,C*-L)(OAc)], where L is a monoanionic pincer ligand derived from 2,6-diacetylpyridine, reacts with 2-iodobenzoic acid at room temperature to afford the very stable pair of Pd^{IV} complexes (OC-6-54)- and (OC-6-26)-[Pd(*O,N,C*-L)(*O,C*-$C_6H_4CO_2$-2)I] (1.5:1 molar ratio, at –55 °C). These complexes and the Pd^{II} species [Pd(*O,N,C*-L)(OX)] and [Pd(*O,N,C*-L')(NCMe)]ClO_4, (X = MeC(O) or ClO_3, L' = another monoanionic pincer ligand derived from 2,6-diacetylpyridine), are precatalysts for the arylation of CH_2=CHR (R = CO_2Me, CO_2Et, Ph) using $IC_6H_4CO_2H$-2 and $AgClO_4$. These catalytic reactions have been studied and a tentative mechanism is proposed. The presence of two Pd^{IV} complexes is detected by ESI(+)-MS during the catalytic process. All data obtained strongly support a Pd^{II}/Pd^{IV} catalytic cycle.

INTRODUCTION

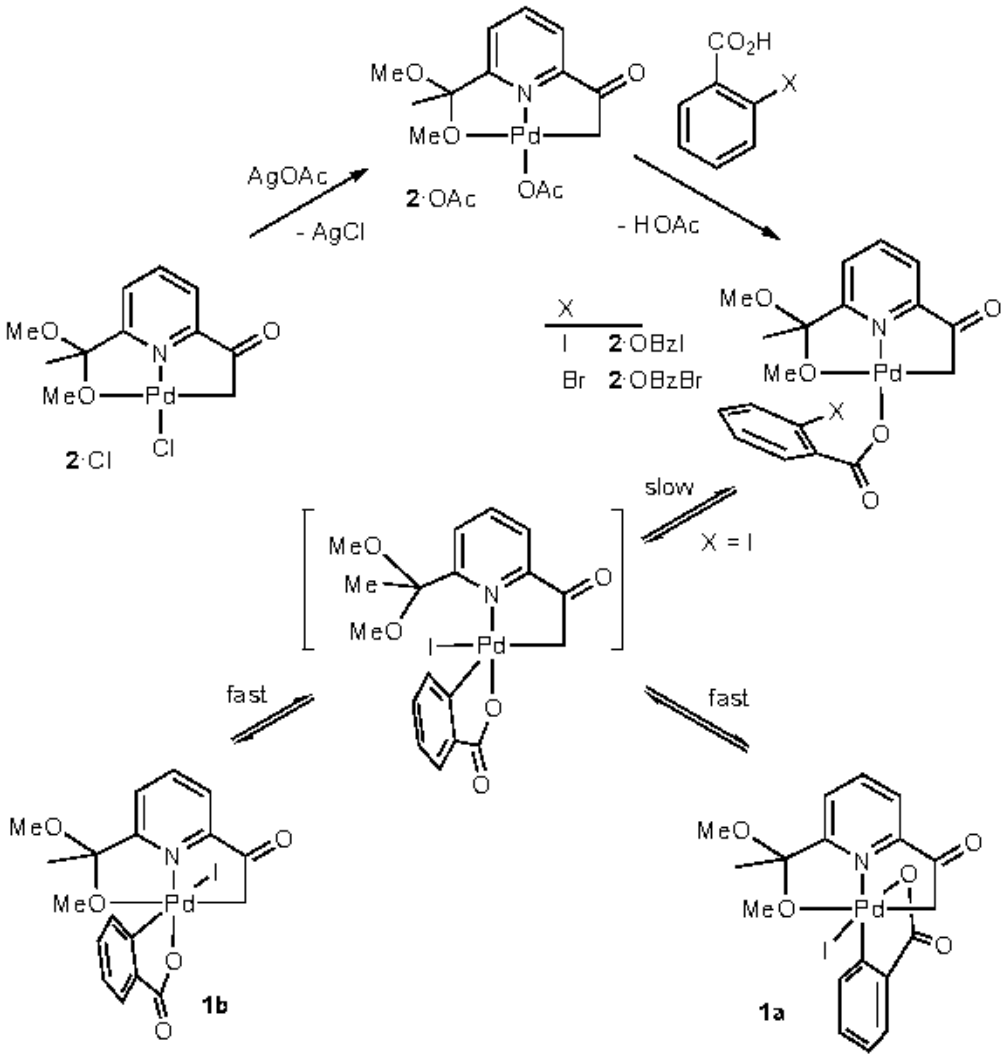
The important role of palladium in organic synthesis has been recognized by the recent award of the 2010 Nobel Prize in Chemistry to Heck, Negishi and Suzuki for their studies on catalytic cross couplings.[1, 2] These reactions, and most of those using Herrmann's palladacycles as precatalysts,[3] involve an aryl halide and a Pd(0) catalyst[4, 5] which forms from Pd(0)[1] or Pd^{II} precatalysts.[6-14] However, based on experimental data[15-17] and computational studies,[8, 18] Pd^{II}/Pd^{IV} cycles have been proposed when using Pd^{II} precatalysts.[19] The present relevance, topicality and interest of this proposal has been covered and emphasised in many papers.[4, 7, 8, 16, 18-22] They insist on the need for experiments addressed to detect some aryl-Pd^{IV} species in those catalytic reactions in which the intermediacy of Pd(0) complexes or Pd nanoparticles has been ruled out. We believe that this has become one of the most intriguing open problems in homogeneous catalysis. Additionally, the use of oxidizing agents stronger than aryl halides (for example, iodonium salts, peroxo-compounds, O_2) to form Pd^{IV} catalysts from Pd^{II} precatalysts is at present one emerging research area of interest in organic synthesis.[16, 20, 23] Although these oxidation reactions are well documented, experimental evidence of the presence of Pd^{IV} species in catalytic cycles has neither been provided so far. The involvement of a bimetallic Pd(III) complex in palladium-catalysed carbon-heteroatom formation has been proved.[21]

Of course, the elusive nature of intermediates in a catalytic cycle is behind the difficulty in proving their presence in the reaction mixture, for example, by using NMR spectroscopy. Fortunately, electrospray ionization mass spectrometry (ESI-MS) is especially useful in detecting ions without destroying molecules. It allows even short-lived intermediates to be captured from the reaction solution to the gas phase.[24] It is so mild that viral material can remain viable after an electrospray ionisation process.[25] Being, in addition, a fast and high-sensitivity technique it can provide accurate information of the ions present in reaction solutions, allowing their capture and characterization, thus facilitating mechanistic studies.[26] In particular, it has been reported that "observation of complexes under catalytic conditions by ESI-MS indicates that they are intermediates in the reaction".[27] The important applications of this technique in studying macromolecules earned John B. Fenn the 2002 Nobel Prize in Chemistry.[28]

Another weak point of the Pd^{II}/Pd^{IV} catalytic cycle proposal was that the required oxidative addition of an aryl halide to a Pd^{II} complex had not been proved.[14] However, we recently communicated the isolation of [Pd(*O,N,C*-L)(*C,O*-$C_6H_4CO_2$-2)I] (**1**, Scheme 1) from the reaction of [Pd(*O,N,C*-L)(OAc)] (**2**·OAc) with 2-iodobenzoic acid (HOBzI).[29] ^{1}H NMR studies showed that **1** exists as an equilibrium mixture of two isomers and that they are also in equilibrium with its Pd^{II} precursor [Pd(*O,N,C*-L)($O_2CC_6H_4I$-2)] (**2**·OBzI). Finally, we reported (1) that **1** is a precatalyst for the synthesis of (*E*)-methyl 2-carboxycinnamate (**3a**, Scheme 2) from CH_2=$CHCO_2Me$ and 2-iodobenzoic acid, in the presence of one equiv of $AgClO_4$ and (2) that the addition to the catalytic reaction of Hg (4000 equiv per Pd) or benzyl chloride (5 equiv/Pd)[30] neither quenched the process nor afforded dibenzyl, respectively, thus excluding the involvement of Pd nanoparticles (see below) [9, 12, 17] or some Pd(0) complex, respectively, as the catalyst in the reaction.[8] These data suggested that Pd^{II}/Pd^{IV} species can be involved in the catalytic cycle.

In spite of the above results, it needs to be taken into account that although the Pd^{IV} complex **1** is a precatalyst, this does not mean that it is involved in the catalytic cycle. Therefore, we found it essential to go some steps further, by studying the catalytic reaction using NMR spectroscopy and ESI-MS to obtain kinetic data and information on species present in solution, particularly some aryl-Pd^{IV} complex, which is our main objective. In addition, these studies could help us to propose a mechanism or to detect some Pd^{II} complex that we could synthesize to use it as precatalyst. This is indispensable because the use of a Pd^{IV}

complex as precatalyst (as we did using **1** in our communication)[29] could introduce reasonable doubts as to whether any detected signal of a Pd^{IV} complex could be attributed to the added Pd^{IV} complex or some derivative not intervening in the catalytic cycle.



Scheme 1

RESULTS AND DISCUSSION

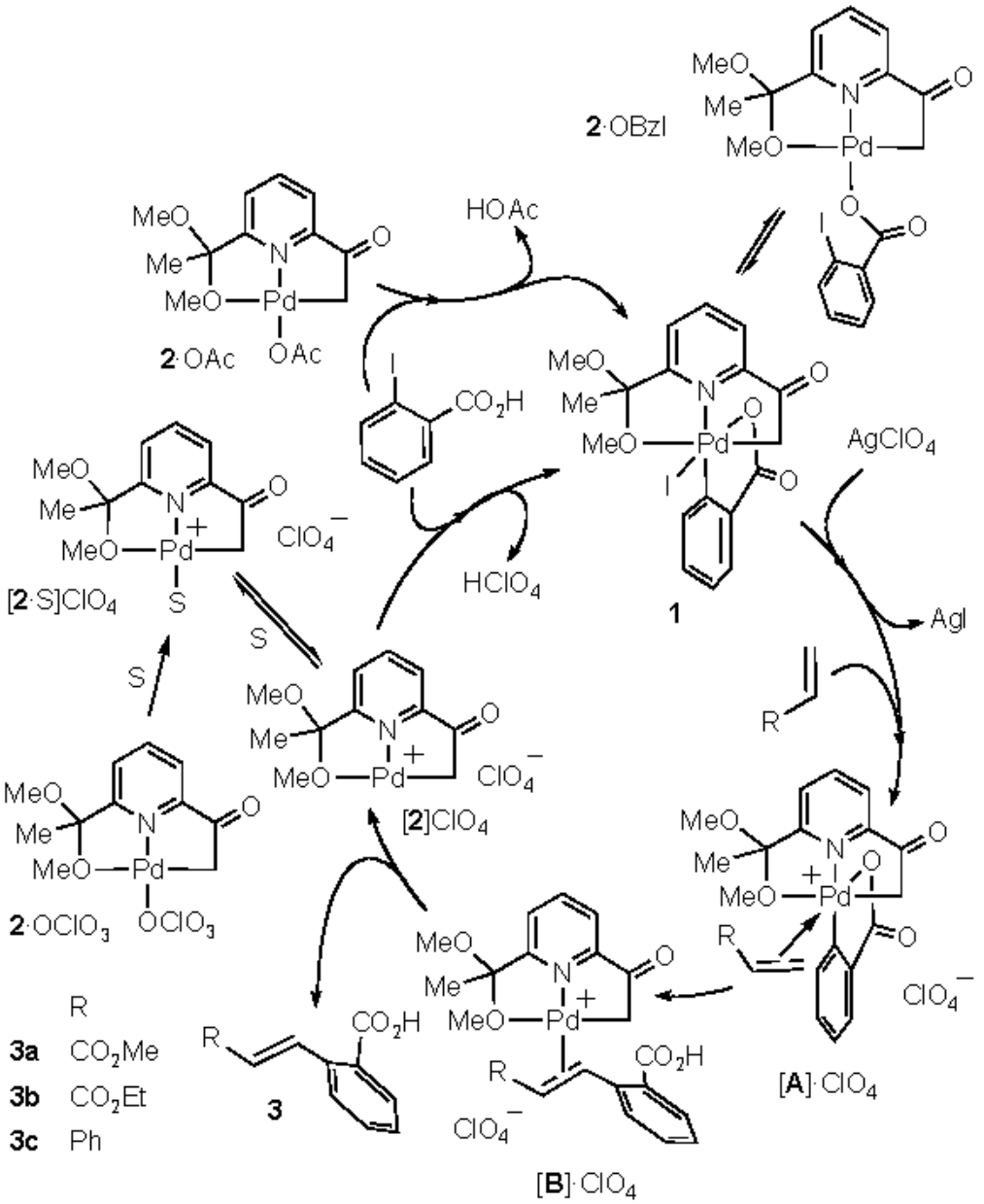
Complex **1** is also a precatalyst for the synthesis of other arylated olefins such as **3b** and **3c** (Scheme 2). The Heck syntheses of these products, using the aryldiazonium salt instead of 2-iodobenzoic acid, have been reported.[31] As expected, complex **1** can be replaced by its precursor **2**·OAc in the catalytic reaction.

The beginning of the catalytic reaction. Use of the Pd^{II} complex [Pd(*O,N,C*-L)($OClO_3$)] (2·$OClO_3$) as precatalyst. Using **1** as precatalyst at room temperature in the synthesis of **3a** (from now on "the reaction"), we initially detected only a Pd^{II} pincer-complex by ^{1}H NMR, which we assumed to be the solvento complex [Pd(*O,N,C*-L)S]ClO_4 ([**2**·S]ClO_4, S = [D_6]acetone, Scheme 2) because (1) it shows the CH_2 ^{1}H NMR resonance at 3.49 ppm, which is similar to that observed in [Pd(*O,N,C*-L)X] (in ppm: X = Cl (**2**·Cl; Scheme 1), 3.52; Br, 3.50, I, 3.49; OAc, 3.54; $O_2CC_6H_4$Br-2 (**2**·OBzBr), 3.66) but more shielded than that in the related Pd^{IV} derivatives [Pd(*O,N,C*-L)X_3] (in ppm: X = Cl, 6.03; Br, 6.04; I, 6.29 and 6.01) and **1**, 4.95, 4.55 ppm),[29, 32, 33] (2) we have prepared solutions of [**2**·S]ClO_4 (2a) by dissolving in acetone [Pd(*O,N,C*-L)($OClO_3$)] (**2**·$OClO_3$), which was isolated by reacting **2**·Cl (Scheme 1)[32] with one equiv of $AgClO_4$ and behaves in acetone as an 1:1 electrolyte (Λ_M = 81 $\Omega \cdot cm^2 \cdot mol^{-1}$),[34] and (2b) from the stoichiometric reactions **1** + CH_2=CHR (R = CO_2Me, CO_2Et, Ph) + $AgClO_4$ + S → [**2**·S]ClO_4 + **3** + AgI (Scheme 2) and (3) **2**·$OClO_3$ behaves as a precatalyst for the reaction (quantitative yield of **3a** in 40 min).

The evolution and the end of the reaction. The new Pd^{II} complex [Pd(*O,N,C*-L')(NCMe)]ClO_4 ([2'·MeCN]ClO_4) can be used as precatalyst. Following the course of the reaction, a decrease of the amount of [**2**·S]ClO_4 with time was observed while MeOH and a new Pd^{II} complex appeared. Its ^{1}H NMR spectrum showed $\delta(CH_2)$ at 3.65 ppm, suggesting it is [Pd(*O,N,C*-L')S]ClO_4 ([**2'**·S]ClO_4; Scheme 3) resulting from the hydrolysis of [**2**·S]ClO_4,[29, 32, 33] where L' is the monoanionic ligand resulting from monodeprotonation of one acetyl group of 2,6-diacetylpyridine. The presence of water (from the non-anhydrous acetone or the atmosphere) and the acidic medium (HOBzI and $HClO_4$; Scheme 2) must be responsible for this acid-catalyzed hydrolytic process.

The proposed nature of [**2'**·S]ClO_4 was confirmed by concentrating a solution of the catalytic reaction, adding MeCN and then precipitating with Et_2O its homologue [**2'**·MeCN]ClO_4 (Scheme 3). Its ^{1}H NMR spectrum in [D_6]acetone shows resonances of the pincer ligand at chemical shifts almost identical to those of [**2'**·S]ClO_4 (± 0.05 ppm), suggesting that replacement of MeCN by acetone occurs in solution to give [**2'**·S]ClO_4. Correspondingly, [**2'**·MeCN]ClO_4 is also a precatalysts for the catalytic reaction. [**2'**·S]ClO_4 was detected in amounts increasing with time, in all catalytic reactions using **1**, **2**·OAc or **2**·$OClO_3$ as precatalysts while the amount of [**2**·S]ClO_4, decreased until its total disappearance.

This means that two catalytic cycles can operate simultaneously while [2·S]ClO_4 and [2'·S]ClO_4 coexist (Schemes 2 and 3).



Scheme 2. Proposed catalytic cycle for the synthesis of 2-vinyl benzoic acids involving precatalyst **1**, **2**·OAc or **2**·$OClO_3$. S = Me_2CO.

Conversion *vs* time plots. Figure 1 shows conversion (%) *vs* time (min) plots for the synthesis of **3a** using the **1**, **2**·OAc or [2'·MeCN]ClO_4 precatalysts (from now "the three precatalysts") . The data show that the reaction rate decreases in the order [2'·MeCN]ClO_4 >

2·OAc > **1**. A ^{1}H NMR study of the catalytic reaction mixture using **2**·OAc or **1** showed almost immediate formation of complex [**2**·S]ClO_4 while [**2'**·S]ClO_4 appeared later in the catalytic reaction from **1** (40% after 30 min) than in that from **2**·OAc (90% in 20 min). This explains that the reaction rate is greater from **2**·OAc that from **1**; in other words, the sooner the best precatalyst [**2'**·S]ClO_4 forms, the faster the reaction goes. The faster formation of [**2'**·S]ClO_4 from **2**·OAc than from **1** is surprising because **1** forms from **2**·OAc. This could be explained if **2**·OAc, or some intermediate in the reaction **2**·OAc → **1**, hydrolyzed faster than **1** to afford [**2'**·S]ClO_4.

