Mechanisms of Cyclopalladation Reactions in Acetic Acid: Not So Simple One-Pot Processes

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The processes operating during the synthetic cyclopalladation reactions of imines in acetic acid have been studied from a kinetico-mechanistic point of view. These reactions include a fast initial coordination to the palladium through the N-donor atom of the imine, followed by the proper C–H bond activation to produce the acetato bridged dimeric species. At this point, the lability of the bridging acetato groups, the hydrolysis of the C–Pd bonds, and/or the hydrolysis of C=N *exo* bonds contribute to the generation of dark red polynuclear compounds. The processes occurring after the C–H activation have been followed kinetically, both from palladium acetate plus imine, and the synthetically pure isolated acetato dimers as starting materials. The kinetic and activation parameters have been found identical within experimental error whatever the starting material was ($k^{323} = 1.5 \times 10^{-4}$ s^{-1}; $\Delta H^{+} = 51$ kJ mol^{-1}; $\Delta S^{+} = -163$ JK^{-1} mol^{-1} $\Delta V^{+} = +19$ cm^3 mol^{-1} for the 4-ClC_6H_4–CH=N–CH_2–C_6H_5 imine derivative **1a**). Acidolysis of C–Pd bonds has been found to occur in these polynuclear species. When alternative monomeric $C_{benzylic}$–Pd bond-containing complexes are possible follow ups of the reactions produce them as final dead-end complexes ($k^{323} = 2.2 \times 10^{-5}$ s^{-1}; $\Delta H^{+} = 61$ kJ mol^{-1}; $\Delta S^{+} =$ JK^{-1} mol^{-1} $\Delta V^{+} \approx 0$ cm^3 cm^{-1} for the [2,4,6-$(CH_3)_3$]C_6H_2–CH=N–CH_2-[2-$(CH_3)C_6H_4$] imine derivative **3d**). The same study has been carried out with primary amines in order to check the validity of the data if C=N bond hydrolysis is taking place in the imine derivatives with *exo* C=N bonds. For complexes with similar type of metallacycles, the results agree reasonably well with the proposed mechanism [$k^{323} = 1.2 \cdot 10^{-4}$ s^{-1}, $\Delta H^{+} = 46$ kJ·mol^{-1}, $\Delta S^{+} = -180$ J·K^{-1}mol^{-1}, $\Delta V^{+} = -16$ cm^3·mol^{-1} for the polynuclear formation of the C_6H_5–CH_2–NH_2 derivative **4e**; $k^{323} = 3.0 \cdot 10^{-4}$ s^{-1}, $\Delta H^{+} = 55$ kJ·mol^{-1}, $\Delta S^{\ddagger} = -147$ J·K^{-1}mol^{-1}, $\Delta V^{+} = -24$ cm^3·mol^{-1} for the polynuclear formation of the C_6H_5–CH_2–N=CH–2,3,6-$(CH_3)_3C_6H_2$ derivative **2c**].

Introduction

Cyclometallation reactions were one of the first known examples of C–H bond activation and cyclometallated compounds of a wide variety of ligands (containing N, P, As, O, or S as heteroatoms) have been described.[1] The cyclopalladation of N-donor ligands has been extensively studied by a number of research groups, and this reaction has acquired great interest because of the applications of metallacycles in many areas including organic synthesis,[2] homogeneous catalysis,[3] the design of new metallomesogenes,[4] and antitumor drugs.[5] The factors that influence the ease and mode of cyclopalladation of N-donor ligands are not entirely understood, but in general the following trends are accepted: intramolecular electrophilic attack of "Pd^{2+}" at the carbon atom, strong tendency to form five-membered metallacycles, and preferential activation of aromatic versus benzylic C–H bonds.[1]

There are few studies on these reactions dealing with kinetico-mechanistic information for the cyclopalladation of N-donor ligands like tertiary amines,[6] imines,[7] 2-phenylpyridines,[8] or triamines.[9] For these reactions, a highly ordered transition state has been proposed, in which the leaving proton is accepted by a base. Recently, the formal relationship that may be established between the cyclometallation reaction and the protonation of σ M–C bonds of d^8 organometallic species has been pointed out, as well as the possible role of arenonium ions in both processes.[10]

Very little information is available about the nature of the species existing in these reaction solutions. It is generally assumed that cyclopalladated compounds maintain their dimeric structure in solution, but recently it has been shown by ^{1}H-NMR spectroscopy that compounds like [Pd(μ-Br){$C_6H_4CH(CH_3)NH_2$}]$_2$ and [Pd{1-CH_2-2-(CH=$NCH_2C_6H_4$)-3,5-$(CH_3)_2C_6H_2$}(CH_3COO)]$_2$ adopt mononuclear structures in acetone[11] and acetic acid respectively.[7a]

Following our research on the cyclopalladation of N-donor ligands[12] and the mechanisms operating on organometallic reactions involving the activation of C–H and C–X bonds,[13] we present, in this paper, the study of the process that occurs between imines and palladium acetate in an acetic acid solution, both from a kinetic and a synthetic point of view. The imines have been selected to allow comparison of the behaviour of *endo*- and *exo*-metallacycles containing $C_{arom.}$–Pd or $C_{benz.}$–Pd bonds. As an extension of this work, the action of palladium acetate on primary amines has also been investigated.

Results and Discussion

The processes taking place when imines ***a***, ***b***, ***c***, and ***d*** (Scheme 1) are treated stoichiometrically with palladium acetate in acetic acid have been studied both from a synthetic and from a kinetic point of view. Although the for-

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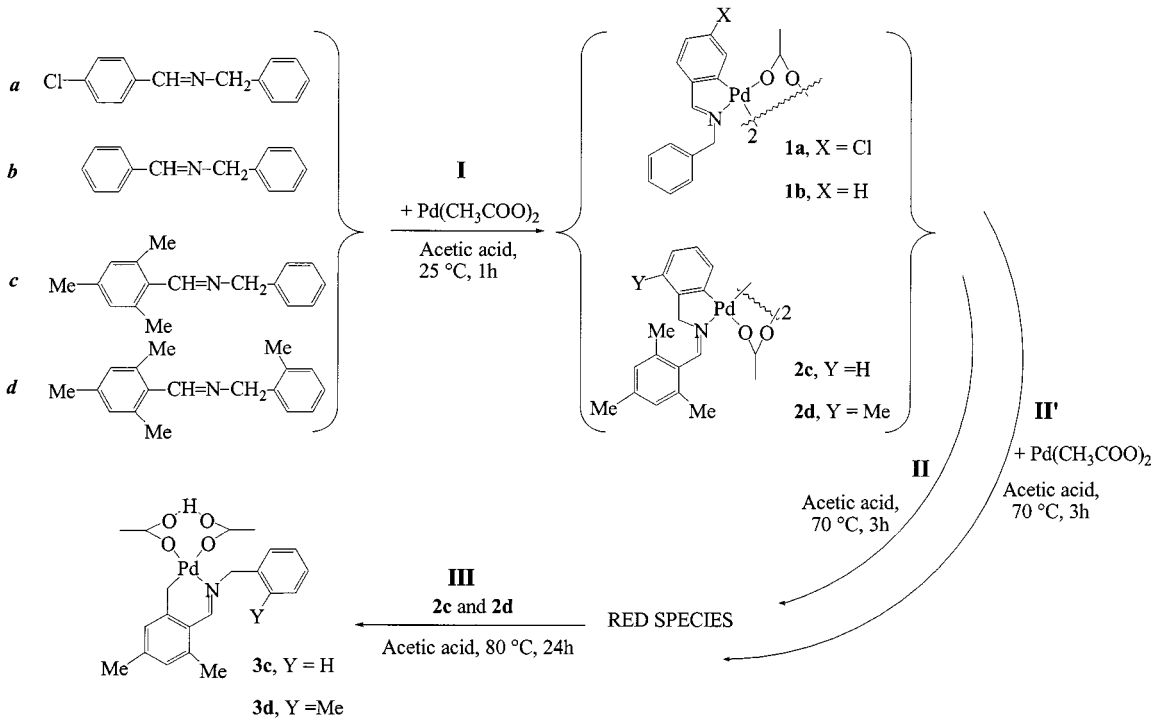
mation of cyclopalladated compounds is a well-established reaction, and even kinetico-mechanistic studies have been carried out by us[7] and other groups,[6] when the compounds are prepared in an acetic acid solution, important quantities of undefined material appear, and reduced yields are evident, compared with the reactions carried out in toluene (20% yield in acetic acid versus 60% in toluene for compounds **2c** and **2d**).[7a,12a] The available kinetic studies carried out in acetic acid also show the presence of further processes, once the main C−H electrophilic bond activation has taken place.[7a] Previous studies have indicated that the isolated acetato-bridged cyclopalladated complexes have significant differences when considered in acetic acid or in toluene. Furthermore, even though the nature of the complexes in solution is also dependent on the nature of the activated C−H bond (benzylic in **3c** and **3d**, versus aromatic in **2c** and **2d**), differences in behaviour for *endo*, **1a** and **1b**, versus *exo*, **2c** and **2d**, compounds are not so certain. In any case, it is clear that the lability of protonated bridging or terminal acetato groups plays a key role in the overall process.

Scheme 1 shows a simplified view of the reactivity involved in these cyclopalladation reactions. Discussion of Scheme 1 has to be carried out very cautiously. Any of the processes depicted (i.e. **I**, **II**, and **III**) does not necessarily have to be a single reaction; in fact, most of them have to be considered as rather complex reactions. Consequently, any rate constants and activation parameters discussed are ***apparent*** values that can only be considered as such, despite the fact that can be very informative about the equivalence of processes between different systems.

Examination of Scheme 1 gives a very good viewpoint of the cyclopalladation process. Reaction **I** takes place by the initial fast formation of a 1:1 coordination compound in stoichiometric conditions, followed by the proper C−H bond activation.[19] Kinetic measurements both in toluene and acetic acid are available at variable temperature and pressure, and the results have already been published.[7a]

The crude yellow acetato-bridged complexes isolated from the reaction **I**, **1a** and **1b**, are stable for days in the solid state, but when dissolved in acetic acid a deep red solution is formed; the process (**II**) is complete after 3 h at 70°C. Kinetic studies at variable temperature and pressure have been carried out. Table 1 collects the available data together with those for all the other processes depicted in Scheme 1. Despite the similar reactivity, the values determined for the volume of activation indicate a dramatic difference between the mechanism for the *endo*, **1a** and **1b**, and *exo*, **2c** and **2d**, complexes. Although in both cases an induction period exists, for the *exo* complexes this period is much better defined.