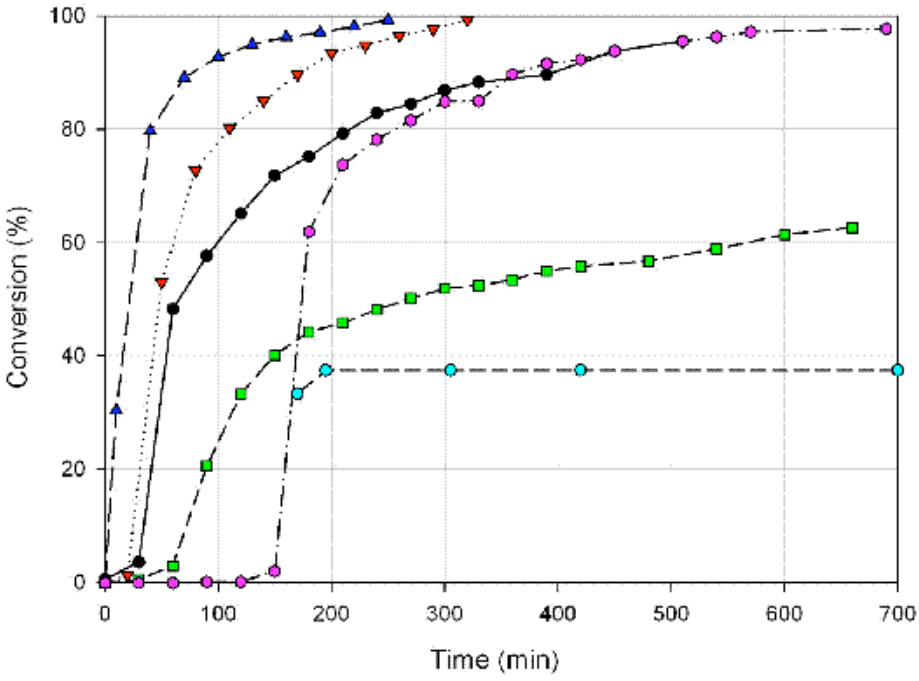
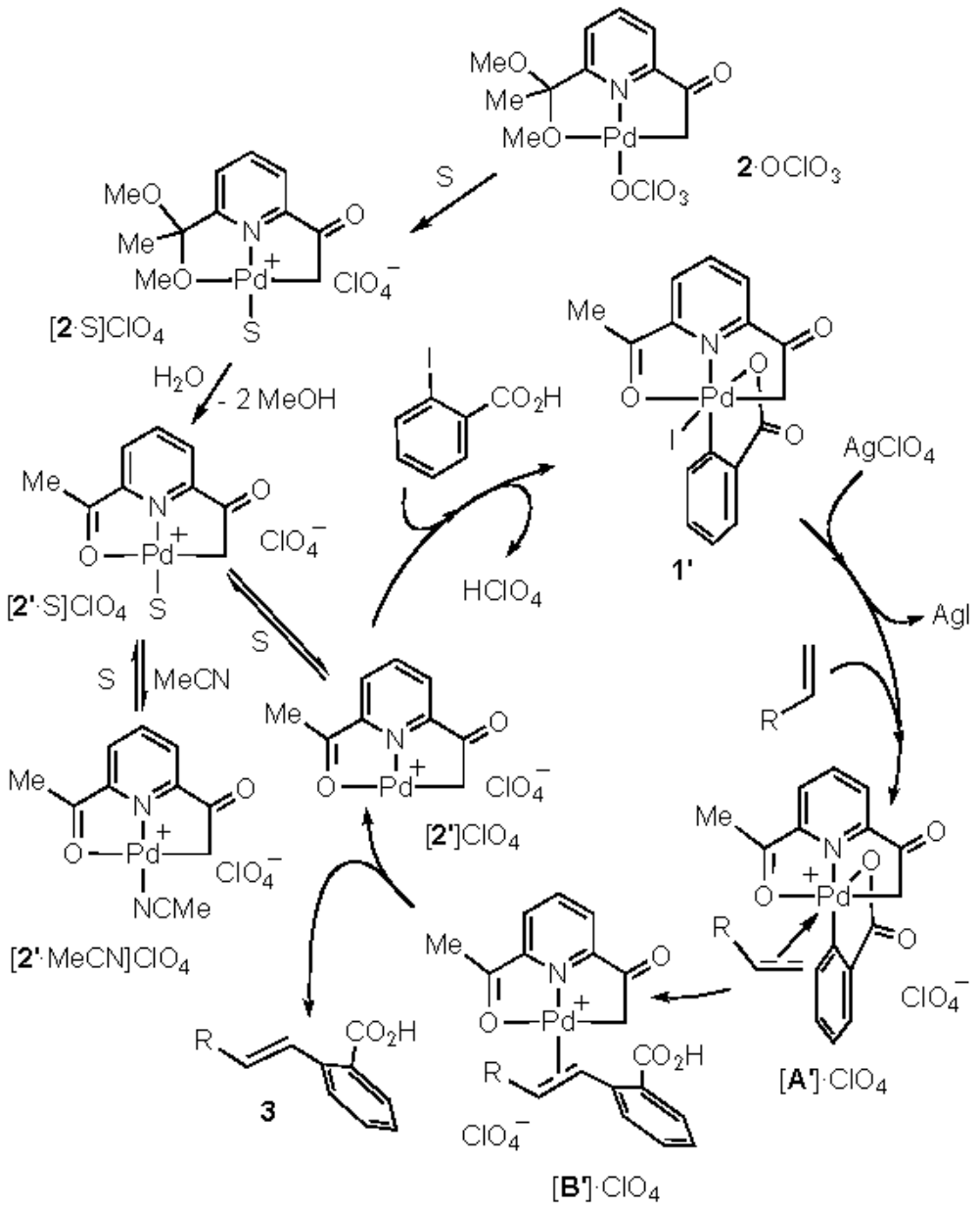


Figure 1. Conversion (%) vs time (min) plots for the catalytic reaction using various precatalysts (10%): [**2'**·MeCN]ClO_4 (—▲-), **2**·OAc (···▼···), **1** (—●—), **2**·OAc+AgOTf (—●—), **2**·OAc+AgOTf+Hg (—○—) or **2**·OAc (1%): —■-·

Homogeneous or heterogeneous catalysis? We have checked that Pd nanoparticles are not involved in the catalytic cycle when using any of the three precatalysts. In fact, Hg addition (4000 equiv of Hg per Pd) did not quench the catalytic reaction[6-8, 10, 35] although reduced its rate. The same behaviour has been previously reported in Heck-type reactions using an homogenous catalyst.[9, 36] This is likely attributable to a decrease in the concentration of some

intermediate in the catalytic cycle. In fact, Figure 1 shows a marked rate decrease when using 1% instead of 10% of precatalyst 2·OAc. This behavior also differs from that of reactions catalyzed by nanoparticles that usually utilize less than 0,1% of catalyst. In some cases at higher concentrations, palladium black forms and the reaction stops.[37] The reaction using 2·OAc as precatalyst was neither quenched upon the addition of any of the poisoning agents CS_2, PPh_3 or thiophene, in amounts of 0.5–1 equiv/Pd.[10]



Scheme 3. Proposed catalytic cycle for the synthesis of 2-vinyl benzoic acids involving precatalyst [**2'**·MeCN]ClO_4 or **2**·$OClO_3$. S = Me_2CO.

We have also considered the possibility that the catalyst were small size soluble Pd nanoparticles (soluble metal clusters). However, as we did not find a test to detect them, we repeated a reported catalytic reaction using such type of nanoparticles[38] in the presence of Hg (300 eq per Pd). The quenching of this reaction means that the Hg test is valid for both types of nanoparticles. Therefore, in our reaction do not involve nanoparticles (soluble or not) as catalysts.

The involvement of some soluble Pd(0) complex was also ruled out because using any of the three precatalysts and 5 equiv/Pd of benzyl chloride in the catalytic reaction gave 98%, 80% (5 h at room temperature) or 97% (3 h at room temperature) yield of **3a**, respectively, while dibenzyl was not detected.[8] In addition, the reaction is carried out under atmospheric conditions, while most catalytic C–C coupling reactions require a protected atmosphere.

The homogeneous nature of the reaction when any of the three precatalysts is used is also supported by the very short induction period (Figure 1), the data reproducibility, and the stricking dependence of the rate on the concentration of the precatalyst.[9, 35, 39]

The catalytic reaction using **2**·OAc, changed to heterogeneous when AgOTf was used instead $AgClO_4$ (Figure 1). In this case, no reaction was observed after 8h at room temperature when 4000 equiv of Hg/Pd were added to the initial mixture. When the same amount of Hg was added after 3 h of catalytic activity, the conversion was instantly quelled (Figure 1). The long induction period for this reaction shows (1) its heterogeneous nature[7, 8, 10, 11, 35] and (2) the difference with respect to those using any of the three precatalysts. In an attempt to isolate [Pd(*O,N,C*-L)(OTf)] (**2**·OTf), we reacted **2**·OAc[29] with one equiv of HOTf in [D_6]acetone at room temperature; however, the resulting product started to decompose after 30 min and finished after approx 5h giving a mixture in which we observed the formation of Pd metal and identified (HL)OTf only. The corresponding salts, (HL)ClO_4 or (HL')ClO_4, were never detected when any of the three precatalysts were used, which suggests the exclusive involvement of the pincer complexes in the catalytic cycle. The inability of **2**·OTf during its lifetime to act as an homogeneous catalyst could be attributed to the Pd–OTf bond being stronger than that in Pd–$OClO_3$ or Pd–$OCMe_2$. This could preclude (1) the coordination of the $OBz I^-$ anion to give **2**·OBzI and, correspondingly, the oxidative addition to afford **1** or (2) the necessary coordination of the olefin. We have reported that the catalyst in the reaction at high temperatures (typical Heck conditions), using **1** as precatalyst in the absence of $AgClO_4$, is Pd in the form of nanoparticles.[29]

All the above tests and observations show that our reaction is neither heterogeneous nor homogeneous through soluble Pd clusters, ligand-free or ligand-containing Pd(0) species.

Looking for intermediates in the catalytic reaction by use of ESI(+)-MS. The above conclusion suggests that the catalysis takes place by oxidizing a Pd^{II} complex with HOBzI. It has recently been reported that a dinuclear Pd^{III} complex bearing two acetato bridging ligands is a catalyst in the reaction of benzo[h]quinoline with $PhICl_2$ or *N*-chlorosuccinimide to afford 10-chlorobenzo[h]quinoline.[21] Although **2**·OAc is a dinuclear complex of the type required for this kind of catalysis, it is monomeric in solution and we have shown its reaction with HOBzI not to give a dinuclear species but the mononuclear aryl-Pd^{IV} complex **1**.[29] In the case of the other Pd^{II} precatalysts [**2**·S]ClO_4 or [**2'**·S]ClO_4 formation of Pd^{III} complexes using HOBzI as oxidant is very unlikely.

One electron oxidation of a Pd^{II} complex using a ferrocinium or a Ag^+ salt has been reported as an intermediate step in a stoichiometric reductive elimination reaction.[40] In our case, oxidation of some Pd^{II} complex by Ag^+ to give a Pd^{III} (or Pd^{IV}) complex can be ruled out because a ^1H NMR study shows that the reaction **2**·$OClO_3$ + $AgClO_4$ + HOBzI does not take place unless the olefin is added. In addition, we have discarded the involvement of $AgClO_4$ and/or AgI in the catalytic reactions after confirming, by ^1H NMR in [D_6]acetone, that the reaction HOBzI + 0.5 AgI + 0.5 $AgClO_4$ + 0.5 $HClO_4$ + 2 CH_2=$CHCO_2Me$ does not take place.

Trying to establish if **1** can be obtained from **2**·$OClO_3$, as suggested in Scheme 2, the ESI(+)-MS of a 1:10 mixture of **2**·$OClO_3$ and HOBzI was measured in acetone with 1% MeCN, to intercept species with this ligand, and 1 mmol/L aq solution of $HClO_4$ (0.3 equiv/HOBzI), to mimic the acidic conditions in the catalytic reaction. The peaks intercepted around 342 and 355 m/z (see supporting information, SI) correspond to the Pd^{II} adducts [**2**·N_2]$^+$,[41] and [**2**·MeCN]$^+$ (both also detected by ESI(+)-MS in a solution of **2**·$OClO_3$). Those around 562 m/z can only be assigned to the Pd^{II} [**2**·OBzI+H^+] and Pd^{IV} [**1**+H^+] isomers (mean error for the 5 more intense peaks of the three groups of signals is 0.3 ppm), which parent neutral species we have reported to be in a slow equilibrium with each other (Schemes 1 and 2).[29] About the ratio [**1**+H^+]:[**2**·OBzI+H^+] in solution, it is realistic to assume that it is much greater than that between the unprotonated species (2.3:1 at 25 °C), because HOBzI (*i.e.*, $OBzI^-$ +H^+) must be a poor donor easily replaceable by acetone or MeCN contributing to the peaks at 342 and 355 m/z. In short, the concentration of the benzoato complex **2**·OBzI in a strong acid

medium ($HClO_4$) must be very low or even zero. Contrarily, in [**1**+H^+] the ligand 2-$C_6H_4CO_2H$ (i.e., 2-$C_6H_4CO_2^-$+H^+) is expected to act as *C,O*-chelating, with a very strong Pd–C bond. An experimental support of the very low or null concentration of **2**·OBzI in the presence of $HClO_4$ was obtained by recording the ESI(+)-MS of an acetone solution (with 1% MeCN and 0.3 equiv of $HClO_4$/HOBzBr) of the Pd^{II} complex **2**·OBzBr ($\mathbf{A}_{Br}$, Scheme 1), which neither intercepts [**2**·OBzBr+H^+] nor its Pd^{IV} isomer, homologue of **1**, [Pd(*O,N,C*-L)(*C,O*-$C_6H_4CO_2$-2)Br] ($\mathbf{1}_{Br}$). This means that (1) **2**·OBzBr, which we have isolated and characterized by X-diffraction,[29] reacts with $HClO_4$ replacing HOBzBr, such as we anticipated for its homologue **2**·OBzI and (2) that it does not convert into $\mathbf{1}_{Br}$, at difference of **2**·OBzI (Scheme 1); we had concluded the same when we studied its ^{1}H NMR spectrum. In summary, *the aryl-Pd^{IV} complex [**1**+H^+] is formed in the stoichiometric reaction **2**·$OClO_3$ + HOBzI, in the presence of $HClO_4$, since the peaks around 562 m/z are mainly, if not exclusively, corresponding to such Pd^{IV} ion.* As the ^{1}H NMR of this reaction mixture does not detect **1**, the equilibrium **2**·$OClO_3$ + HOBzI ⇆ $HClO_4$ + **1** must be very displaced to the left. However, minute amounts of **1** in this equilibrium (shown by ESI-MS) would be enough to allow its role in the catalytic reaction (Scheme 2).

We have also monitored by ESI(+)-MS (acetone with 1% MeCN) the reaction using precatalyst **2**·$OClO_3$ after 20 min. Apart from peaks attributed to Ag^+ adducts and aggregate products, the peaks around 342, 355 and 562 m/z, found in the mixture **2**·$OClO_3$ + HOBzI, were also intercepted (see SI). In agreement with the above discussion, the peaks around 562 m/z *represent the first detection of an aryl-Pd^{IV} species in a catalytic process.*

We have also monitored by ESI(+)-MS (acetone with 1% MeCN) the catalytic reaction using precatalyst [**2'**·MeCN]ClO_4 and detected Pd^{II} adducts [**2'**·N_2]$^+$, [**2'**·MeCN]$^+$, [**2'**·N_2·MeOH]$^+$, [**2'**·MeCN·MeOH]$^+$ as well as a molecular ion of around 515 m/z that, as in the case of the precatalyst **2**·$OClO_3$, indicates the presence of the Pd^{IV} intermediate [**1'**+H^+] (mean error of the 5 more intense peaks 1.8 ppm; see SI). Howewer, the relative intensity of these peaks is much smaller than that corresponding to [**1**+H^+]. The minor concentration of these intermediates could be related with the reaction rate; the faster it is, the lower is the concentration of intermediates, other factors being similar. In fact, the ESI(+)-MS of the stoichiometric reaction of **2'**·MeCN with 10 equiv de HOBzI (acetone with 1% MeCN and 0.3 equiv of $HClO_4$/HOBzI), detects the same group of peaks around 515 m/z but more intense than in the catalytic reaction. This means that the oxidative addition is an equilibrium in which

the Pd^{IV} complex exists in a ratio greater than that in the catalytic reaction because it is not consumed by reacting with $AgClO_4$ and the olefin. This also supports the involvement of Pd^{IV} in the catalytic cycle. All attempts to isolate **1'** or its acetato precursor by using the method we applied for its homologue **1** or **2**·OAc were unfruitful.

A tentative proposal for the mechanism. Although the present work did not intend to study the mechanism of the reaction but providing support in favour of the existence of some Pd^{IV} intermediate during this catalysis, we tentatively represent in Schemes 2 and 3 our proposal of mechanism. Complex **1** neither reacts appreciably with CH_2=$CHCO_2Me$ nor with $AgClO_4$ (by ^{1}H NMR). However, it does when the three reagents are present. We think that the use of $AgClO_4$ is justified by the need to create a coordination vacancy around Pd^{IV} to coordinate the olefin before the migratory insertion. Therefore, we postulate that complex **1** reacts first with $AgClO_4$ to give a pentacoordinate complex, which reacts with the olefin to afford the intermediate [**A**]ClO_4 (Scheme 2). The following steps replicate those proposed in the Pd(0)/Pd^{II} cycle: migratory insertion of the aryl ligand to the olefin and β-hydride elimination to give the Pd^{II} complex [**B**]ClO_4, which dissociates the ortho vinylated benzoic acid, regenerating the catalyst [**2**]ClO_4. The reaction from **1'** could follow a similar pathway (Scheme 3). DFT studies on Pd^{II}/Pd^{IV} catalytic cycles find that T-shaped complexes, like [**2**]ClO_4, are the active catalysts.[18]

CONCLUSIONS

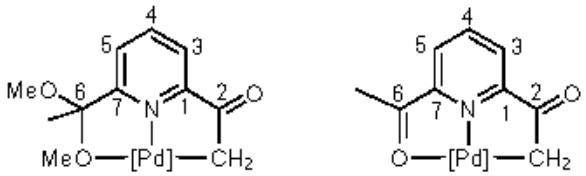
In conclusion, using the Pd^{IV} complex **1** or the Pd^{II} derivatives **2**·OAc, **2**·$OClO_3$, or [**2'**·MeCN]ClO_4 as precatalyst for the room temperature Heck-type synthesis of olefins (E)-ArCH=CHR from CH_2=CHR and 2-$IC_6H_4CO_2H$, we have succeeded in (1) the detection, for the first time, by ESI(+)-MS of some peaks mainly, if not exclusively, corresponding to aryl-Pd^{IV} species [**1**+H^+] during the catalytic reaction; to assume they were exclusively attributable to a Pd^{II} isomer is not tenable, on the basis of elemental chemical concepts and the negative test with A_{Bt}, (2) the detection by ESI(+)-MS of peaks corresponding to the aryl-Pd(IV) complex **1'**; the fact that these peaks were weaker in the catalytic mixture than in the stoichiometric reaction **2'**·MeCN + 10 HOBzI also suggests the involvement of **1'** as intermediate in the catalytic cycle, (3) obtaining experimental data that exclude the intervention of soluble or insoluble nanoparticles of Pd or soluble Pd(0) complexes or Ag^+, (4) the detection of

intermediates ([**2**·S]ClO_4 and [**2'**·S]ClO_4) in solution, the synthesis of their precursors (**2**·$OClO_3$ and [**2'**·MeCN]ClO_4, respectively) and their use as precatalysts, (5) studying the conversion (%) *vs* time for the catalytic synthesis of **3a** using three different precatalysts; the data establish the homogeneous nature of the catalysis and the following order of reaction rates depending on the precatalyst: [**2'**·MeCN]ClO_4 > **2**·OAc > **1**, and (6) changing the catalysis to heterogeneous by replacing the anion ClO_4^- by OTf^- or by increasing the temperature reaction in the absence of $AgClO_4$; these reactions differ from those using the homogeneous precatalysts in the conversion *versus* time plots, their quenching in the presence of Hg and in the fact that we detect the corresponding HL^+ or HL'^+ salt. We are convinced that our catalytic reaction can not be taken as model for most Heck-type catalytic reactions. Still, its value stands on the long awaited detection of an aryl-Pd^{IV} complex in a catalytic reaction, which is facilitated by the use of a Pd^{II} pincer complex and the use of HOBzI as the aryl halide. We expect our work will encourage those which have argued that some C–C coupling reactions could occur through a Pd^{II}/Pd^{IV} cycle, to find more examples like ours to establish the limits of this alternative to the main Pd^0/Pd^{II} mechanism.

EXPERIMENTAL SECTION

General Procedures

Complexes **1**, **2**·OAc,[29] and **2**·Cl[32] were obtained following previously described procedures. Compounds **3b** and **3c** were prepared as **3a**.[29] Their spectroscopic properties are in agreement with the data previously reported.[31] Chart 1 shows the atom numbering used in NMR assignments.



[Pd](*O,N,C*-L) [Pd](*O,N,C*-L')

Chart 1

Unless otherwise stated, the reactions were carried out without precautions against light or atmospheric oxygen or moisture. Melting points were determined on a Reichert apparatus

and are uncorrected. Elemental analyses were carried out with a Carlo Erba 1106 microanalyzer. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on Bruker Avance 200, 300 or 400 spectrometers at room temperature. Chemical shifts were referred to TMS. NMR assignments were performed with the help of APT, HMQC and HMBC techniques. Complexes **1**,[29] **2**·OAc,[29] and **2**·Cl[32] were prepared following previously described procedures. Compounds **3b** and **3c** were prepared as for **3a**.[29] Their spectroscopical properties are in agreement with the data previously reported.[31]

Typical Kinetic Run. An NMR tube was charged with 2-iodobenzoic acid (10.90 mg, 0.044 mmol), $AgClO_4$ (9.11 mg, 0.044 mmol), **1** (2.46 mg, 0.004 mmol) and a solution of methyl acrylate (7.92 μL, 0.088 mmol) in [D_6]acetone (800 μL). The sample was manually stirred for 1 min and then the ^{1}H NMR spectrum was recorded. Every 30 min, the relative concentration of the coupling product was determined by ^{1}H NMR. We monitored the NMR signals of a cinnamate olefin proton (8.54 ppm, d, 1 H, $^3J_{HH}$ = 16 Hz) and an aromatic benzoic acid proton (7.25 ppm, m, 1 H) to calculate the reaction conversion.