Where possible, spectroscopic and kinetic measurements for the initiation have been made (Table 1). If the reaction is carried out in the presence of palladium acetate (**II′**) the intensity of the red colour increases with its concentration, and the induction period decreases. The kinetic results agree with those of the experiments carried out in the absence of $Pd(CH_3COO)_2$, that is, the palladium acetate concentration does not affect the rate constant, only its extent. The deep red reaction mixture formed when the reaction was carried out with *exo* complexes, **2c** and **2d**, contains free aldehyde, as detected by ^{1}H-NMR spectroscopy. For the *endo* com-



Scheme 1. Reactivity involved in the cyclopalladation reactions of imines in acetic acid

Table 1. Available kinetic data for the processes depicted in Scheme 1. Apparent thermal activation parameters are obtained from 4−5 measures in a range of at least 35 degrees and apparent pressure activation parameters from 5−6 measures in a range of 1500 atm. Parameters indicated for process labeled as **I** + **II** correspond to the process following the C−H bond activation, i.e. process **II**, under synthetic conditions starting from imine plus palladium acetate mixtures

Imine[a]	Process	k^{323} s^{-1}	$\Delta H^{\neq}$ $kJ{\cdot}mol^{-1}$	$\Delta S^{\neq}$ $J{\cdot}K^{-1}mol^{-1}$	$\Delta V^{\neq}$ $cm^3{\cdot}mol^{-1}$
a	**I** + **II**	$1.5{\cdot}10^{-4}$	51	−163	+19
	II	$1.4{\cdot}10^{-4}$	id **I** + **II**	id **I** + **II**	
	II′[b]	$8.5{\cdot}10^{-5}$	id **I** + **II**	id **I** + **II**	
b	**I** + **II**	$1.7{\cdot}10^{-4}$	78	−74	+11
c	**II**	$3.0{\cdot}10^{-5}$	55	−147	−24
	III	$1.5{\cdot}10^{-5}$	70	−123	*ca.* 0
d	**I** + **II**	$1.0{\cdot}10^{-4}$	id **II**	id **II**	
	II	$9.7{\cdot}10^{-5}$	70	−108	−25
	II initiation[c]	$3.7{\cdot}10^{-3}$	66	−89	[d]
	I + II	$2.2{\cdot}10^{-5}$	61	−149	*ca.* 0

[a] Only compounds with the best spectroscopic handles are included. − [b] $[Pd(CH_3COO_2)_2]$ in the 5−15% range from that of the cyclometallated complex. − [c] Initial fast process corresponding to the appearance of aldehyde (see text). − [d] Reaction with too small spectroscopic changes to be measured.

plexes, **1a** and **1b**, the amount of aldehyde is less important, and appears after longer periods. Furthermore, practically no free or metallated amine is found by NMR spectroscopy, indicating that most of it remains coordinated to the palladium through the N atom. The presence of polynuclear species in the red reaction mixture has been detected by FAB and ion-spray (IS) mass-spectrometry. While mass spectra for the isolated yellow material (**1a**, **1b**, **2c**, and **2d**) indicate molecular peaks corresponding to the formulated dimer complexes, the isolated red material following process **II** has peaks at masses that correspond to species containing further acetato and palladium groups.

The IS mass spectrum of the red solid obtained from the reaction between palladium acetate and imine ***a*** shows peaks up to 1121, while the molecular weight of the dinuclear compound **1a** is 786. Furthermore, proton NMR spectroscopy of this red material shows an extremely complicated pattern in the 2.0 ppm zone, indicating that many different types of acetato ligands are present in the material, as should correspond to an undefined polynuclear compound. Further confirmation of our assumptions comes from the fact that in spite of pure dinuclear acetato bridged compounds usually being obtained in solid state after a purification process (recrystallization or column chromatography), the action of palladium acetate on 2-dimethylaminotoluene in acetic acid affords a trinuclear species, of general formula $[Pd_3(C-N)_2(\mu_2\text{-}O_2CCH_3)_4]$ (C−N≡metallated amine), as a mixture of *cis* and *trans* isomers [in relation to the $Pd_3(CH_3COO)_4$ moiety].[14] In addition, the formation of trinuclear species containing acetato bridges, isostructural to palladium acetate, has recently also been described for ligands containing C,S donor atoms.[15]

Process **I** + **II** corresponds, *de facto*, to the standard synthetic procedure in acetic acid. Under these conditions, besides cyclometallated complexes, the red coloured solution is always observed to some extent. Purification of the obtained product by column chromatography produces the final acetato-bridged dimer plus some quantities of an unidentified red material. The existence, in the acetic acid reaction medium, of palladium acetate and the final cyclometallated complex should enable the formation of polynuclear species according to reaction sequence **I** and **II′**. Kinetic measurements at variable temperature and pressure are available for this reaction sequence starting from imine and palladium acetate. Table 1 collects the data corresponding to the process that follows the C−H bond activation already described in previous studies.[7] The results agree with those obtained from the reactions carried out with the crude isolated yellow acetato dimers, **1a**, **1b**, **2c**, and **2d** (processes **II** and **II′**).

Figure 1 collects all the spectroscopic changes observed in the UV/Vis spectrum for the sequence **I** + **II**. For the reactions carried out with *exo* compounds, **2c** and **2d**, keeping these intense red solutions for 24 h at 80°C produces the light yellow *endo* monomeric complexes, **3c** and **3d**, as indicated by NMR experiments in deuterated acetic acid (process **III**).[7a] Kinetic measurements at variable temperature and pressure are available for this process starting from the isolated *exo* dimers, and these are also collected in Table 1. These *endo*, $C_{benz.}-Pd$ bond containing, complexes seem to be the dead-end of the whole process given their stability over very long periods in acetic acid.

The results, although difficult to interpret unequivocally, can be rationalized by taking into account the different stabilities in acid medium of the $C_{benz.}-Pd$ and $C_{arom.}-Pd$ bonds, as well as the reactivity of the labile acetato bridging groups. From the results presented, it is evident that, while the $C_{arom.}-Pd$ bond-containing complexes can be hydrolyzed in acetic acid, the stability of the metallacycles containing $C_{benz.}-Pd$ bond is much higher. This stability can be related both to the nature of the C−Pd bond, and to the final form of the complex in acetic acid (dimeric or polynuclear in the case of $C_{arom.}-Pd$ bond-containing complexes and monomeric for the $C_{benz.}-Pd$ bond-containing complexes). The presence of monomeric cyclometallated complexes containing $C_{benz.}-Pd$ bonds in acetic acid that do not evolve during long periods indicate that these are the most thermodynamically favourable compounds under these conditions. These results can be related with the ligand exchange reaction of N-donor ligands on cyclopalladated compounds. It has been shown that Pd^{II} effectively migrates to the ligand, forming the palladacycle less susceptible to acidolysis.[16]

As for the details of the reactivity, from the kinetic and activation parameters data, *endo* and *exo* cyclometallated $C_{arom.}-Pd$ bond-containing complexes present dramatic differences in their reaction mechanism. This can be attributed to the greater ease of Pd−C acidolysis of *exo*-metallacycles[16c] and the hydrolysis of the C=N imine bond, as seen by NMR spectroscopy. Given the fact that the reaction mixture contains "all the necessary ingredients", and that the cyclopalladated amine derivatives react with benzaldehydes to form imine *endo*-metallacycles (see below), long

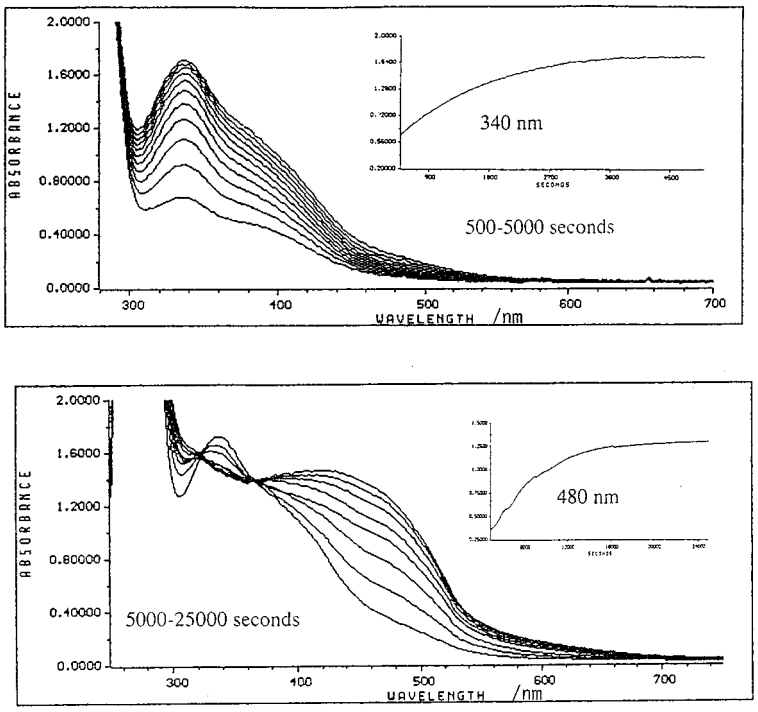
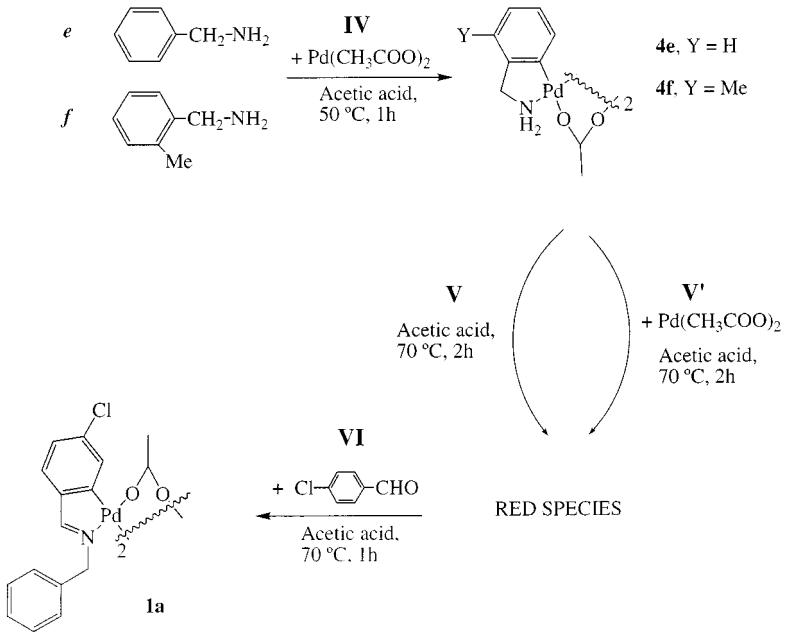