Poisoning Experiments. *Hg drop tests*. Hg drop tests were performed with 4000 equiv of Hg relative to the metal complex. Hg was added either at t = 0 min and 180 min to the reaction mixture and it was vigorously stirred with a magnet. In the case of the reaction mixture with AgOTf the points in the graph was determined by taking the supernatant solution from the flask, adding to an NMR tube and recording the ^{1}H NMR spectrum. In a typical experimental procedure, a 10 mL flask was charged with 2-iodobenzoic acid (21.10 mg, 0.085 mmol), $AgClO_4$ (17.61 mg, 0.085 mmol), **2**·OAc (3.26 mg, 0.009 mmol) and a solution of methyl acrylate (15.30 μL, 0.170 mmol) in [D_6]acetone (800 μL). Immediately, Hg (6.76 g, 33.70 mmol) was added and the mixture was vigorously stirred.

Quantitative poisoning experiments. CS_2, PPh_3 and thiophene were used to carry out quantitative poisoning experiments. These agents were added to the reaction mixture at t = 0 min and the amounts varied from 0.5 to 1 eq per metal complex. In a typical experimental procedure, an NMR tube was charged with 2-iodobenzoic acid (13.60 mg, 0.055 mmol), $AgClO_4$ (11.41 mg, 0.055 mmol), **2**·OAc (2.12 mg, 0.005 mmol) and a solution of methyl

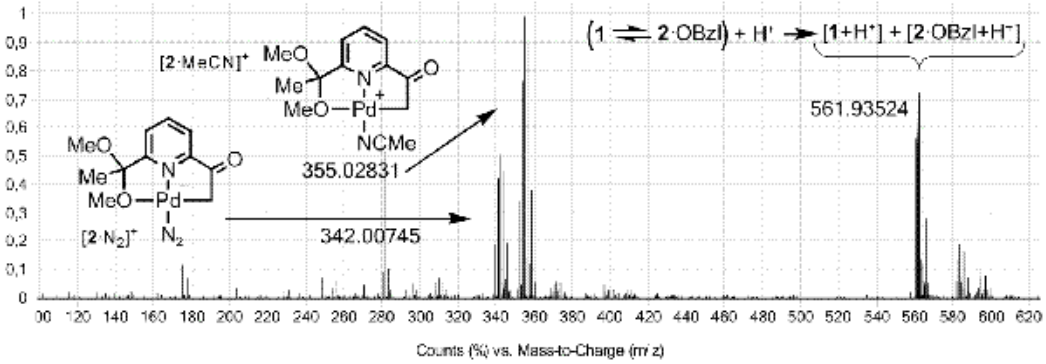
acrylate (9.90 μL, 0.110 mmol) in [D_6]acetone (800 μL). Immediately, PPh_3 (0.72 mg, 0.003 mmol) was added and the mixture was stirred. The reaction was followed by ^{1}H NMR.

ESI-MS(+) Experimental Conditions. All high resolution ESI-MS experiments were performed on a Agilent 6620 time-of-flight mass spectrometer. For typical electrospray ionization conditions, mass spectrometer were operated in the positive ion mode and direct insertion of the sample. Main conditions were ionization voltage, 3000 V; fragmentor, 150 V; mobile phase, MeOH/H_2O (0.4 mL/min) and drying gas N_2 (350 °C, 11 L/min). The solvent composition was acetone with 1% MeCN to minimize the number of adducts that intermediates could form in the gas phase or to allow formation and detection of more stable adducts. To study reactions of **2**·$OClO_3$ + 10 HOBzI and [**2'**·MeCN]ClO_4 + 10 HOBzI, 0.3 equiv of $HClO_4$ per HOBzI was added.

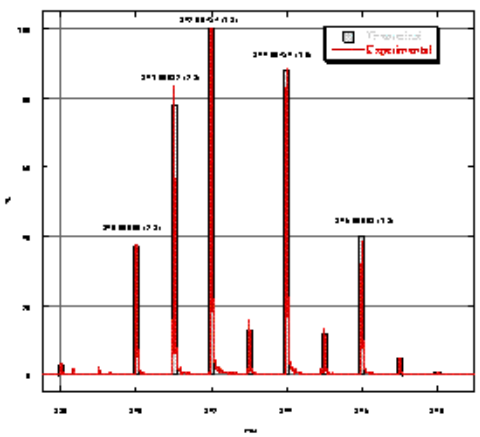
In all of the mass spectra that we recorded, we detected palladium aggregation products between 700 and 900 m/z, also detected when we used pure samples of the precatalyst. Thus, we assume this aggregation products are formed in the ionization process so they do not come from the catalytic reaction. Moreover, when we analized the catalytic reactions we detected free silver cation (Ag^+) and its adducts with solvents that have not been labeled in the figures. Finally, all molecular ions we have not been identified, have empirical formulas that do not correspond with any real chemical structure. In addition, most of them are also observed when we used pure samples of precatalyst. In other ESI-based mechanistic studies many peaks also remain unassigned, which we assume it is due to the difficulty of assign them.[42]

Mixture of 2·$OClO_3$ and 2-iodobenzoic acid (1:10).

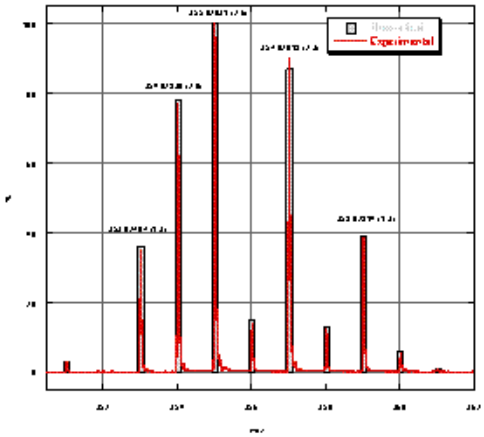
A vial was charged with 2-iodobenzoic acid (5.11 mg, 0.021 mmol), **2**·$OClO_3$ (0.91 mg, 0.0021 mmol) and acetone (1% MeCN + 1 mM $HClO_4$) (6 mL). The solution was stirred at room temperature and after 5 min a mass spectrum was recorded.



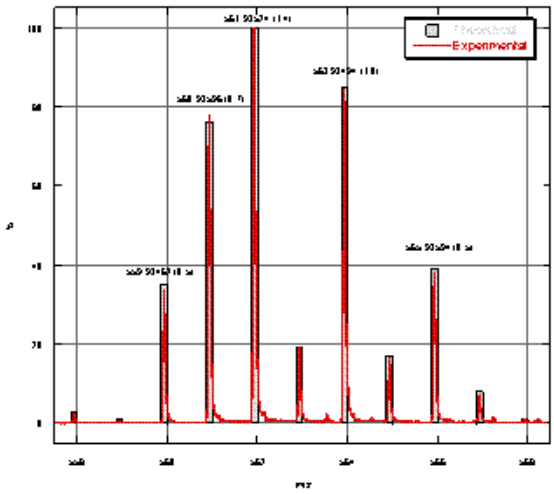
Comparison between theoretical and experimental isotopic distribution of the molecular ions $[Pd(O,N,C\text{-L})(N_2)]^+$ (a), $[Pd(O,N,C\text{-L})(NCMe)]^+$ (b) and $[Pd(O,N,C\text{-L})(C_6H_4CO_2H\text{-}2)I]^+$ + $[Pd(O,N,C\text{-L})(IC_6H_4CO_2H\text{-}2)]^+$ (c), in the reaction mixture (error in ppm in parentheses).



(a)



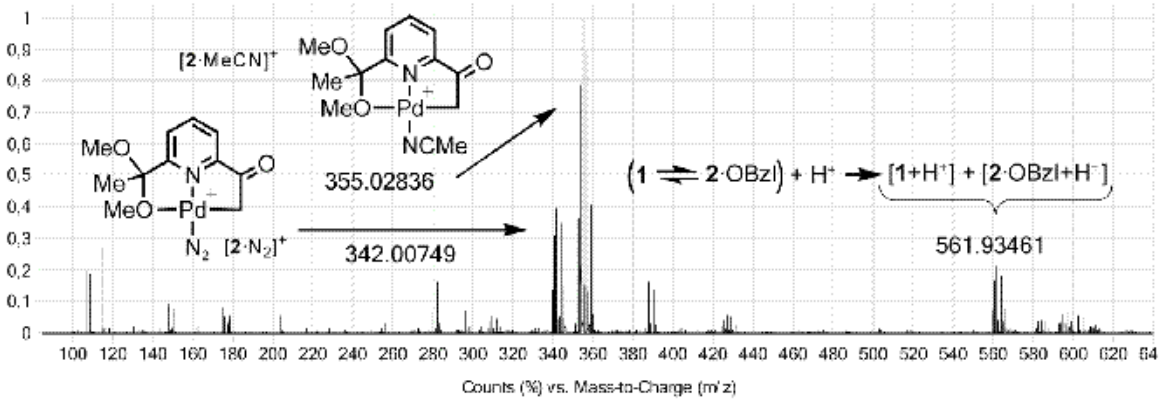
(b)



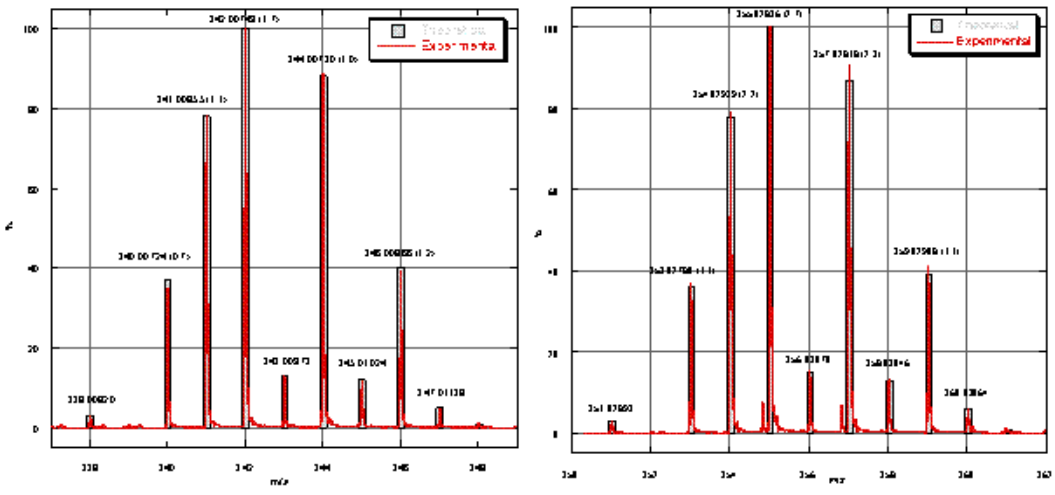
(c)

Reaction mixture using 2·$OClO_3$ as precatalyst.

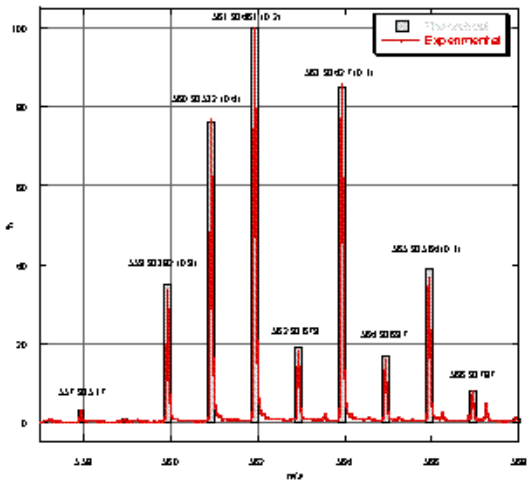
A vial was charged with 2-iodobenzoic acid (10.20 mg, 0.041 mmol), $AgClO_4$ (8.51 mg, 0.041 mmol), 2·$OClO_3$ (1.80 mg, 0.0041 mmol) and a solution of methyl acrylate (7.40 μL, 0.082 mmol) in acetone + 1% MeCN (7 mL). The mixture was stirred at room temperature and after 20 min a mass spectrum was recorded.



Comparison between theoretical and experimental isotopic distribution of the molecular ions [Pd(*O,N,C*-L)(N_2)]$^+$ (a), [Pd(*O,N,C*-L)(NCMe)]$^+$ (b) and [Pd(*O,N,C*-L)($C_6H_4CO_2$H-2)I]$^+$ + [Pd(*O,N,C*-L)($IC_6H_4CO_2$H-2)]$^+$ (c), in the reaction mixture (error in ppm in parentheses).



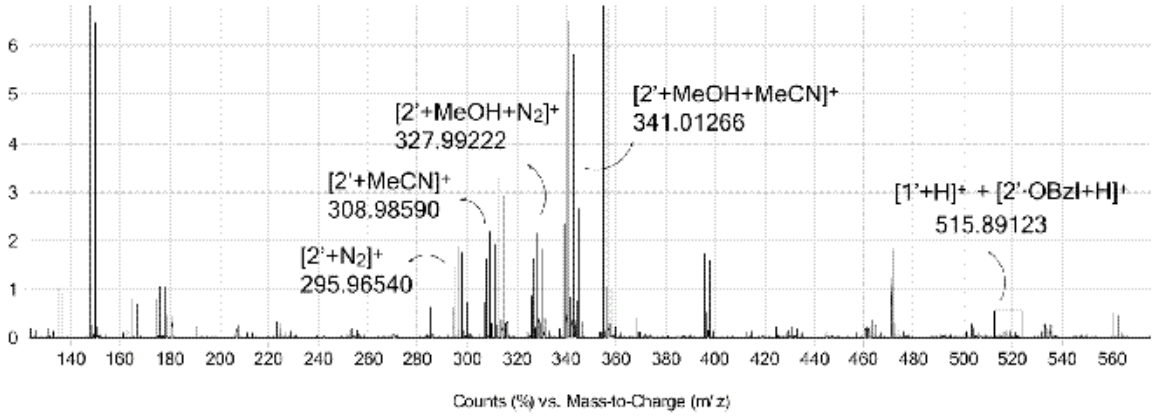
(a) (b)



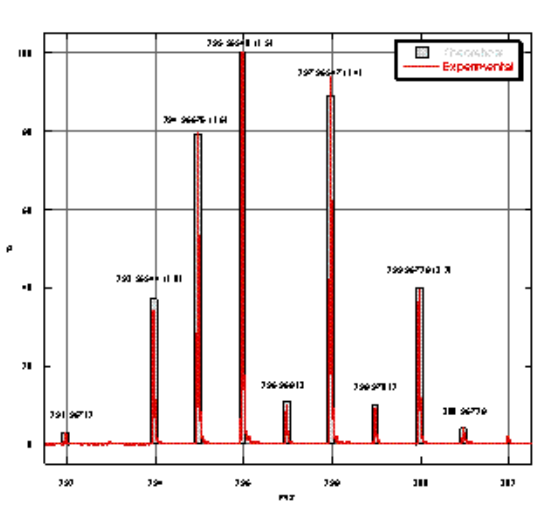
(c)

Reaction mixture using [2'·MeCN]ClO_4 as precatalyst.

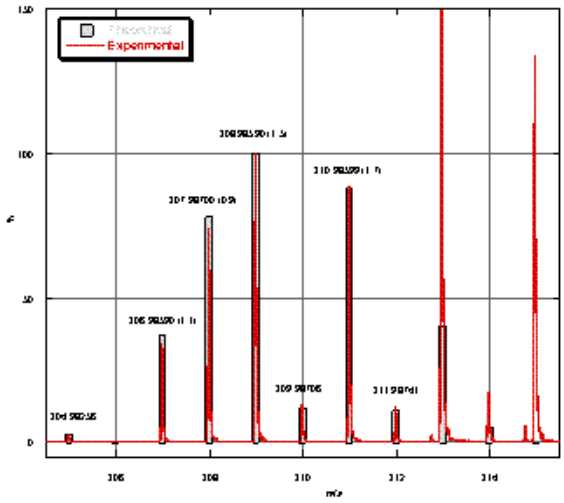
A vial was charged with 2-iodobenzoic acid (8.91 mg, 0.036 mmol), $AgClO_4$ (7.49 mg, 0.036 mmol), [2'·MeCN]ClO_4 (1.48 mg, 0.0036 mmol) and a solution of methyl acrylate (6.48 µL, 0.072 mmol) in acetone + 1% MeCN (6 mL). The mixture was stirred at room temperature and after 25 min a mass spectrum was recorded.



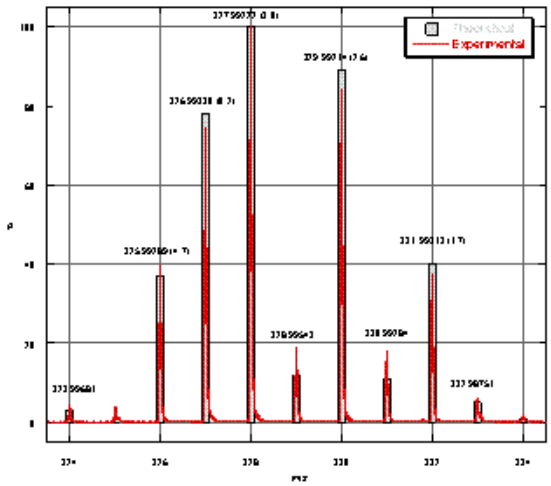
Comparison between theoretical and experimental isotopic distribution of the molecular ions [**2'**+N_2]$^+$ (a), [**2'**+MeCN]$^+$ (b), [**2'**+MeOH+N_2]$^+$ (c), [**2'**+MeOH+MeCN]$^+$ (d) and [Pd(*O,N,C*-L')($C_6H_4CO_2H$-2)I]$^+$ + [Pd(*O,N,C*-L')($IC_6H_4CO_2H$-2)]$^+$ (e), in the reaction mixture (error in ppm in parentheses).