Figure 1. UV/Vis spectroscopic changes for the synthetic process, **I** + **II**, at 50°C between palladium acetate ($1\cdot10^{-3}$ M) and imine ***a*** ($1\cdot10^{-3}$ M) depicted in Scheme 1; above, metallation process (**I**); below, polynuclear formation process (**II**)

standing periods at high temperature of these red solutions produce the final dead-end monomeric *endo* $C_{benz.}-Pd$ bond-containing complex. On the other hand, the induction period for the *endo* metallacycle for the same process has to be the formation of palladium acetate via the initial $C_{arom.}-Pd$ *endo* bond hydrolysis, given the fact that the presence of palladium acetate seems to somehow reduce this induction period. From then on, the complex reaction to produce polynuclear red material (and a certain degree of decomposition) takes place with kinetic and activation parameters independent of the presence of palladium acetate in the reaction medium. The pressure activation parameters derived for the processes agree with this differentiation. While the activation volume for the polynuclear formation process for the ***a*** and ***b*** imines *endo* $C_{arom.}-Pd$ bond-containing complexes is positive, in spite of the extremely negative activation entropy, the value measured for the process that takes place for the *exo* $C_{arom.}-Pd$ bond-containing complexes is very negative. Kinetic factors seem to be dominant in the differentiation of these two processes as seen for the inverse cyclometallation reaction already studied.

In view of the interest of the processes labeled as **II** and **III** for **2c** and **2d**, the action of palladium acetate on primary amines has also been studied. It is generally accepted that primary amines are inert towards cyclometallation reactions, but they can undergo cyclopalladation if experimental conditions are appropriate. The action of $AgClO_4$ on coordination compounds $[PdCl_2L_2]$ (L=primary amine), or the action of palladium acetate on the amines in a 1:1 ratio leads to the cyclopalladation of primary amines with good yields. These results have been explained by the generation of coordinatively unsaturated species that experience the metallation.[11][17] The cyclopalladated derivative of benzylamine was prepared by refluxing a 1:1 mixture of palladium acetate and the amine in acetonitrile, as has been reported,[17e] and the cyclopalladation of the 2-methylbenzylamine was accomplished under the same reaction conditions. The dimeric compound obtained in this latter case $[Pd(CH_3COO)(3\text{-}CH_3C_6H_3CH_2NH_2)]_2$ (**4f**) was characterized by elemental analyses and NMR spectra. The monomeric triphenylphosphane complex $[PdBr(3\text{-}CH_3C_6H_3CH_2NH_2)(PPh_3)]$ (**5f**) was prepared by reaction of the acetate bridged derivative with LiBr and PPh_3 in acetone.

The action of palladium acetate on these primary amines in acetic acid was also studied; in this case the addition of deuterated pyridine to a deuterated chloroform solution of the compounds obtained, shows the formation of the $[Pd(CH_3COO)(C-N)([D_5]py)]$ (C−N ≡ ***e*** or ***f*** metallated amine, see Scheme 2) derivatives, indicating that the metallation of these ligands can take place even in acetic acid. The proton NMR spectra of the compounds obtained in absence of deuterated pyridine show, in addition to the signals of the dimeric derivatives, new signals at $\delta = 2.2-1.7$ suggesting that, under these reaction conditions, polynuclear acetato bridged complexes are also formed. This fact has been confirmed by mass spectra. The overall process depicted in Scheme 2 and its study from a kinetic point of view has also been carried out. Again, reaction **IV** takes place by the initial fast formation of the 1:1 coordination



Scheme 2. Reactivity involved in the cyclopalladation reactions of amines in acetic acid

compound in stoichiometric conditions, followed by the $C_{arom.}-H$ bond activation.

The metallation process has been studied kinetically in toluene solution at variable temperature and pressure. Table 2 collects the kinetic and thermal and pressure activation parameters for this process together with relevant comparative data; the results in solution agree with those obtained for the already published[7] metallation reactions. For the reactions studied in acetic acid solution, the activation parameters show important differences with respect to the systems already published. These observations can be explained by the fact that the metallation product obtained in acetic acid, although containing the palladacycle depicted in Scheme 2, does not correspond to that isolated according to literature procedures. As in the processes depicted in Scheme 1, the isolated solid dimer prepared according to the literature procedure is stable indefinitely, but when dissolved in acetic acid evolves to produce intense red coloured solutions. This reaction has been studied, both in neat acetic acid and in an acetic acid solution of palladium acetate, on the crude isolated acetato dimer (processes **V** and **V′** respectively). After an induction period, the formation of an intense red coloured solution takes place; the kinetic and activation parameters determined for this process are the same, within experimental error, in both cases and are characterized by extremely negative activation entropies and a negative volume of activation. Table 3 collects these data together with those for all the processes depicted in Scheme 2.

The induction period can be detected spectrophotometrically, although it implies very small absorbance changes; the kinetic and thermal activation parameters associated indicate dramatic changes with respect to the other processes involved in the overall reaction scheme. As seen in Table 3, the activation enthalpy is extremely large and the

Table 2. Kinetic and activation parameters for the cyclometallation reaction of palladium acetate with the amines ***e*** and ***f*** indicated in Scheme 2 in toluene and acetic acid solutions (process **IV**); literature data from the related imines ***c*** and ***d*** from Scheme 1 are also included.[7]

Ligand	Solvent	$10^4 k^{323}$ s^{-1}	ΔH^{+} $kJ \cdot mol^{-1}$	ΔS^{+} $J \cdot K^{-1} mol^{-1}$	ΔV^{+} $cm^3 \cdot mol^{-1}$
e	Toluene	2.6	73	−91	−16
	Acetic acid[a]	76	100	+3	−11
f	Toluene	2.5	55	−145	−20
c	Toluene	70	67	−100	−12
	Acetic acid	13[b]	49	−138	−13
d	Toluene	9.2	62	−120	−17
	Acetic acid	2.2[b]	69	−91	−13

[a] In acetic acid solution process **IV** cannot be completely separated from process **V**, consequently the kinetic and activation parameters indicated have a limited reliability (see text). – [b] Measured at 298 K.

Table 3. Available kinetic data for the processes depicted in Scheme 2. Apparent thermal activation parameters are obtained from 4−5 measures in a range of at least 35 degrees and apparent pressure activation parameters from 5−6 measures in a range of 1500 atm. Parameters indicated for process labeled as **IV + V** correspond to the process following the C−H bond activation, *i.e.* process **V**, under synthetic conditions starting from amine plus palladium acetate mixtures

Amine[a]	Process	k^{323} s^{-1}	ΔH^{+} $kJ \cdot mol^{-1}$	ΔS^{+} $J \cdot K^{-1} mol^{-1}$	ΔV^{+} $cm^3 \cdot mol^{-1}$
e	**IV + V**	$2.5 \cdot 10^{-4}$	82	−63	+14
	V initiation[b]	$3.4 \cdot 10^{-3}$	121	80	>>0
	V	$1.2 \cdot 10^{-4}$	46	−180	−16
	V′ initiation[b,c]	id **V** initiation[b]			
	V′[c]	id **V**			

[a] Only compounds with the best spectroscopic handles are included. – [b] Initial fast process (see text). – [c] $[Pd(CH_3COO_2)_2]$ in the 5−15% range from that of the cyclometallated complex.

value found for the activation entropy is very positive. As for the activation volume, an extremely large positive value is estimated from the experiments. Its determination has not been possible due to the fact that there is an important pressure retardation of the initiation process with small spectroscopic changes implied, and that the above mentioned process has a large pressure acceleration with important differences in the spectra. The presence of polynuclear species in the red reaction mixture is clearly indicated in solid state by mass spectrometry, as well as in solution (^{1}H-NMR spectroscopy). Peaks up to 757 are observed in the FAB mass spectrum of the red solid obtained from the reaction of palladium acetate and amine ***e***. The molecular weight of the dinuclear compound **4e** is 543. From gas chromatography analysis of the crude red solution small quantities of free amine are also detected. Under synthetic conditions in acetic acid solution (process **IV** + **V**) the final red coloured solution is always observed. Kinetic measurements have been carried out at variable temperature and pressure for the reaction following the C−H bond activation process; the results obtained for both thermal and pressure activation parameters and collected in Table 3. When *para*-chlorobenzaldehyde is added to the crude deep red solution in acetic acid, condensation with the amine takes place, producing the *endo* cyclometallated compound, **1a**, derived from the corresponding imine as detected by NMR spectroscopy.

The results from the data in Scheme 2 have to be interpreted together with those for the imine derivatives. It is noteworthy to indicate that the behaviour of the cyclometallated amine has to be directly related to the reactivity of the *exo* cyclometallated complexes, **2c** and **2d**, containing $C_{arom.}$−Pd bonds, once the initial C=N bond hydrolysis has taken place (see above). The fact that formation of an intense red coloured solution is observed, both in synthetic conditions in acetic acid and by further treatment of the isolated acetato dimers in neat acetic acid or acetic acid solutions of palladium acetate, is a clear indication that the reactivity is related to the acidolysis of the $C_{arom.}$−Pd bond in the complexes. Again mass spectra indicate that important amounts of polynuclear species are present in the isolated red material. Nevertheless, even in these intense red polynuclear containing solutions, the presence of cyclometallated complexes is always detected, no full decomposition of the cyclopalladated compound is taking place.