Theoretical
Experimental

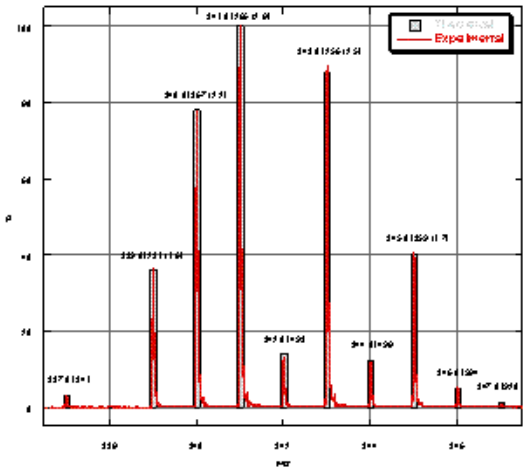
(a)


Theoretical
Experimental

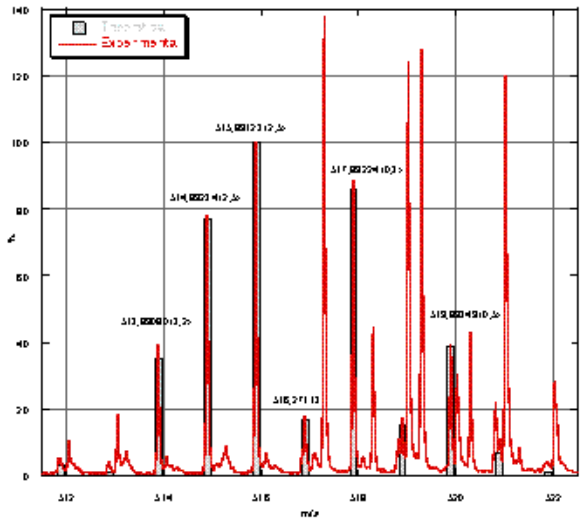
(b)


Theoretical
Experimental

(c)


Theoretical
Experimental

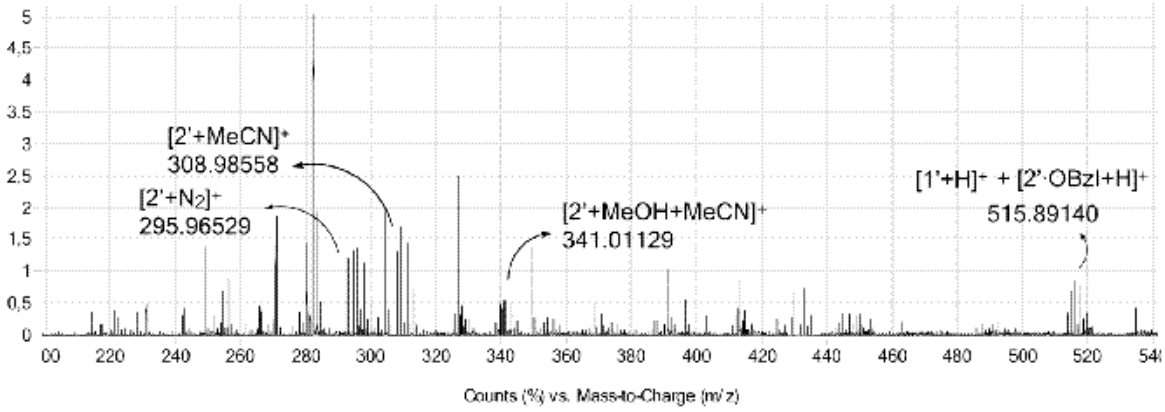
(d)


Theoretical
Experimental

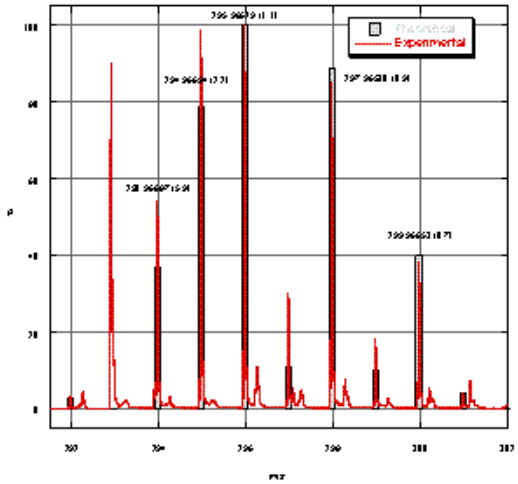
(e)

Mixture of [2'·MeCN]ClO_4 and 2-iodobenzoic acid (1:10).

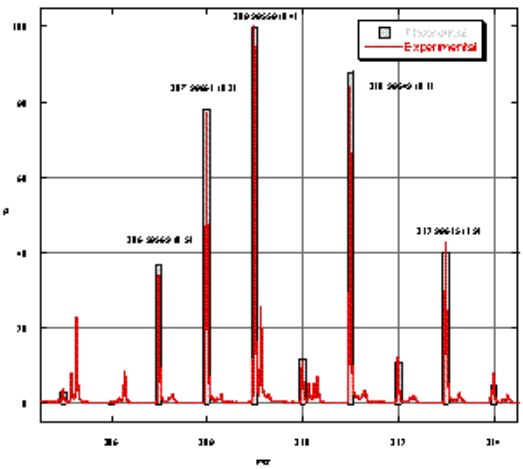
A vial was charged with 2-iodobenzoic acid (6.74 mg, 0.027 mmol), [2'·MeCN]ClO_4 (1.12 mg, 0.0027 mmol) and acetone (1% MeCN + 1 mM $HClO_4$) (6 mL). The solution was stirred at room temperature and after 10 min a mass spectrum was recorded.



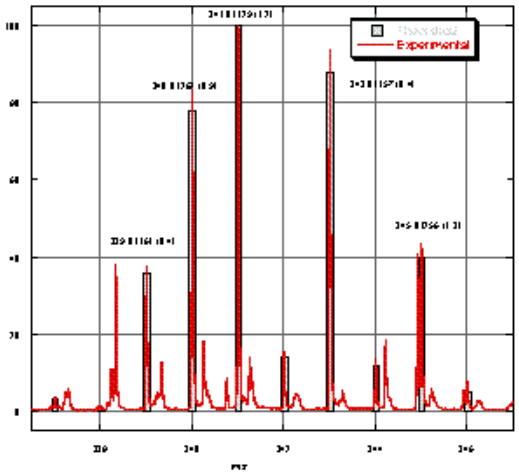
Comparison between theoretical and experimental isotopic distribution of the molecular ions $[\mathbf{2'}+N_2]^+$ (a), $[\mathbf{2'}+MeCN]^+$ (b), $[\mathbf{2'}+MeOH+MeCN]^+$ (c) and $[Pd(O,N,C\text{-}L')(C_6H_4CO_2H\text{-}2)I]^+$ + $[Pd(O,N,C\text{-}L')(IC_6H_4CO_2H\text{-}2)]^+$ (d), in the mixture (error in ppm in parentheses).



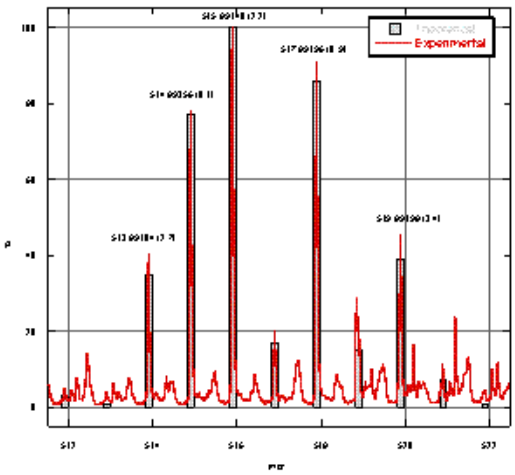
(a)



(b)

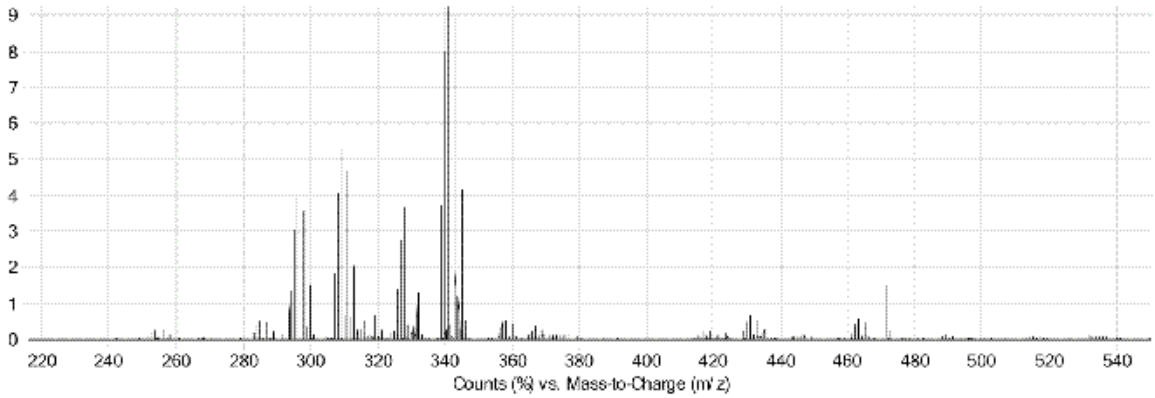


(c)



(d)

Major ions detected that have not been assigned, also appear in pure sample of [**2'**·MeCN]ClO_4 so it should not be due to the equilibrium.



ESI(+)-MS of pure [**2'**·MeCN]ClO_4

Soluble metal clusters poisoning test.

In order to check the efficiency of poisoning experiment respect to small size Pd nanoparticles (soluble metal clusters) we have decide to test Pd nanoparticles that have been previously characterized. In this context, we chose Pd colloids with an average particle size of 1.6 nm reported by M. T. Reetz and E. Westermann.[38] The system is based on the Heck coupling of ethyl acrylate (10 mmol) and iodobenzene (5 mmol) under Jeffery conditions:[38] NaOAc (12.5 mmol), TBABr (5 mmol), $Pd(OAc)_2$ (0.25 mmol), *N,N*-dimethylacetamide (5 mL), 50 °C/1 h. In one case, we run the reaction in the presence of 75 mmol of Hg (300 eq per Pd). The mixture

was heated at 50 °C during 1 h. After extraction, no coupling product was detected by ^{1}H NMR, proving that Hg poisoning test is also valid for small size Pd nanoparticles.

We also run the reaction in the presence of 1.25 mmol of benzyl chloride (5 eq per Pd) to check if dibenzyl forms. After one hour at 50 °C and extraction, 85% conversion of coupling product was detected but dibenzyl wasn't. Therefore, soluble metal clusters do not behave toward the benzyl chloride test as a mononuclear Pd(0) complex.

Synthesis

Synthesis of [Pd(O,N,C-L)(OClO$_3$)]·1/4 CH$_2$Cl$_2$ (**2**·OClO$_3$)**.** To a solution of **2**·Cl (29.1 mg, 0.08 mmol) in CH_2Cl_2 (5 mL) was added $AgClO_4$ (34.4 mg, 0.17 mmol). The reaction mixture was vigorously stirred for 15 min and then filtered through Celite. The resulting solution was concentrated (1 mL) and the addition of Et_2O (6 mL) gave a suspension, which was filtered under N_2. The solid was washed with Et_2O and dried under a N_2 stream to give **3**·OClO$_3$ as a yellow solid. Yield: 31.2 mg, 87%. Mp: 138 °C dec. Λ_M = 81 Ω·cm^2·mol^{-1}. IR (Nujol, cm^{-1}): ν(C=O) 1700, ν(C=N) 1604, ν(Cl–O) 1005. ^{1}H NMR (200 MHz, [D$_6$]acetone): δ 8.48 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.99 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 7.89 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 3.50 (s, 2H, CH_2), 3.48 (s, 6H, OMe), 1.90 (s, 3H, Me). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (t, 1 H, H4, $^3J_{HH}$ = 7.8 Hz), 7.80 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 7.65 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ =1.2 Hz), 3.75 (s, 2H, CH_2), 3.46 (s, 6H, OMe), 1.81 (s, 3H, Me). Anal. Calcd for $C_{11}H_{14}NO_7ClPd·1/4CH_2Cl_2$: C, 31.04; H, 3.36; N, 3.22. Found: C, 31.04; H, 3.27; N, 3.43.

Synthesis of [Pd(O,N,C-L')(NCMe)]ClO$_4$ ([**2'**·MeCN]ClO$_4$). To a mixture of 2-iodobenzoic acid (168.7 mg, 0.68 mmol), $AgClO_4$ (141.0 mg, 0.68 mmol) and **1** (39.3 mg, 0.07 mmol) was added a solution of CH_2=$CHCO_2Me$ (122.5 μL, 1.36 mmol) in acetone (10 mL). The mixture was stirred for 4 h in the dark and then filtered through Celite. The filtrate was concentrated (1 mL) and MeCN (1 mL) and Et_2O (20 mL) were added. The resulting precipitate was filtered off, washed with Et_2O (2x5 mL) and dried under N_2, giving orange [**2'**·MeCN]ClO$_4$. Yield: 21.2 mg, 76%. Mp: 148 °C dec. IR (Nujol, cm^{-1}): ν(C≡N) 2328, ν(C=O) 1707, 1637, ν(C=N) 1594, ν(Cl–O) 1099. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ 8.84 (dd, 1 H, H5 or H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 8.70 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.18 (dd, 1 H, H3 or H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 3.68 (s, 2 H, CH_2), 3.08 (s, 3 H, Me). ^{1}H NMR (200

MHz, [D_3]acetonitrile): δ 8.40 (t, 1 H, H4, $^3J_{HH}$ = 8 Hz), 8.14 (dd, 1 H, H5, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 8.03 (dd, 1 H, H3, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1.2 Hz), 3.61 (s, 2H, CH_2), 2.85 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (50.30 MHz, [D_3]acetonitrile): δ 200.0 (s, C6), 197.7 (s, C2), 156.9 (s, C1), 156.1 (s, C7), 143.9 (s, C4), 129.8 (s, C3), 126.5 (s, C5), 39.0 (s, CH_2), 28.5 (s, Me). Anal. Calcd for $C_{11}H_{11}N_2O_6ClPd$: C, 32.30; H, 2.71; N, 6.85. Found: C, 32.33; H, 2.80; N, 6.82.

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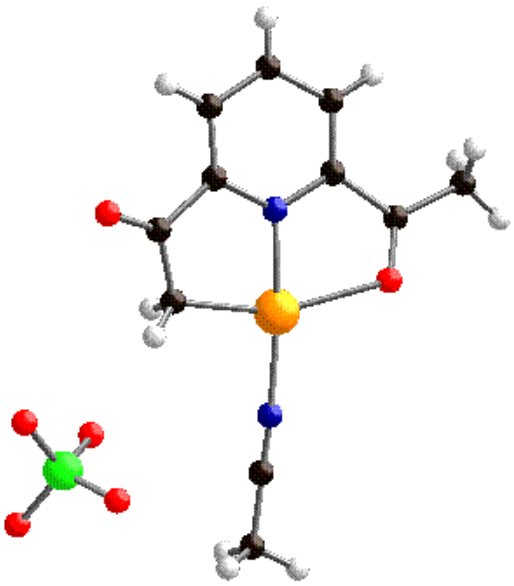
CHAPTER V

Pd(II)–Catalyzed Deprotection of Acetals and Ketals Containing Acid Sensitive Functional Groups



The results of this chapter are currently preparing to be published:

F. Juliá-Hernández, A. Arcas, J. Vicente, *Manuscript in preparation*

The results reported in this chapter are the subject of an *Applied Patent P201031021/2010* (Spain).

SUMMARY CHAPTER V

Apart from the pure research that generates fundamental knowledge about chemical transformations, it is a field of great interest to apply these results to the design of green, efficient and atom-economic processes, which have really interest to the industry. In this context, the development of new catalytic species is strongly useful because of their important effects in the selectivity and rate of many reactions with biological and pharmaceutical applications.

When we studied the reactivity of the cationic Pd(II) complexes in Section II.2 and we observed the hydrolysis of the pincer-type ligand, we wondered if some of these compounds could catalyze the deprotection of carbonyl groups in organic compounds by hydrolysis of the corresponding ketals and acetals moieties. Because of these transformations are one of the most used reactions in multistep organic synthesis, we considered interesting to carry out a study on this topic.

In **Chapter V** are presented the results corresponding to the palladium-catalyzed hydrolysis of acetals and ketals in the presence of other acid sensitive functional groups. After a series of preliminary tests, we found that the acetonitrile Pd(II) complex with metallated 2,6-diacetylpyridine, presented a high activity in carbonyl deprotection reactions. We have obtained very good yields starting from acyclic, cyclic, aromatic and aliphatic acetals and ketals leading to the corresponding aldehydes and ketones.

In addition, the catalytic reaction shows a very high selectivity to the hydrolysis of acetals and ketals, without affecting alcohol protecting groups such as silyl ethers or THP. Moreover, we checked the behaviour of substrates containing easily dehydratable primary alcohol, not detecting the disturbance of these functional groups.

These results, which leave our catalyst as one of the most useful active species in the hydrolysis of acetals and ketals, have been protected with the application of a patent.

ABSTRACT

The pincer complex **1** is used for the high-yield and selective catalytic hydrolysis of aliphatic, aromatic, cyclic and acyclic dimethyl-acetals, -ketals and dioxolanes, even in the presence of large substituents. Other protecting groups, as THP or TBDMS, or very acid-sensitive alcohols were not affected. The catalyst is easily prepared in situ from commercially available reagents, stable to air and moisture and easily recoverable.

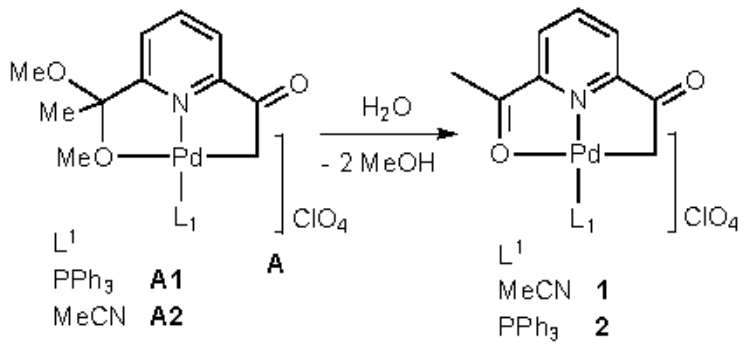
INTRODUCTION

Protection and deprotection of functional groups are key in many multi-steps organic synthesis. Therefore, the development of mild, efficient and selective reactions are crucial for such processes. In particular, the deprotection of acetals and ketals to give the corresponding carbonyl compounds have a very important role in total synthesis.[1-8] Consequently, many reagents have been developed with this purpose, for example, organic acids,[9] metal chlorides,[7,10-13] coordination complexes,[14-16] inorganic salts[1,2,4,17-21] and organic compounds.[3,5,8,22-25] While these reagents are useful towards low functionalized substrates, most of them have some limitations as (1) not being efficient to all kind of acetals and ketals,[1,2,5,12,14,19,20,24] (2) using acidic medium that prevents the use of acid sensitive functional groups[1,9,11,13,17,25] and (3) giving unwanted side-reactions with other protecting groups (tetrahydropyranyl (THP), methoxymethyl ether (MOM) or silyl ethers).[15,16,21,22,26] In the last decade, some methodologies have been highlighted over the rest, such as triethylsilyl trifluoromethanesulfonate (TESOTf) + base,[3,23] that selectively unmasks acetals in the presence of ketals in good yields, Bi(III)[7] and In(III)[4,10] salts that easily deprotect acetals and ketals in the presence of THP and silyl ether protecting groups. Only one example of Pd-catalyzed deprotection of acetals and ketals has been reported by Lipshutz *et al.*[16] Low amounts of $[PdCl_2(NCMe)_2]$ are able to afford the corresponding carbonyl groups in good yields but competitive reactions are given with THP alcohol protecting group.

RESULTS AND DISCUSSION

We have recently reported the isolation of a family of Pd(II) pincer complexes $[Pd(O^I,C^I,N^I\text{-L})(L^1)]ClO_4$[27] (L = monoanionic ligand resulting from cyclopalladation of 2,6-diacetylpyridine, L^1 = MeCN (**1**), PPh_3 (**2**); Scheme 1, and other N-, P- and C-donor ligands) obtained from the spontaneous hydrolysis of the corresponding monoketal derivatives

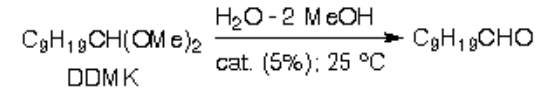
([Pd(O^1,C^1,N^1-L')(L^1)]ClO_4 (**A**), Scheme 1). As it did not occur from neutral homologous of **A**, for example [Pd(O^1,C^1,N^1-L)Cl], we interpreted that it was caused by the increase in the acidic character of Pd(II) in the cationic complexes **A**. To test if this hydrolysis could occur with an 'external' ketal we attempted to use **A1** (L^1 = MeCN) or **A2** (L^1 = PPh_3) as catalyst for the hydrolysis of decanal dimethylketal (DDMK). However, although it occurred, the process was very slow (Table 1) and curiously, the 'internal' hydrolysis did not occur while there was DDMK in solution. This suggested us that the external hydrolysis occured by replacing the ketal group of the pincer ligand by DDMK, preventing the internal hydrolysis, and not by replacement of the ligand L^1, which would be very improbable in the case of PPh_3 (**A2**). The greater reaction rate when **A1** was used as catalyst instead of **A2** could be attributable the voluminous nature of PPh_3. Consequently, we thought that complex **1** could be better as catalyst then complexes **A** because the acetyl is smaller than the ketal group, it is electron-withdrawing instead of electron-donating, making the metal center more acidic, and the Pd–O bond is weaker than the **A**-type complex.[27] We selected DDMK for the test because the catalytic deprotection of some large substrates have failed[20] and, particularly, the only reported catalytic hydrolysis of DDMK reached only 17% yield.[28]



Scheme 1

The deprotection of DDMK using **1** as catalyst was compared with that of [$PdCl_2(NCMe)_2$], because it is the only palladium compound reported for this type of catalytic reactions,[16] as well as with $Pd(OAc)_2$ or 10% of HAcO. The reactions were performed at room temperature in wet acetonitrile, with 5 mol% amount of the catalyst. Complex **1** was by far the best catalyst for the reaction (Table 1). We have recently reported that **1** showed also to be a good precatalyst for some room temperature Pd(II)/Pd(IV) Heck-type reactions.[29]

Table 1. Deprotection of DDMK with various catalysts.[a]



catalyst	time (h)	yield (%)[a]
A1	16	6
A2	16	36
1	8	95
$[PdCl_2(NCMe)_2]$[16]	16	30
$[Pd(OAc)_2]$	16	0
10 % HOAc	16	0

[a] Room temperature, 5% catalyst. Determined by ^{1}H NMR.

In order to optimize reaction conditions, we carried out some experiments at room temperature varying the amount of **1** added to the mixture (Table 2). Decanal was obtained in very good yields after 36 to 5.5 h depending on the concentration of the catalyst (1 to 10%, respectively). When the temperature of the reaction was increased to 50 °C, 98% yield was obtained after 5 min using 1% mol of **1**. Therefore, the latter reaction conditions can be used with non temperature sensitive substrates

Table 2. Deprotection of DDMK at concentrations of **1**

% of **1**	temp (°C)	time	yield (%)[a]
1	25	36 h	92
3	25	12 h	96
5	25	8 h	95
10	25	5.5 h	97
1	50	5 min	98

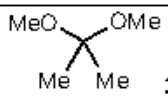
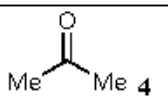
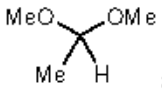
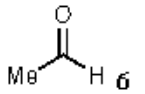
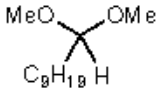
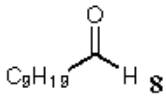
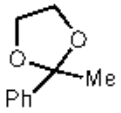
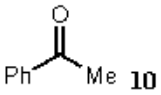
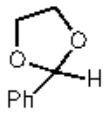
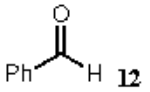
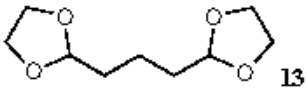
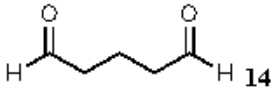
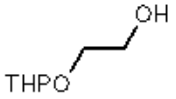
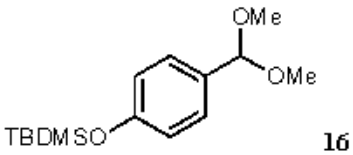
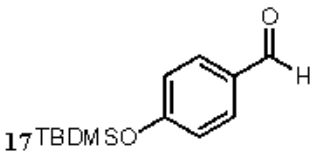
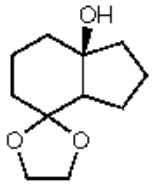
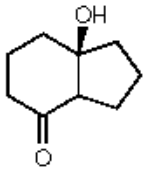
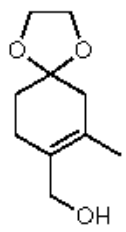
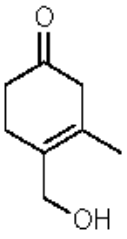
[a] Determined by ^{1}H NMR.

To know the scope of the reaction we selected some aliphatic, aromatic, cyclic and acyclic dimethylacetals, dimethylketals and dioxolanes as substrates (Table 3). The reactions were performed in wet acetonitrile and using 1 mol% of **1** as catalyst.

All deprotection reactions led to the corresponding carbonyl compounds in more than 95% yield in the range of 1-120 min at room temperature or by heating at 50 °C. As expected, ketals (entry 4, Table 3) were easier hydrolyzed than the corresponding acetals (entry 5). Moreover, dioxolane ketals and acetals were somewhat more resistant than dimethoxy compounds (entry 6). This methodology is compatible with other acid sensitive protecting groups such as tetrahydropyranyl (THP, entry 7) tert-butyldimethylsilylether (TBDMS, entry8). However, in $[PdCl_2(NCMe)_2]$-catalyzed reactions of THP protected acetals both hydrolytic processes are in competition.[16] We have also successfully deprotected two ketals containing one OH group (entries 9 and 10) that could easily dehydrate, giving the corresponding α,β–unsaturated carbonyl compounds, if acid deprotecting reagents were used. These are very remarkable results, because deprotection of compound **18** has only been accomplished with $(NH_4)_2Ce(NO_3)_6$ (CAN)[21] but the hydrolysis of substrates similar to **20** has failed using TiCl4 as catalyst.[13] We have found that $[PdCl_2(NCMe)_2]$ (1%, 50°C, 1 h) does not deprotect **20**. However, neither $(MeO)_2CH(CH_2)_3NH_2$, or its boc-protected derivative, nor $(MeO)_2CHCH_2CN$ were hydrolyzed in the presence of **1**, probably because they N-coordinate to Pd preventing the coordination of the ketal group.

Complex **1** is stable during the hydrolysis reaction and can be easily recovered (95%) and reused. As complex **1** can also be obtained (and isolated in 94% yield) by reaction of $Pd(OAc)_2$ and 2,6-diacetylpyridinium perchlorate,[27] we have also used complex **1** as catalyst for the deprotection of DDMK preparing it *in situ* by succesive addition of equimolecular amounts of 2,6-diacetylpyridinium perchlorate and $Pd(OAc)_2$ to MeCN. We have proved that palladium acetate or the acetic acid by-product did not affect the catalytic hydrolysis of DDMK (Table 1). The ^{1}H NMR of [D_3]acetonitrile solutions of reaction mixtures show that the formation of the catalyst is quantitative and instantaneous.

Table 3. **Deprotection of acetals and ketals**

Entry	Substrate	Time	Temp	Product	Yield (%)[a]
1	 **3**	10 min	25 °C	 **4**	99
2	 **5**	1 min	50 °C	 **6**	99
3	 **7**	5 min	50 °C	 **8**	98
4	 **9**	7 min	50 °C	 **10**	98
5	 **11**	12 min	50 °C	 **12**	98
6	 **13**	120 min	50 °C	 **14**	95
7	 **15**	16 h	25 °C	No reaction	---
8	 **16**	10 min	25 °C	 **17**	99
9	 **18**	10 min	50 °C	 **19**	96
10	 **20**	5	50 °C	 **21**	98

[a] Yield determined by proton NMR.

CONCLUSIONS

In conclusions, we have developed a new efficient and mild methodology for the deprotection of cyclic and acyclic acetals and ketals using [Pd(O^1,C^1,N^1-L)(NCMe)]ClO_4 (**1**) as catalyst. We achieved quickly, with very good yields and under mild conditions the corresponding carbonyl compounds without side-reactions even in the presence of others protecting groups as THP, TBDMS and very acid sensitive alcohols. The catalyst is easily prepared *in situ* from commercially available palladium acetate and 2,6-diacetylpiridinium perchlorate, fully recoverable, reusable and stable in the solid state and in solution even in the presence of air and moisture.

EXPERIMENTAL SECTION

General Procedures.

Unless otherwise stated, the reactions were carried out without precautions to exclude light, atmospheric oxygen or moisture. Melting points were determined on a Reicher apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 16F PC FT-IR spectrometer with Nujol mulls between polyethylene sheets. NMR spectra were recorded on a Bruker AC 200, or Avance 300 or 400 spectrometers. Chemical shifts were referred to TMS (^{1}H, ^{13}C). When needed, NMR assignments were performed with the help of APT, HMQC and HMBC techniques. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS; the exact masses have been calculated for the combination of the most abundant isotopes. Chart 1 shows the atom numbering used in NMR assignments. Complexes **A1**, **A2**, **1** and **2** were obtained following previously described procedures,[27] as well as compounds **18**[30] and **20**.[31]

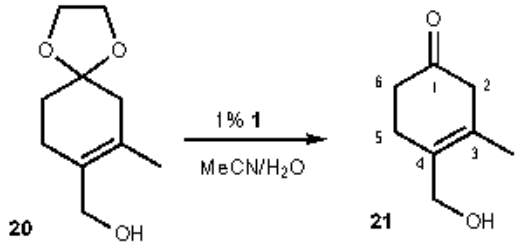
Typical experimental procedure for catalytic deprotection reaction by NMR.

An NMR tube was charged with decanal dimethylketal (48.3 μL, 0.198 mmols), water (100 μL), catalyst **1** (8.07 mg, 0.002 mmols) and acetonitrile-d_3 (500 μL). The tube was shaken until completion solution and put it on the magnet. The sample was heated at 50 °C and NMR spectra was recorded every 5 min. Conversion was calculated integrating the aldehyde proton and referenced with the solvent residual peaks.

Large-scale hydrolysis of decanal dimethylketal catalyzed by complex 1.

To a solution of decanal dimethylketal (10 mL, 41.02 mmols) and water (2 mL) in acetonitrile (50 mL), compound **1** was added (168.1 mg, 0.41 mmols). The resulting orange solution was heated at 50 °C. After 20 min, the solution was concentrated (6 mL) and diethyl ether was added (15 mL) to precipitate an orange solid that was filtered off, washed with diethyl ether and dried in vacuo. Yield: 161.3 mg, 0.39 mmols (95% recovering). The filtrate was washed with saturated aqueous solution of $MgSO_4$ and the solvent was removed in vacuo to obtain decanal in 98% of purity. Yield: 6.20 g, 39.42 mmols, 96%.

Experimental procedure for the synthesis of compound 21.



An NMR tube was charged with compound **20** (24.80 mg, 0.135 mmols), water (100 μL), catalyst **1** (0.53 mg, 0.0013 mmols) and acetonitrile-d_3 (500 μL). The tube was shaken until complete dissolution. The sample was heated at 50 °C and NMR spectra was recorded after 5 min. Compound **21** was detected in 98% conversion. ^{1}H NMR (300 MHz, acetonitrile-d_3): δ 4.07 (s, 2 H, CH_2OH), 2.78 (br, 2 H, H2), 2.48-2.37 (m, 4 H, H6+H5), 1.69 (s, 3 H, Me). ^{13}C{^{1}H} NMR (75.45 MHz, acetonitrile-d_3) δ 212.9 (C1), 131.5 (C4), 128.3 (C3), 61.5 (CH_2OH), 46.0 (C2), 39.5 (C6), 28.0 (C5), 18.4 (Me).

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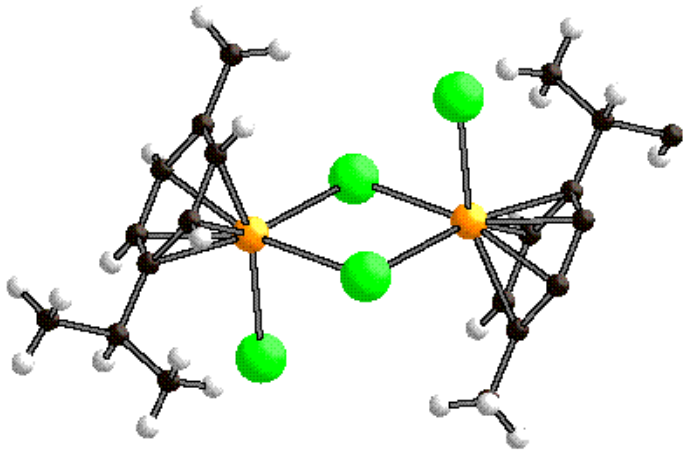
CHAPTER VI

Kinetics and Activation Parameters of the Dimerization of Terminal Alkynes Catalyzed by [Ru(*p*-cymene)Cl_2]$_2$ in Acetic Acid

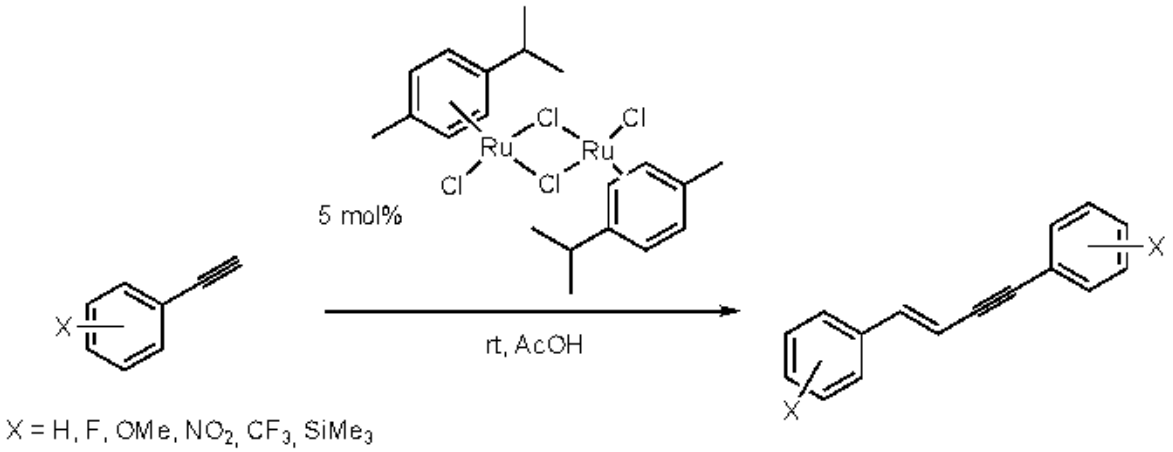


The results of this chapter are currently preparing to be published:

M. Bassetti, C. Pasquini, F. Juliá-Hernández, *Manuscript in preparation*

During my PhD I moved for a three months stay at the Consiglio Nazionale della Ricerca, Sezione Meccanismi di Reazione in the Dipartimento de Chimica at the Università La Sapieza in Rome (Italy), under the supervision of Dr. Mauro Bassetti. The main aim of this short stay was to improve my knowledge about reaction mechanism elucidation and, specifically, the use of chemical kinetics for this purpose.

When I joined Bassetti's group, one of the main research lines was focused on the preparation of 1,4-disubstituted enynes by catalytic dimerization of terminal alkynes. These C-4 unsaturated moieties are key units in naturally occurring compounds, and in organic materials, especially when derived from aromatic alkynes. Actually, they had found a very active catalytic system for this reaction based on an homogeneous metal catalyzed process. In addition, they had been recently published that commercially available di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] complex, [Ru(*p*-cymene)Cl_2]$_2$, catalyzes the dimerization of aromatic alkynes in acetic acid at room temperature to form the corresponding (*E*)-1,4-diarylbut-1-ene-3-yne derivatives, with high stereoselectivity. (Scheme 1)



Scheme 1

Due to the simplicity of the catalytic system/reaction conditions, the compatibility with aqueous media, and the excellent *E*-stereoselectivity, the study of the catalytic cycle was presented as a challenging objective.

To address this goal, I had to do a literature revision of metal-catalyzed dimerization of alkynes and understand how similar catalytic system worked. Then, we designed and carried out a vast of experiments to obtain information about reaction rate and reaction order at different conditions. Finally, we made a rigorous data processing and draw conclusions.

In order to determinate reaction rate and reaction order, we performed reactions in pseudo first order conditions and following the catalytic process by UV spectroscopy, stopped-flow spectroscopy, NMR and GC/MS. With these data we could make concentration *vs* time plots and calculate reaction rate for each experimental conditions.

The range of the dataset was patterned towards different main aims. On one hand, we carried out experiments varying the nature of substituents in *meta* and *para* position in the aromatic ring. This change produced an important shift in the reaction rate because of the variation of the electronic properties of the alkyne, providing us information about the slow reaction step. In addition, we could quantify it by using the Hammett plot, which describes a linear free-energy relationship relating reaction rates and equilibrium constants (Figure 1). The value of the slope gave notice of the existence of a excess of positive charge in the transition state of the slow reaction step.

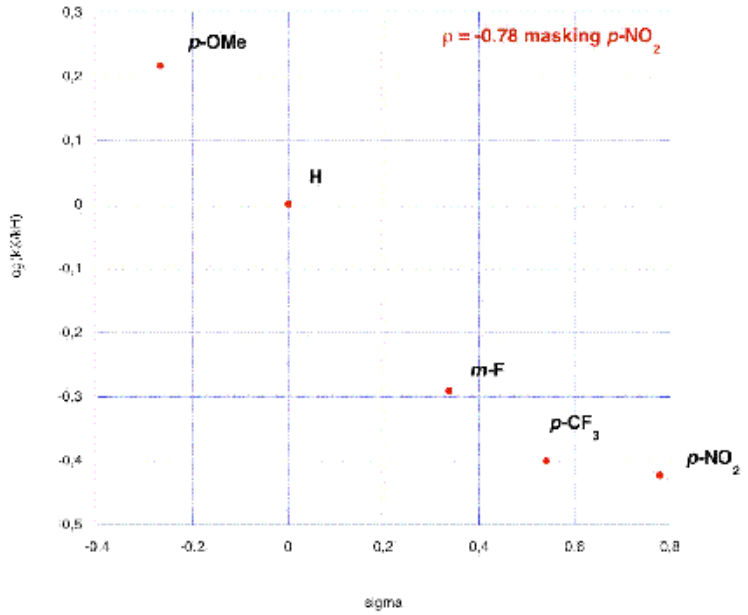


Figure 1

On the other hand, we performed experiments at different temperatures in order to calculate the activation parameters of the catalytic cycle. This dataset allowed us to determinate the activation entropy and activation energy by using the Eyring equation (Figure 2). From the slope and the intercept we could obtain a negative value for the entropy and 16 kcal/mol of

activation energy, meaning that the rate-determining step corresponds to an associative process.