Reaction of these red solutions with the corresponding aldehyde produces solutions where the *endo* cyclometallated complex **1a**, already described, is detected. We assume that the presence of the free amine in the polynuclear material solutions allows for the amine-aldehyde condensation;[20] thereafter the cyclometallation process, already described for the imine derivatives, takes place. As for the kinetic and activation parameters measured, an interesting fact is that those related to reaction **V** are in perfect agreement with those measured for the appearance of the polynuclear-containing red solutions for the reactions of the *exo* imine derivative complexes, **II**. In both cases, an initiation reaction is detected, while for the *exo* imine complexes it has been proven to be partly due to the hydrolysis reaction of the C=N bond, for compounds **4e** and **4f** this reaction has to be related solely to the hydrolysis of the main $C_{arom.}$−Pd bond. It is also interesting to note that, although in the presence of palladium acetate in the acetic acid solution medium this initiation also exists, it involves smaller spectral changes. It seems evident that the initiation process in this reaction needs the presence of $Pd(CH_3COO)_2$ in order to start the formation of the red polynuclear material. In this respect, the values measured for the activation parameters (specially the activation volume) for the synthetic process **IV** + **V**, have to be looked into more carefully. Given the fact that the $C_{arom.}$−H bond activation of the amines (process **IV**) is much slower (see Table 2) than the fast initiation process of reaction **V**, detected when the isolated acetato dimer **4e** is dissolved in acetic acid (see Table 3), the values determined for the polynuclear formation process starting from amine and palladium acetate mixtures, probably also contain a contribution from the C−H bond activation reaction, **IV**.

Conclusions

In summary, our mechanistic studies have shown that the reaction between imines and palladium acetate, in acetic acid solution, is a rather complex process in which several different reactions, such as acidolysis of Pd−C and C=N bonds, and substitution on the acetato bridging positions take place. It has also been found that cyclopalladated amine compounds react with benzaldehydes to afford the corresponding metallated imines in the *endo* form. Even the structures generally assumed for all these complexes are not so simple and they strongly depend on the reaction conditions. Under smooth conditions (25°C, 1 h), dimeric species containing five-membered metallacycles in *endo* (**1a** and **1b**) and *exo* (**2c** and **2d**) conformations, are formed and can be isolated as yellow solids in good yields. Longer reaction periods or higher temperatures induce the formation of polynuclear red materials due to the reactivity of the acetato bridging groups, as well as the reactivity of the C−Pd and C=N bonds. Obviously these more drastic reaction conditions favour the formation of the more thermodynamically stable metallacyclic species (*endo* six-membered monomeric cycles versus *exo* five-membered dimeric cycles, for ligands ***c*** and ***d***). In any case, the reaction mixture contains polynuclear species that can be detected, both in solution by NMR spectroscopy and in solid state by mass spectrometry. The cyclometallation of amines ***e*** and ***f*** in acetic acid has also been accomplished for the first time; in an analogous way, dimeric cyclopalladated compounds are initially formed, but the existence of dynamic processes affords some final polynuclear species.

Deeper interpretation of the kinetic and activation data available would be speculative at this point, given the multitude of steps taking place in any of the processes depicted in the reaction schemes. Further detailed studies for some of these systems are currently under way in order to establish a better kinetic understanding.

Experimental Section

General: ^{1}H- and ^{31}P{^{1}H}-NMR spectra were recorded on a Varian XL-200 (200 MHz) or Bruker 250 DRX (101.25 MHz) spectrometer. Chemical shifts (in ppm) are relative to $SiMe_4$ for ^{1}H and to 85% H_3PO_4 for ^{31}P spectra. The solvents used were $CDCl_3$ for ^{1}H spectra and $CHCl_3$ for ^{31}P spectra. − IR spectra were recorded as KBr disks on a Nicolet 520 FT-IR spectrometer. − GC analyses were performed on a Hewlett-Packard 5890 Series II gas chromatograph (50-m Ultra 2 capillary column 5% phenylmethylsilicone and 95% dimethylsilicone) with a FID detector. − Microanalyses were performed by the Institut de Química Bio-Orgànica de Barcelona (CSIC) and by the Serveis Científico-Tècnics de la Universitat de Barcelona. − Mass spectra (FAB and IS) were recorded on a Micromass VG-Quattro spectrometer; the samples were introduced in a matrix of 2-nitrobenzyl alcohol for FAB spectra and a mixture of water/acetonitrile was used as eluent for ion-spray spectra. − Imines **a**−**d** and cyclopalladated compounds **1a**, **1b**, **2c**, **2d**, and **4e** were prepared according to literature procedures.[12a,17e,18]

[Pd(CH$_3$COO)$_2$(4-ClC$_6$H$_4$CH=NCH$_2$C$_6$H$_5$)$_2$]: 0.100 g ($0.45\cdot10^{-3}$ mol) of palladium acetate and 0.21 g of **a** ($0.90\cdot10^{-3}$ mol) were dissolved in 10 cm^3 of toluene and stirred at room temperature for 2 hours, affording a pale yellow precipitate. The solid was filtered off and washed successively with toluene and diethyl ether, and dried under reduced pressure. Yield: 0.24 g (80%). − $C_{32}H_{30}Cl_2N_2O_4Pd$ (683.91): calcd. C 56.22, H 4.42, N 4.10; found C 56.26, H 4.48, N 4.38. − ^{1}H NMR: δ = 9.06 (br. s, 1 H, C*H*=N), 7.70−7.10 (m, 9 H, aromatic), 5.39 (s, 2 H, CH_2N), 1.60 (s, 3 H,CH_3).