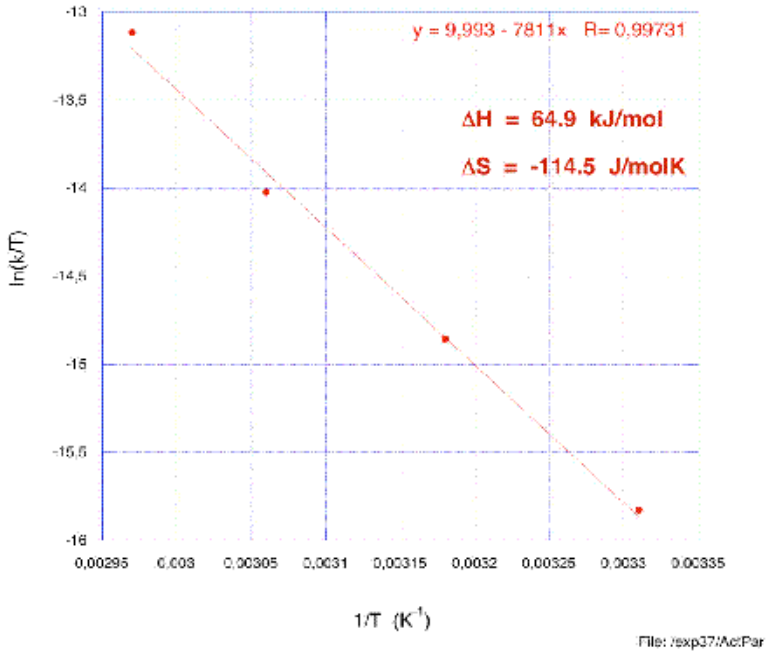
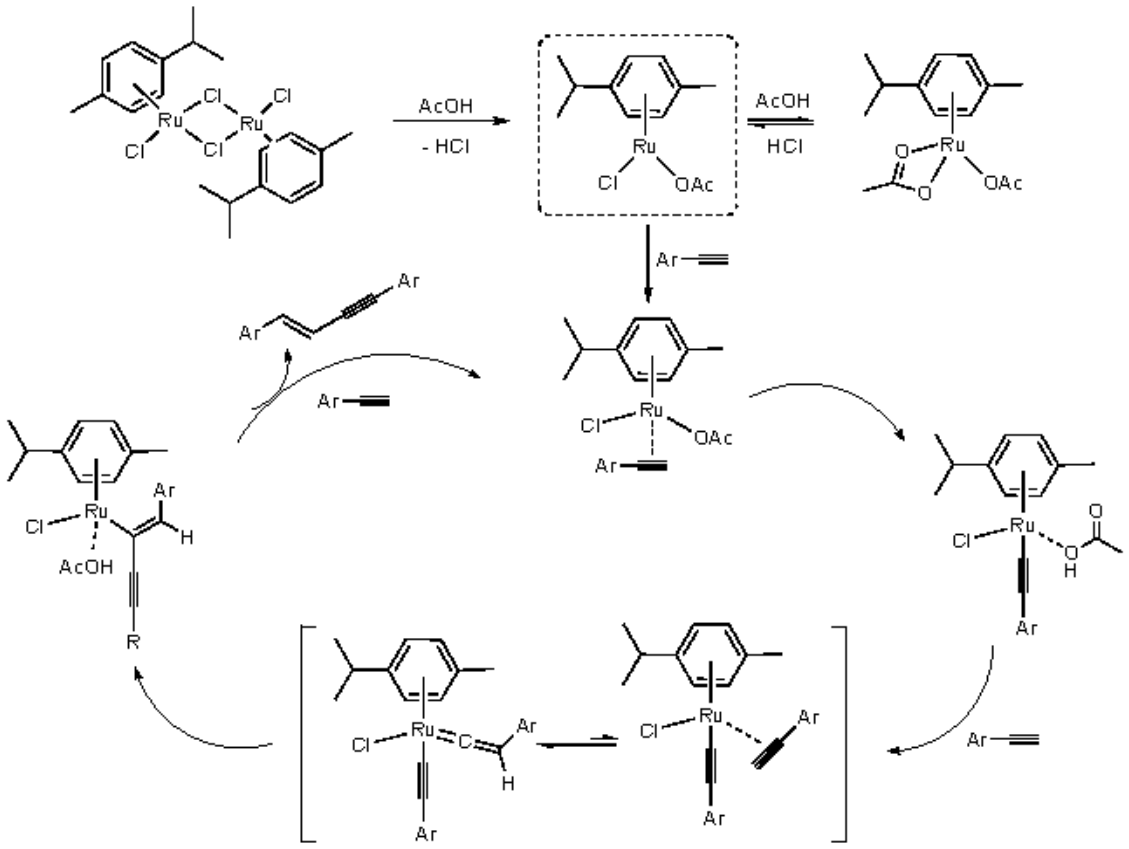


Figure 2

Finally, with the activation parameters, Hammett plot values, reaction orders, shape of the kinetic curves and other considerations, we could suggest a mechanism for the ruthenium-catalyzed dimerization of terminal alkynes. (Scheme 2)

First, there is a coordination of the alkyne to the active species, which corresponds to a mononuclear ruthenium complex with one acetate ligand. We suggested this process as the rate-determining step for the catalytic cycle because an associative process is involved and a formal positive charge can be created due to coordination of the alkyne. Then, the metalation of the terminal alkyne is supported to the acetate base ligand, generating a Ru(II) intermediate that reacts with another alkyne to form an equilibrium between a π-η^2-alkyne species and a vinylidene complex. After insertion of the coordinated alkyne into the Ru–C bond an alkenyl complex is formed. Finally, this compound is protanted by acetic acid and the desired enyne is released, regenerating the catalyst.



Scheme 2

The work done during my stay in Rome served to introduce me to the study of reaction mechanisms. The techniques and knowledge learnt were useful for my later work developing my doctoral thesis in Murcia. In addition, the **results obtained are preparing to be published.**

GENERAL CONCLUSIONS

Organometallic Complexes of Pd(II) and Pd(IV) Derived from 2,6-Diacetylpyridine. Catalytic Applications.

1. We have prepared a diaryl Pd(II) complex by a rare example of disproportionation when [Pd(κ^2-Ar)(*O,O*-acac)] is reacted with 4 equiv of XyNC. We attribute this to the transphobia effect between the aryl and *C*-acac ligands in an intermediate.

2. 2,6-Diacetylpyridine can be cyclopalladated using palladium chloride in methanol via its transformation into its monodimethylketal. The resulting complex reacts with isocyanides, giving complexes resulting from coordination or, additionally, insertion of the ligand followed by a tautomerization process from β-ketoimine to β-ketoenamine.

3. The synthesis of cationic complexes derived from 2,6-diacetylpyridine dimethylmonoketal have been carried out. Some of these complexes hydrolyzed spontaneously to give MeOH and the corresponding complexes with the pincer ligand resulting from deprotonation of one acetyl group of 2,6-diacetylpyridine.

4. We have prepared and fully characterized the first family of organopalladium(IV) complexes containing a pincer-type ligand. The great stability of these complexes is due to the specific ligand used in this work. These complexes undergo C–X (X = Cl, Br, I) reductive elimination reactions to give the corresponding halogenated compounds that have been also characterized.

5. The thermodynamic parameters of the formation of the triiodo organopalladium(IV) complex have been determined by proton NMR and using the van't Hoff equation.

6. The synthesis of a mixture of two Pd(IV) isomers, by oxidative addition of an aryl halide to Pd(II), has been reported. The reaction proceeds through a benzoate Pd(II) intermediate, which has been detected by NMR. Methyl acrylate and 2-iodobenzoic acid are coupled in the presence of silver perchlorate and catalytic amounts of these Pd(IV) complexes.

7. We have used these Pd(IV) complexes and some of our Pd(II) compounds as precatalysts in a Heck-type coupling reaction. An investigation about the reaction mechanism have been carried out, ruling out the participation of palladium

nanoparticles or Pd(0) complexes. Two Pd(IV) intermediates have been detected in the catalytic reaction by ESI-MS.

8. All experimental data strongly support our proposal of a Pd(II)/Pd(IV) catalytic cycle in this Heck-type coupling reaction.

9. The acetonitrile Pd(II) complex, containing the metallated 2,6-diacetylpyridine behaves as an efficient and mild catalyst for the hydrolysis of acetals and ketals in the presence of other acid sensitive functional groups.

10. The kinetics and activation parameters determination of the dimerization of terminal alkynes catalyzed by $[Ru(p\text{-cymene})Cl_2]_2$ in acetic acid, have been carried out.

DISSERTATION
SUMMARY

Pd(II) and Pd(IV) Complexes

Derived from 2,6-Diacetylpyridine.

Catalytic Applications.

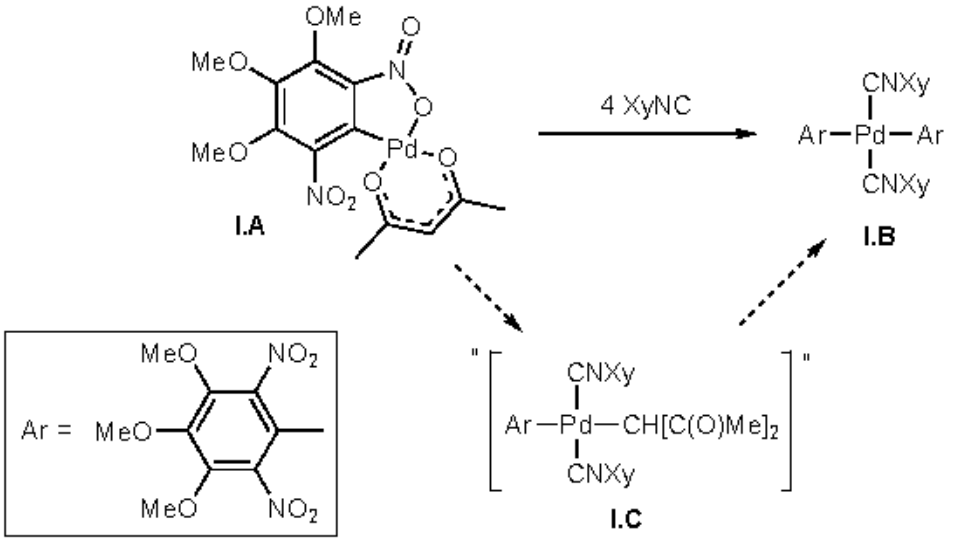
One of the most interesting topics developed by our research group is focus on the synthesis of new *ortho*-functionalized organometallic complexes, as well as the study of its reactivity, to find novel chemical behaviour and applications in organic synthesis. In this context, palladium is highlighted as many of its organometallic derivatives are intermediates in numerous stoichiometric and catalytic reactions, some of which are key steps in industrial processes.

Most of this memory corresponds to the synthesis of Pd(II) and Pd(IV) complexes with ligands derived from 2,6-diacetylpiridine and the study of the reactivity and catalytic properties of the new compounds (Chapters II-V). Moreover, it is included a preliminary work regarding the preparation, reactivity and structural study of Pd(II) complexes with the ligand 3,4,5-trimethoxy-2,6-dinitrophenyl (Chapter I). In addition, the memory concludes with a summary of the work carried out in my predoctoral short stay at La Sapienza – Università di Roma, under the supervision of Dr. Mauro Bassetti.

Chapter I

We decided to use $C_6(NO_2)_2$-2,6-$(OMe)_3$ as a pincer-type ligand in order to prepare and study the behaviour of the corresponding palladium complexes. Although we were not able to obtain any of such kind of compounds, we found other interesting results.

The complex [Pd(κ^2-Ar)(*O,O*-acac)] (**I.A**, Scheme 1) reacts with 4 equivalents of XyNC leading to the formation of *trans*-[Pd(κ^1-Ar)$_2$(CNXy)$_2$] (**I.B**). This reaction, in which we obtain a diaryl starting from a monoaryl complex, corresponds to a rare example of disproportion. We attribute it to the instability of the intermediate **I.C**, as a consequence of the high transphobia between aryl and acac C-donor ligands. We were not able to synthesize intermediate **I.C** by other ways, always obtaining the compound **I.B**. This result is a new method of synthesis of diaryl complexes [Pd](Ar)$_2$, (Ar = $C_6(NO_2)_2$-2,6-$(OMe)_3$). Previously attempts to prepare such kind of complexes using [Hg(Ar)$_2$] as a transmetallation reagent were unsuccessful, even when using an excess of the organomercury complex.



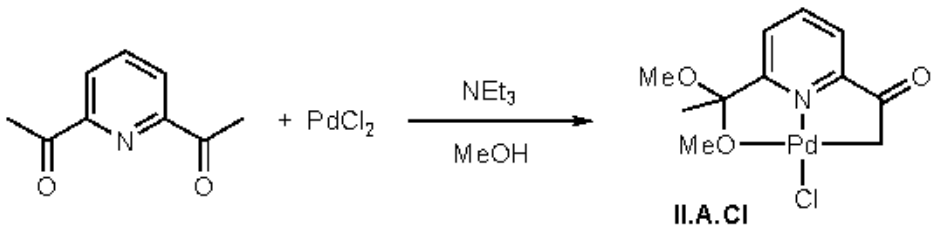
Scheme 1

Then, we decided to synthesize pincer-type complexes by 2,6-diacetylpyridine (dap) metallation.

Chapter II

The synthesis and reactivity of Pd(II) complexes derived from 2,6-diacetylpyridine are reported. New organic ligands have been prepared, which can act as monodentate, chelate or pincer-type.

Specifically, **Section II.1** describes reactions with the aim of palladation 2,6-diacetylpyridine. After a serie of failed experiments, the preparation of a kentonyl Pd(II) complex containing a *C,N,O* pincer-type ligand, resulting from the deprotonation of the acetyl group of the 2,6-diacetylpyridine dimethylketal was achieved (**II.A.Cl** , Scheme 2).



Scheme 2

Using this complex as starting material, we studied reactions with phosphines, diimines and [Tl(acac)] affording the corresponding neutral complexes **II.A**, **II.B** and **II.C** (Figure 1). In

addition, we investigated the reactivity of complex **II.A.Cl** towards isocyanides, detecting the insertion of these unsaturated molecules into the Pd–CH_2 bond and tautomerization processes from β-ketoimine to β-ketoenamine, obtaining complexes with new ligands (**II.D**, **II.E**, **II.F**, Figure 1). Controlling reaction conditions, we could isolate the coordination intermediates preceding to the insertion processes.

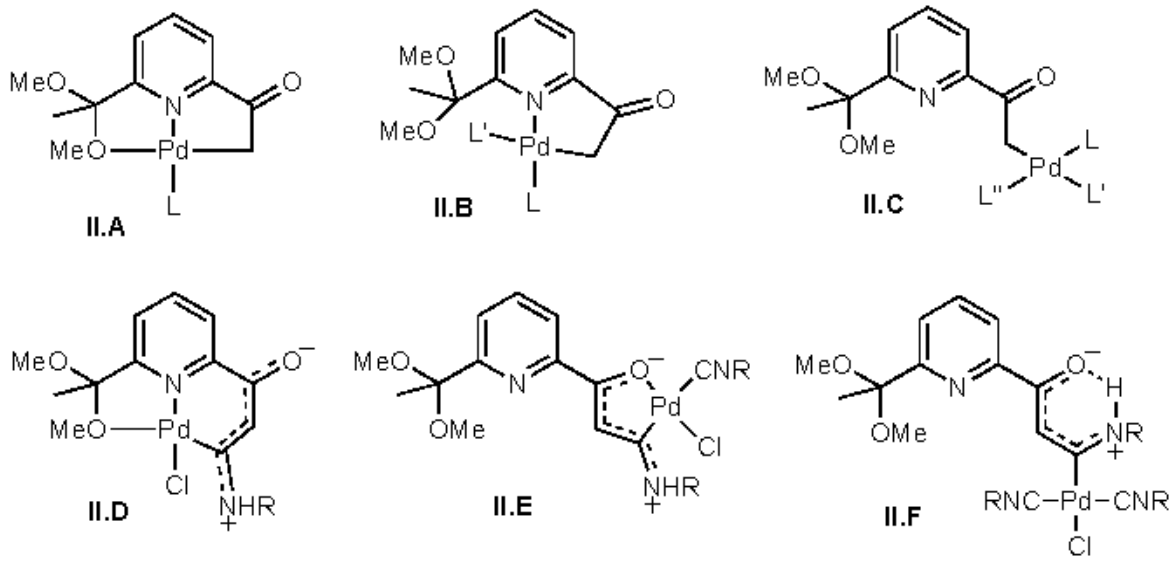
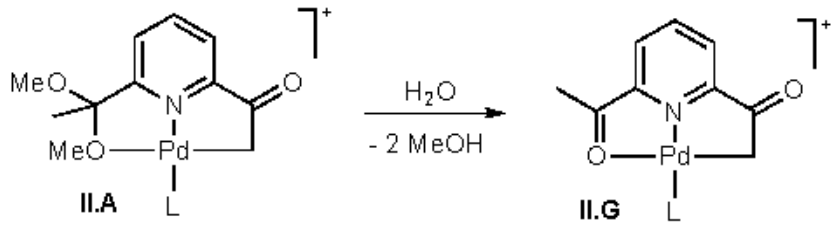


Figure 1

On the other hand, we decided to prepare cationic complexes to look into its reactivity towards various compounds. These results are presented in **Section II.2**. The perchlorate complex **II.A.OClO$_3$** (**II.A**, L = $OClO_3$, Figure 1), which was prepared by reaction of **II.A.Cl** with silver perchlorate, has been used as starting material. We carried out substitution reactions with C–donor (isocyanides and carbon monoxide), P–donor (phosphines and diphosphines) and N–donor ligands (amines, diamines and diimines). We obtained a family of cationic compounds with general structure **II.A**, **II.B** y **II.C** (Figure 1). Most of these compounds are not stable in solution at room temperature and they release methanol because of the hydrolysis of the ketal group of the ligand. In some cases, we could isolate the hydrolysis products with the deprotonated ligand dap acting as pincer (Scheme 3). By this way, we could synthesize the complexes resulting from the palladation of the 2,6-diacetylpyridine (**Section II.2**).



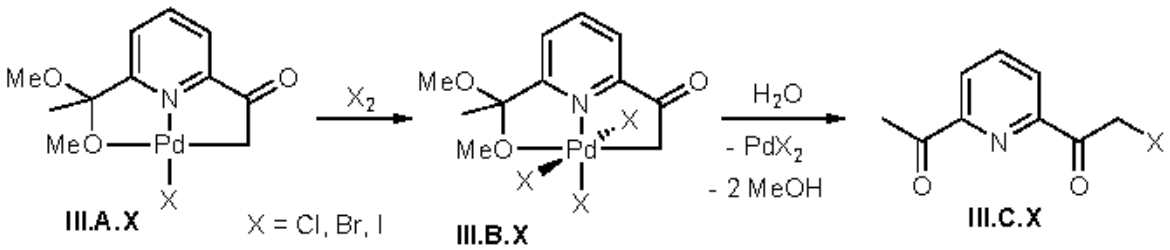
Scheme 3

By reacting 2,6-diacetylpyridinium perchlorate with palladium acetate, the synthesis of complexes **II.G** (Scheme 3) was efficiently simplified.

Chapter III

In view of the versatility of the ligand 2,6-diacetylpyridine dimethylketal and the excellent stability of the Pd(II) complexes prepared, we decided to carry out oxidation reaction in order to obtain the corresponding Pd(IV) derivatives. Palladium complexes in oxidation state IV are considered as rare species because of their high thermal instability. The need to incorporate chelate ligands, usually diimines, in the structure of such compounds is key to improve their thermal stability. Organometallic Pd(IV) complexes are interesting because they have been proposed as intermediates in the most used organic synthesis reactions, both C–C bond formation and C–H activation. Furthermore, this topic became even more interesting when we realized about the absence of pincer-type Pd(IV) complexes isolated.

Section III.1 presents oxidation reactions of the Pd(II) complexes **III.A.X** with chlorine and bromine (Scheme 4), leading to the corresponding **III.B.Cl** and **III.B.Br**, which are the first pincer-type Pd(IV) complexes isolated and completely characterized. The reactivity of such compounds is based on their reductive elimination processes. Thus, it was possible to quantitative and regioselective isolate the corresponding C–X (X = Cl, Br) coupling products (Scheme 4).



Scheme 4

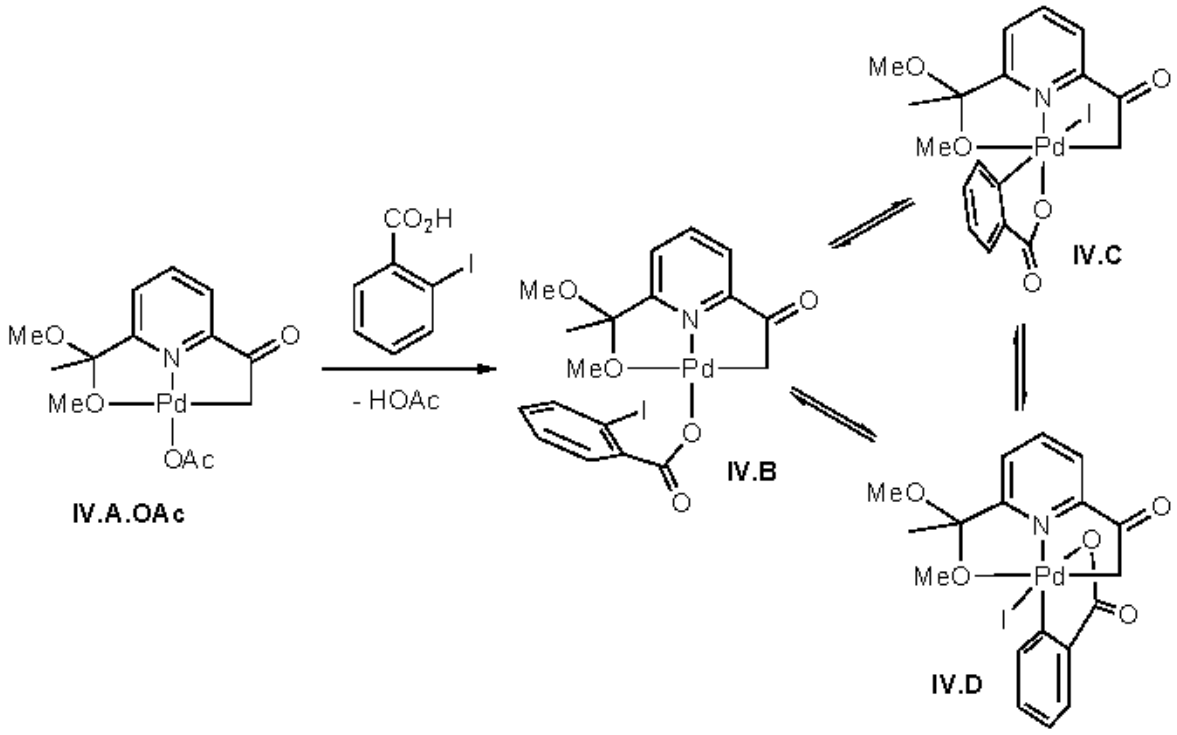
Section III.2 deals with the preparation of the iodo Pd(IV) derivative **III.B.I** (Scheme 4) by reaction of the iodo Pd(II) complex (**III.A.I**) with iodine. The isolation and characterization by X-Ray diffraction of this compound needs to be highlighted in terms that three reducing iodo ligands are bonded to a highly oxidizing metal center. Actually, it is the most iodated organometallic Pd(IV) complex reported. Moreover, the oxidation reaction is not quantitative and an equilibrium is formed between Pd(II) and Pd(IV) species, which allowed us to determinate thermodynamic parameters using the van't Hoff equation. In the same way as the chloro and bromo derivatives, a C–I reductive elimination reaction quantitative and regioselective afforded the corresponding iodated ligand (**III.C.I**, Scheme 4).

Chapter IV

As as result of the extraordinary stability of the Pd(IV) complexes prepared, we decided to investigate the reactivity of our pincer-type Pd(II) compounds with other oxidizing agents. First of all, we applied the experience learned with the synthesis of the trihalo complexes, to the preparation of intermediates proposed in palladium-catalyzed reactions. Within this kind of reactions, C–C bond formations are by far the most used, and its importance has been recognized by awarding the 2010 Nobel Prize in Chemistry. Although the reaction mechanism assumes a catalytic cycle in which Pd(0) and Pd(II) species are involved, the development of new Pd(II) precatalysts with chelate or pincer type ligands, which improve the efficiency of the reaction, led some authors to speculate about a possible Pd(II)/Pd(IV) catalytic cycle. However, while some theoretical calculations suggested this possibility, the lack of definitive experimental proofs left unresolved one of the main open problems in homogeneous catalysis.

The study of a C–C Heck-type coupling reaction begins in **Section IV.1**, looking into the oxidative addition reaction, which corresponds to the first step in a Pd(II)/Pd(IV) catalytic cycle. The oxidative addition of an aryl halide to a Pd(0) species, generating a Pd(II) intermediate, is described in the classic mechanism. The similar step in a Pd(II)/Pd(IV) catalytic cycle would suppose an oxidative addition of a haloarene to the Pd(II) catalyst leading to a Pd(IV) intermediate. Since this kind of reaction had not been previously reported, we decided to address it by using our pincer-type complexes, as a previous step to the catalytic reaction. For this reason, we prepared the acetate Pd(II) complex, **IV.A.OAc**, and 2-iodobenzoic acid was used as haloarene (Scheme 5). The choice of the aryl halide is not trivial

and, in addition, it is crucial to the success of the reaction. We chose a carboxylic group in the *ortho* position because of 1) the rapid acid/base reaction would leave the Ar–I bond closer to the metal, facilitating the oxidation reaction and 2) the formation of two bonds would lead to a chelate ligand that would improve the stability of the Pd(IV) intermediate, making easier its isolation.



Scheme 5

By this way, the reaction of the acetate complex with 2-iodobenzoic acid afforded two Pd(IV) isomers (**IV.C** y **IV.D**, Scheme 5) that are in equilibrium, and correspond to the first Pd(IV) complexes synthesized by oxidative addition of a halorene to a Pd(II) complex.

Because this reaction corresponds to the first step in a Pd(II)/Pd(IV) catalytic cycle, we studied and tested, for the first time, that Pd(IV) complexes **IV.C** and **IV.D** are precatalysts in Heck-type coupling reactions. The reaction of methyl acrylate with 2-iodobenzoic acid in the presence of silver perchlorate and catalytic amounts of the Pd(IV) complexes afforded with good yield the desired C–C coupling product, (*E*)-methyl-2-carboxycinnamate. This result shows the ability of the Pd(IV) complexes to act as precatalysts in this reaction, but don't demostrate its participation in a Pd(II)/Pd(IV) catalytic cycle.

In **Section IV.2** we carried out a comprehensive study of this catalytic reaction for the purpose of elucidating its mechanism. In this way, we used different kind of olefins and expanded the number of precatalysts of the reaction (**IV.A.OClO$_3$**, **IV.A.OAc**, **IV.E**, Figure 2).

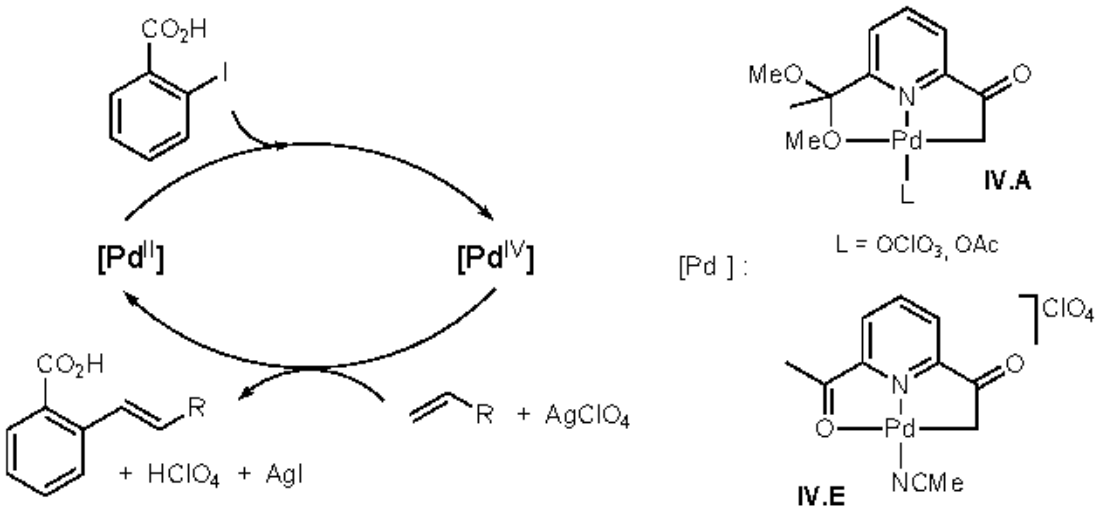


Figure 2

We looked into the reaction kinetics and realized a serie of tests (Hg drop test, quantitative poisoning, dibenzyl) to figure out the homogeneous or heterogeneous nature of the catalyst. Thereby, we ruled out the presence of palladium nanoparticles and Pd(0) complexes in the reaction mixture. Finally, we carried out a study by ESI-MS that allowed us to detect two Pd(IV) intermediates in the reactions catalyzed by complexes **IV.A.OClO$_3$** and **IV.E**. This result is specially novel because it involves the first experimental detection of Pd(IV) intermediates in a Heck-type coupling reaction.

These experimental proofs, which support the existence of a Pd(II)/Pd(IV) catalytic cycle, can not be generalized from other reactions that, usually, are performed at higher temperatures in which Pd(IV) intermediates, if they occur, would decompose leading to nanoparticles that presumably could catalyze the reaction. These evidences just show that it is possible, under very specific circumstances, that a Pd(II)/Pd(IV) mechanism operates in a C–C coupling reaction.

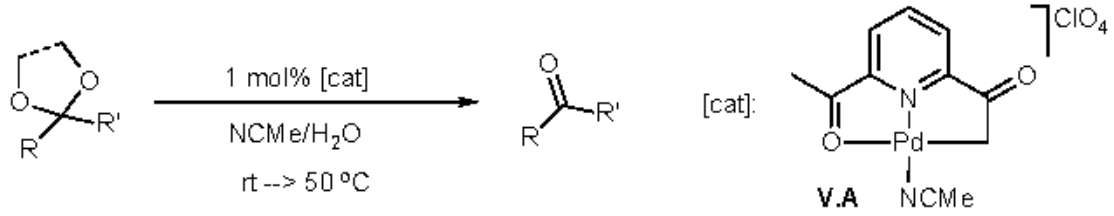
As fundamental research, the search for applications to the organometallic synthesis is one of the main aims of the researchers that work in this field. In this sense, the use of organometallic compounds as catalysts in organic reactions corresponds to the main potential application of such complexes.

Chapter V

The use of one of the palladium complexes prepared as catalyst in one of the most used organic synthesis reaction, the hydrolysis of ketals and acetals, is reported.

The need to use protecting groups in organic synthesis is considered as one of the most important reaction to optimize in multistep processes, having an important role the carbonyl protecting groups (acetals and ketals). Thus, the study of new methodologies for the hydrolysis of acetals and ketals is extremely useful in industrial synthesis of fine chemical drugs. It has been developed many compounds that efficient hydrolyze acetal and ketal groups in simple organic substances. However, most of them present some limitations as: 1) lack of generality, 2) using acidic mediums that prevent the use of acid sensitive substrates or 3) giving undesirable side-reaction with other protecting groups (THP, MOM).

After some preliminary experiments, we determined that complex **V.A** (Scheme 6) is a good catalyst for the deprotection of aldehydes and ketones. Using 1 mol% of the complex, we achieved good yields for cyclic, acyclic, aliphatic and aromatic acetals and ketals. Moreover, the methodology neither affect to acid sensitive functional group nor alcohol protecting groups as THP and sylyl ethers.



Scheme 6

Because of the high activity, efficiency and selectivity, and the easily preparation of the catalyst, we decided to protect these results with the application of a patent.

Chapter VI

This chapter corresponds to a summary of the work I carried out in my predoctoral short stay at La Sapienza – Università di Roma (Italy), under the supervision of Dr. Mauro Bassetti, Consiglio Nazionale della Ricerca. During three months I was studying the reaction mechanism of the dimerization of terminal alkynes catalyzed by a dinuclear ruthenium

complex. It was based on the use of reaction kinetics as the tool to determinate the activations parameters and the Hammett plot of the rate-determining step.

All the new species that have been reported in this memory have been completely characterized by NMR, IR, HRMS and elemental analysis. In addition, some complexes have been also characterized by X-ray diffraction. Apart from the synthetic work, it has been carried out a rigorous study regarding the mechanism of a catalytic reaction, by the use of experimental test and instrumental techniques. From this work, we propose a Pd(II)/Pd(IV) catalytic cycle in a Heck-type C–C coupling reaction, that the author of this memory considers as the greater scientific relevance result of this dissertation.

The scientific contribution which has resulted in this thesis is summarized in the participation in four national and international conferences (3 poster + 1 oral communication), the application of a patent and the publication of the results in this high impact journals:

- J. Vicente, A. Arcas, M.-D. Gálvez-López, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2008**, *27*, 1582.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2010**, *29*, 3066.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Chem. Comm.* **2010**, *46*, 7253.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Inorg. Chem.* **2011**, *50*, 5339.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Angew. Chem. Int. Ed.* **2011**, *50*, 6896.
- F. Juliá-Hernández, A. Arcas, J. Vicente *Chem. Eur. J. Submitted.*
- F. Juliá-Hernández, A. Arcas, J. Vicente *Organometallics Submitted.*
- F. Juliá-Hernández, A. Arcas, J. Vicente *Manuscript in preparation.*

RESUMEN
EN CASTELLANO

Complejos de Pd(II) y Pd(IV) Derivados

de la 2,6-Diacetilpiridina.

Aplicaciones Catalíticas.

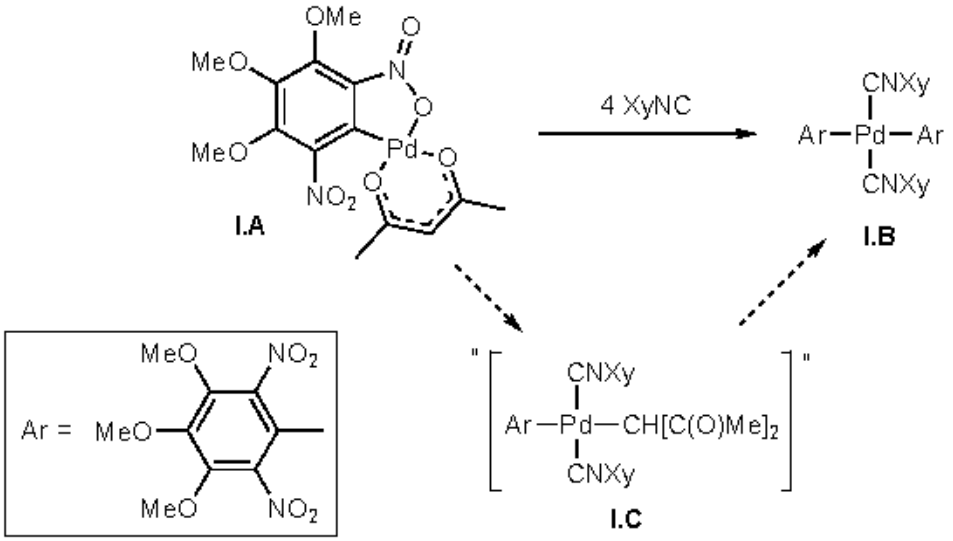
Uno de los focos de interés de nuestro grupo de investigación consiste en la síntesis de nuevos complejos organometálicos de paladio funcionalizados en *orto*, así como el estudio de su reactividad, con el fin de encontrar comportamientos químicos novedosos y aplicaciones en síntesis orgánica. Estos complejos son intermedios en numerosas reacciones catalíticas o estequiométricas, algunas de las cuales constituyen etapas clave en procesos industriales.

La mayor parte de esta memoria se dedica a la síntesis de complejos de paladio (II) y (IV) con ligandos derivados de la 2,6-diacetilpiridina, así como al estudio de su reactividad y propiedades catalíticas (Capítulos II-V). Además se incluye un trabajo inicial, dedicado a la preparación, reactividad y estudio estructural de complejos de paladio (II) con el ligando 3,4,5-trimetoxi-2,6-dinitrofenilo (Capítulo I), y se concluye con un trabajo realizado en el grupo del Dr. Mauro Bassetti durante una estancia de tres meses en La Sapienza – Università di Roma (Capítulo VI).

Capítulo I

El objetivo que nos propusimos al estudiar el comportamiento químico de algunos derivados de paladio con el ligando $C_6(NO_2)_2$-2,6-$(OMe)_3$) fue preparar complejos en los que este ligando actuara como pincer. Aunque no conseguimos obtener ningún compuesto de este tipo, encontramos otros resultados interesantes.

El complejo [Pd(κ^2-Ar)(*O,O*-acac)] (**I.A**, Esquema 1) reacciona con 4 equivalentes de XyNC conduciendo a la formación de *trans*-[Pd(κ^1-Ar)$_2$(CNXy)$_2$] (**I.B**). Esta reacción, en la que se obtiene un di- a partir de un mono-aril complejo, es un ejemplo raro de desproporción, que atribuimos a la inestabilidad del intermedio [Pd(Ar)(*C*-acac)(CNXy)$_2$] (**I.C**), como consecuencia de la transfobia entre los ligandos C-dadores arilo y acac. No fue posible preparar este intermedio inestable por otras rutas; en su lugar se aísla **I.B**. Este resultado supone un nuevo método de síntesis de diaril complejos [Pd](Ar)$_2$, (Ar = $C_6(NO_2)_2$-2,6-$(OMe)_3$). Intentos anteriores de obtener complejos de este tipo usando [Hg(Ar)$_2$] como reactivo de transmetalación fueron infructuosos, incluso cuando las reacciones se llevaron a cabo usando un exceso de mercurial.



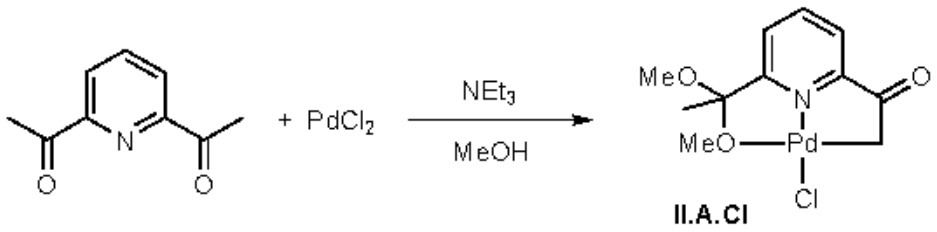
Esquema 1

A continuación decidimos preparar complejos de tipo pincer por metalación de la 2,6-diacetilpiridina (dap).

<u>Capítulo II</u>

Se describe la síntesis y reactividad de complejos de Pd(II) con ligandos derivados de la 2,6-diacetilpiridina. Se han preparado diferentes ligandos orgánicos, que pueden actuar como monodentados, quelato o pincer.

Concretamente, en la Sección II.1 se describen las reacciones llevadas a cabo para paladiar la 2,6-diacetilpiridina. Tras varios experimentos fallidos, se consiguió preparar un cetonil complejo de Pd(II) que contiene un ligando pincer *C,N,O*, resultante de la desprotonación del grupo metilo del acetilo del dimetilcetal de la 2,6-diacetilpiridina (II.A.Cl , Esquema 2).



Esquema 2

Utilizando este complejo como material de partida, estudiamos reacciones con fosfinas, diiminas y Tlacac, obteniéndose los complejos neutros **II.A**, **II.B** y **II.C** (Figura 1), donde el ligando pincer puede descoordinarse formando un quelato o incluso puede actuar como monodentado. Además, investigamos la reactividad del complejo **II.A.Cl** frente a isocianuros, observando procesos de inserción en el enlace Pd–CH_2 y tautomerizaciones de *β*-cetoimina a *β*-cetoenamina. De esta manera, se obtuvieron complejos con nuevos ligados (**II.D**, **II.E**, **II.F**, Figura 1). Controlando las condiciones de reacción, se pudieron aislar los intermedios de coordinación que preceden a los procesos de inserción.

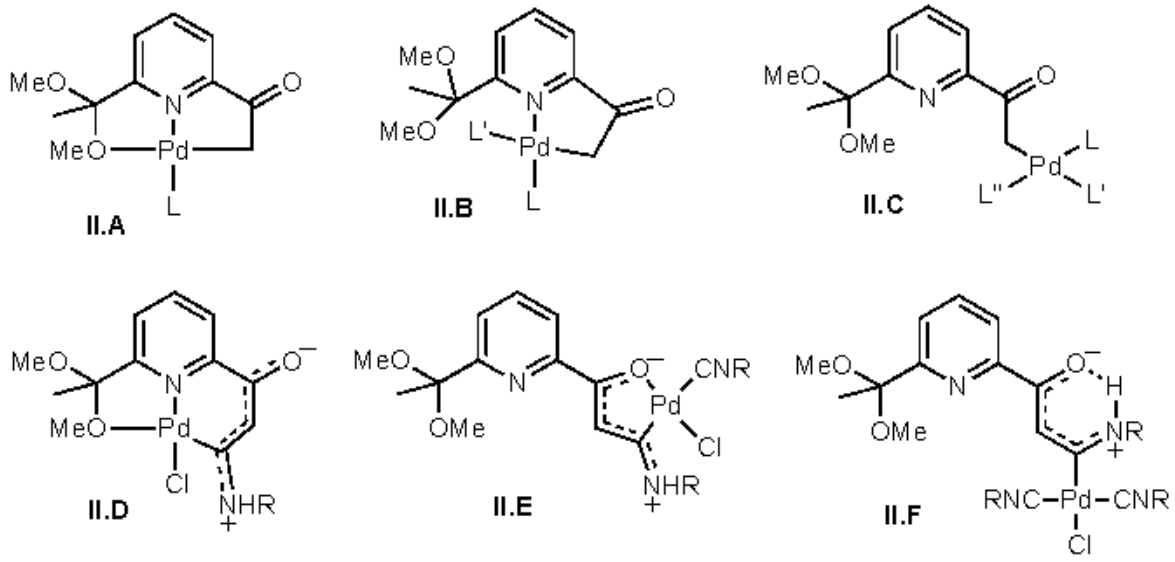
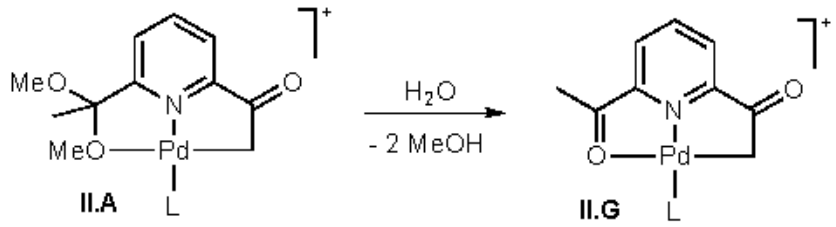


Figura 1

Por otro lado, decidimos preparar complejos catiónicos para investigar su reactividad frente a diversos compuestos. Estos resultados se describen en la **Sección II.2**. Utilizamos como material de partida el perclorato complejo **II.A.OClO$_3$** (**II.A**, L = $OClO_3$, Figura 1), resultado de la reacción del complejo **II.A.Cl** con perclorato de plata. Llevamos a cabo reacciones de sustitución con ligandos dadores de carbono (isocianuros y monóxido de carbono), dadores de fósforo (fosfinas y difosfinas) y dadores de nitrógeno (aminas, diaminas y diiminas). Se obtuvo una familia de complejos catiónicos de estructura general **II.A**, **II.B** y **II.C** (Figura 1). La mayoría de estos productos no son estables en disolución a temperatura ambiente, puesto que eliminan metanol como consecuencia de la hidrólisis del grupo cetal. En algunos casos, fue posible aislar los productos de la hidrólisis, con el ligando dap desprotonado

actuando en todos ellos como pincer (Esquema 3). De esta forma se han obtenido los complejos resultantes de la paladación de la 2,6-diacetilpiridina (**Sección II.2**).