Synthesis of 1a: 0.080 g of **4e** ($0.15\cdot10^{-3}$ mol) and 0.082 g of 4-chlorobenzaldehyde ($0.60\cdot10^{-3}$ mol) were treated with 5 cm^3 of acetic acid at 75°C overnight. The solution was filtered over celite, and the solution was concentrated under reduced pressure. After addition of diethyl ether, a yellow solid was precipitated. The solid **1a** was filtered off and washed successively with hexane and diethyl ether, and dried in vacuo.

[Pd(CH$_3$COO)(3-CH$_3$C$_6$H$_3$CH$_2$NH$_2$)]$_2$ (4f): 0.3 g ($0.25\cdot10^{-3}$ mol) of 2-methylbenzylamine, ***f***, were treated with palladium acetate ($0.25\cdot10^{-3}$ mol, 0.55 g) in acetonitrile at reflux for 4 h and then filtered. The solution was concentrated in vacuo, and the solid, obtained after addition of diethyl ether was recrystallised from chloroform/diethyl ether to obtain **4f** in 60% yield (0.4 g). Anal. [found (calcd. for $C_{20}H_{26}N_2O_4Pd_2$ (571.24): C 42.3 (42.05), H 4.7 (4.59), N 5.0 (4.90)%. − ^{1}H NMR: δ = 7.25 (m, 1 H, aromatic), 6.80 (br m, 2 H, aromatic), 4.00 (br m, 2 H), 3.05 (br. s, 2 H), 2.05 (br. s, 6 H, CH_3−C$_6$H$_3$, CH_3COO). ^{1}H NMR (**4f**+[D$_5$]py): δ = 7.15 (m, 1 H, aromatic), 7.05 (br m, 1 H, aromatic), 6.0 (br d, 1 H, aromatic), 4.62 (br. s, 2 H, NH_2), 4.42 (s, 2 H, CH_2N), 2.26 (s, 3 H, CH_3), 1.98 (s, 3 H, CH_3COO).

[PdBr(3-MeC$_6$H$_3$CH$_2$NH$_2$)(PPh$_3$)] (5f): 0.15 g ($0.25\cdot10^{-3}$ mol) of **4f** were treated with PPh_3 ($0.50\cdot10^{-3}$ mol, 0.14 g) and LiBr ($0.5\cdot10^{-3}$ mol, 0.046 g) in acetone at room temperature for 45 min and then filtered. The solution was concentrated in vacuo, and the solid, obtained after addition of diethyl ether was recrystallized from chloroform to obtain **5f** in 80% yield (0.23 g). − $C_{26}H_{25}BrNPPd$ (568.77): calcd. C 54.91, H 4.43, N 2.46; found C 54.5, H 4.5, N 2.60. − ^{1}H NMR: δ = 7.90−7.70 (m, 6 H, aromatic),7.60 7.40 (m, 9 H, aromatic), 6.75 (d, 7.2 Hz, 1 H, aromatic), 6.46 (t, 7.2 Hz, 1 H, aromatic), 6.36 (br t, 1 H, aromatic), 4.46 (s, 2 H, CH_2N), 4.05 (br. s, 2 H, NH_2), 2.35 (s, 3 H, CH_3). − ^{31}P{^{1}H} NMR: δ = 41.5 (s).

Kinetics: The reactions at atmospheric pressure were followed by UV/Vis spectroscopy in the full 750−300 nm range on a HP8542A instrument equipped with a multicell transport, thermostated (±0.1°C) with a circulation bath. Observed rate constants were derived from the absorbance versus time traces at the wavelengths where a maximum increase or decrease of absorbance was observed. The general kinetic technique is that previously described.[13] The concentration range for the different compounds used in this work is the same as that in previous papers;[7] no dependence on the different concentrations has been found for any of the rate constants in the $0.7-1.3\cdot10^{-3}$ M range. For runs at high pressure, a previously described pressurizing system and high pressure cell were used.[7][13] In these cases, the absorbance versus time traces were recorded on a J&M TIDAS instrument. Rate constants were derived from exponential least-square fitting by the standard routines. Least-square errors for the rate constants were always in the range of 10−15% of the calculated value. All post-run fittings to rate laws were done by standard, commercially available fitting programmes.

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[19] Formation of *bis*-coordination complexes, $[Pd(CH_3COO)_2(imine)_2]$, has also been achieved by precipitation from toluene solution when a 1:2 Pd/imine ratio is used. in addition, further treatment of $[Pd(CH_3COO)_2(\boldsymbol{a})_2]$ in acetic acid for 3 h at 70 °C produces mainly mono-cyclometallated acetato dimer plus free imine.
[20] The direct condensation of ***e*** plus *p*-clorobenzaldehyde in acetic acid yields quantitatively imine ***a***. In addition, after 3 hours in refluxing acetic acid only a 3% of decomposition of imine ***a*** is observed as monitored by GC chromatography.

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