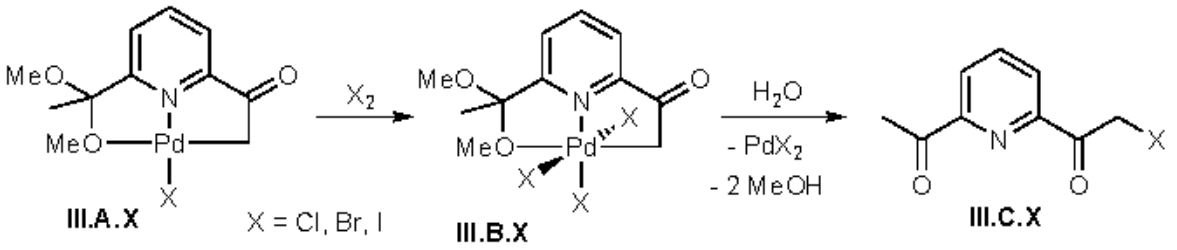
Esquema 3

Mediante reacción del perclorato de 2,6-diacetilpiridinio con acetato de paladio, se simplificó y mejoró la síntesis de los complejos **II.G**.

Capítulo III

A la vista de la versatilidad del ligando 2,6-diacetilpiridina dimetilcetal y la excelente estabilidad de los complejos de Pd(II) preparados, decidimos realizar reacciones de oxidación para intentar obtener los correspondientes derivados de Pd(IV). Los complejos de paladio en estado de oxidación IV están considerados como especies raras debido a su elevada inestabilidad. La necesidad de incorporar ligandos de tipo quelato, normalmente diiminas, en la estructura de estos productos, es clave para aumentar su estabilidad térmica. Los compuestos organometálicos de Pd(IV) son interesantes porque se han propuesto como intermedios en muchas de las reacciones más utilizadas en síntesis orgánica, tanto en formación de enlaces C–C como en activación C–H. Además, la ausencia en la bibliografía de complejos de Pd(IV) de tipo pincer aislados, nos supuso un incentivo.

En la **Sección III.1** se describen las reacciones de oxidación de los complejos de Pd(II) **III.A.X** con cloro y con bromo (Esquema 4), para dar los correspondientes **III.B.Cl** y **III.B.Br**, que son los primeros complejos de Pd(IV) de tipo pincer aislados y totalmente caracterizados. La reactividad de estos compuestos se centra en los procesos de eliminación reductora a los que dan lugar. Se aislaron los correspondiente productos orgánicos de acoplamiento C–X (X = Cl, Br), de manera cuantitativa y regioselectiva (Esquema 4).



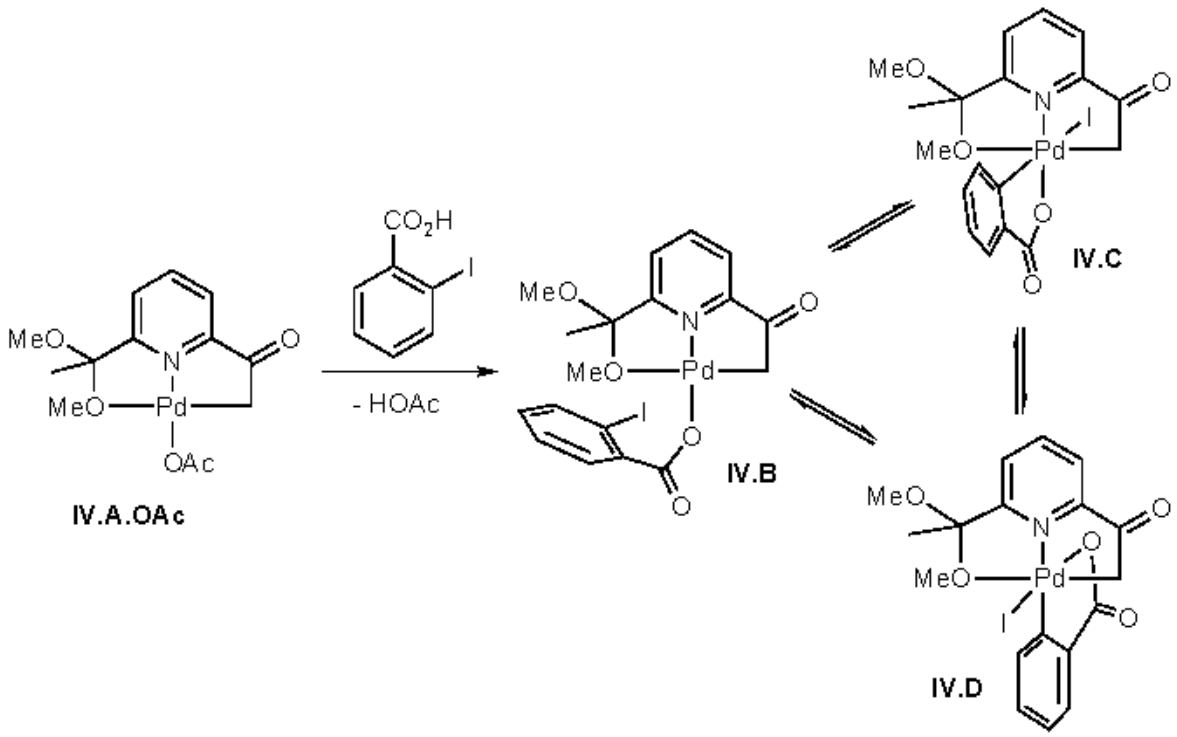
Esquema 4

La **Sección III.2** versa sobre la preparación del derivado iodado de Pd(IV) **III.B.I** (Esquema 4), por reacción del iodo complejo de Pd(II) **III.A.I** con yodo molecular. El haber aislado este producto y haber podido estudiar su estructura mediante difracción de RX, es un resultado digno de resaltar, teniendo en cuenta que están presentes tres ligandos ioduro, con carácter reductor, unidos a un catión metálico fuertemente oxidante. De hecho, es el complejo organometálico de Pd(IV) con mayor número de ligandos ioduro que se ha descrito. Además, el proceso de oxidación no es cuantitativo y da lugar a un equilibrio de especies Pd(II)/Pd(IV), que nos permitió obtener valores experimentales termodinámicos haciendo uso de la ecuación de van't Hoff. Del mismo modo que los derivados de cloro y bromo, se produce la eliminación reductora C–I, dando lugar cuantitativamente y regioselectivamente al producto **III.C.I** (Esquema 4).

Capítulo IV

Como consecuencia de la extraordinaria estabilidad de los complejos de Pd(IV) preparados, decidimos explorar la reactividad de nuestros complejos pincer de Pd(II) con otros agentes oxidantes. En primer lugar, decidimos aplicar la experiencia adquirida con la síntesis de los trihalocomplejos, a la preparación de intermedios propuestos en reacciones catalizadas por paladio. Dentro de estas reacciones, las de acoplamiento C–C son las más utilizadas y su importancia ha sido reconocida con la concesión del Premio Nobel de Química de 2010. Aunque el mecanismo de estas reacciones asume un ciclo catalítico donde participan especies de Pd(0) y Pd(II), el desarrollo de nuevos precatalizadores de Pd(II) con ligandos quelato o pincer, que mejoran la eficiencia de la reacción, determinó que algunos autores especularan sobre un posible ciclo catalítico Pd(II)/Pd(IV). Sin embargo, aunque algunos cálculos teóricos sugieren la posibilidad de este ciclo catalítico, la falta de pruebas experimentales definitivas dejan sin resolver uno de los principales problemas actuales en catálisis homogénea.

El estudio de una reacción de acoplamiento C–C de Heck comienza en la **Sección IV.1** con la investigación de la reacción de adición oxidante, que es la primera etapa del ciclo catalítico Pd(II)/Pd(IV). En el mecanismo clásico se describe la adición oxidante de un haluro de arilo a una especie de Pd(0) generándose un intermedio de Pd(II). La etapa semejante en un ciclo Pd(II)/Pd(IV) supondría la adición oxidante del haloareno al catalizador de Pd(II) dando lugar a un intermedio de Pd(IV). Puesto que este tipo de reacción no se había descrito experimentalmente, nos propusimos abordar su realización usando nuestros complejos pincer, como paso previo al estudio del proceso catalítico. Para ello, preparamos el acetato complejo de Pd(II) **IV.A.OAc** y como haloareno al ácido 2-iodobenzoico (Esquema 5). La elección del haluro de arilo no es trivial y además, es determinante para el éxito de la reacción. Elegimos un grupo carboxilo en la posición en *orto* al iodo por dos razones fundamentales: 1) la rápida reacción ácido/base acercaría el enlace Ar–I al metal facilitando la adición oxidante y 2) la formación de los dos enlaces daría lugar a un ligando quelato, que aumentaría la estabilidad del intermedio de Pd(IV), facilitando su aislamiento.



Esquema 5

De esta forma, por reacción del acetato complejo con ácido 2-iodobenzoico se obtienen dos isómeros en equilibrio (**IV.C** y **IV.D**, Esquema 5), que son los primeros complejos de Pd(IV) preparados por adición oxidante de un haloareno a un complejo de Pd(II).

Debido a que esta reacción se corresponde con la primera etapa de un ciclo catalítico Pd(II)/Pd(IV), estudiamos y probamos, por primera vez, que los complejos de Pd(IV) **IV.C** y **IV.D** son precatalizadores en reacciones de acoplamiento de tipo Heck. Para ello, hicimos reaccionar acrilato de metilo con ácido 2-iodobenzoico, en presencia de perclorato de plata y cantidades catalíticas de los complejos de Pd(IV), aislándose con buen rendimiento el producto esperado de acoplamiento C–C de tipo Heck, (*E*)-metil-2-carboxicinamato. Este resultado muestra la capacidad de los complejos de Pd(IV) para actuar como precatalizadores en esta reacción, pero no su operatividad en un ciclo catalítico Pd(II)/Pd(IV).

En la **Sección IV.2** llevamos a cabo un estudio exhaustivo de esta reacción catalítica, con el objetivo de elucidar su mecanismo. Para ello, utilizamos olefinas de distinta naturaleza y ampliamos el número de precatalizadores para la reacción (**IV.A.OClO$_3$**, **IV.A.OAc**, **IV.E**, Figura 2).

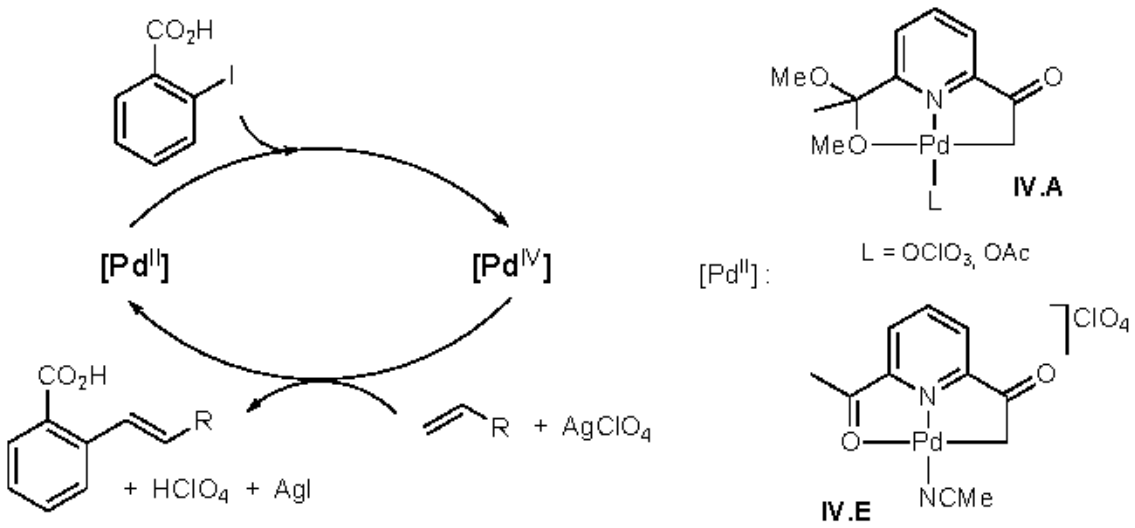


Figura 2

Investigamos la cinética de la reacción y realizamos una serie de tests (gotas de Hg, envenenamiento cuantitativo, dibencilo) para averiguar la naturaleza homogénea o heterogénea del catalizador. De este modo, descartamos la presencia de nanopartículas activas de paladio y complejos de Pd(0) en la mezcla de reacción. Finalmente, un estudio mediante espectroscopía

de masas (ESI-MS) nos permitió detectar intermedios de Pd(IV) en las reacciones catalizadas por los complejos **IV.A.OClO$_3$** y **IV.E**. Este resultado es especialmente novedoso, ya que supone la primera detección experimental de intermedios de Pd(IV) en una reacción de acoplamiento de tipo Heck.

Estas evidencias experimentales, que apoyan la existencia de un ciclo catalítico Pd(II)/Pd(IV) en una reacción de tipo Heck, no pueden ser generalizadas para otras reacciones de la misma naturaleza que, normalmente, se llevan a cabo a elevadas temperaturas, donde los intermedios de Pd(IV), caso de formarse, se descompondrían formando presumiblemente nanopartículas que catalizarían la reacción. Estas evidencias sólo prueban que es posible, bajo circunstancias muy determinadas, que opere un mecanismo Pd(II)/Pd(IV) en esta reacción de acoplamiento C–C.

Al igual que la investigación básica, la búsqueda de aplicaciones a la síntesis organometálica es uno de los principales objetivos de los investigadores que trabajan en este campo. En este sentido, el uso de complejos organometálicos como catalizadores en reacciones orgánicas se corresponde con la principal aplicación potencial de estos compuestos.

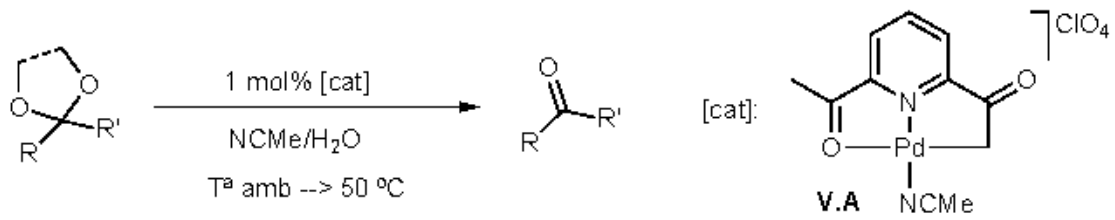
Capítulo V

Se describe la utilización de uno de los complejos de paladio que hemos preparado como catalizador en una de las reacciones más utilizadas en síntesis orgánica: *la hidrólisis de cetales y acetales*.

El uso de grupos protectores en síntesis orgánica está considerado como una de las reacciones para optimizar más importantes en procesos multietapa, teniendo un importante papel los grupos protectores de las funciones carbonilo (cetales y acetales). Por lo tanto, el estudio de nuevas metodologías para la hidrólisis de cetales y acetales, de una forma eficiente y selectiva, es extremadamente útil para la síntesis industrial de fármacos en química fina. Se han desarrollado muchos compuestos que hidrolizan eficientemente los grupos cetales y acetales en sustancias orgánicas sencillas. Sin embargo, la mayor parte de ellos presenta algunas limitaciones como: 1) no son generales para cetales y acetales de distinta naturaleza, 2) usan medios ácidos que limita su uso para sustratos sensibles a ácidos o 3) presentan reacciones secundarias con otros grupos protectores (THP, MOM).

Tras varios experimentos preliminares, determinamos que el complejo **V.A** (Esquema 6) es un buen catalizador para la desprotección de aldehídos y cetonas. Utilizando un 1% de

catalizador se obtienen buenos rendimientos para cetales y acetales, cíclicos, acíclicos, alifáticos y aromáticos. Además, la reacción catalítica no afecta a grupos funcionales sensibles a medios ácidos, así como a otros grupos protectores de alcoholes como THP y silil éteres.



Esquema 6

Debido a la elevada actividad, eficiencia y selectividad, y a la fácil preparación del catalizador, decidimos proteger estos resultados con una patente.

Capítulo VI

En este capítulo se incluye un resumen del trabajo que realicé durante mi estancia predoctoral en La Sapienza – Università di Roma (Italia), bajo la supervisión del Dr. Mauro Bassetti, perteneciente al Consiglio Nazionale della Ricerca. Durante tres meses llevé a cabo el estudio del mecanismo de la reacción de dimerización de alquinos terminales catalizada por un complejo dinuclear de rutenio. El estudio mecanístico se basó en la utilización de la cinética química como herramienta para determinar los parámetros de activación y la gráfica de Hammett de la etapa lenta del ciclo catalítico.

Todas las nuevas especies que se describen en esta memoria, han sido totalmente caracterizadas mediante espectroscopía de resonancia magnética nuclear, espectroscopía infrarroja, espectrometría de masas de alta resolución y análisis elemental. Además, se han determinado las estructuras cristalinas de alguno de los complejos preparados mediante difracción de RX. Aparte del trabajo de síntesis, se ha llevado a cabo un estudio riguroso del mecanismo de una reacción catalítica, mediante el uso de técnicas instrumentales y tests experimentales. De este trabajo se deriva la propuesta de un ciclo catalítico Pd(II)/Pd(IV) para una reacción de acoplamiento C–C de tipo Heck, que el autor de esta memoria considera como el resultado de mayor relevancia científica de esta tesis doctoral.

La producción científica a la que ha dado lugar esta tesis doctoral se resume en la participación en cuatro congresos nacionales e internacionales (3 pósteres + 1 comunicación

oral), la solicitud de una patente y la publicación de los resultados en estas revistas de elevado prestigio internacional:

- J. Vicente, A. Arcas, M.-D. Gálvez-López, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2008**, *27*, 1582.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista, P. G. Jones *Organometallics* **2010**, *29*, 3066.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Chem. Comm.* **2010**, *46*, 7253.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Inorg. Chem.* **2011**, *50*, 5339.
- J. Vicente, A. Arcas, F. Juliá-Hernández, D. Bautista *Angew. Chem. Int. Ed.* **2011**, *50*, 6896.
- F. Juliá-Hernández, A. Arcas, J. Vicente *Chem. Eur. J. Enviado.*
- F. Juliá-Hernández, A. Arcas, J. Vicente *Organometallics Enviado.*
- F. Juliá-Hernández, A. Arcas, J. Vicente *Manuscrito en preparación.*