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Variable-Temperature and -Pressure Kinetics and Mechanism of the Cyclopalladation Reaction of Imines in Aprotic Solvent

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The cyclometalation reactions of benzylidenebenzylamines, -anilines, and -propylamine with palladium acetate have been studied in toluene solution. The cyclometalated compounds are formed *via* C−H electrophilic bond activation to produce different types of metallacycles, depending upon the polyfunctional nature of the ligand selected. If a five-membered *endo* metallacycle is possible, it is formed *via* aromatic C−H bond activation. Formation of a five-membered *exo* metallacycle only takes place when *endo* cyclometalation requires the formation of a six-membered compound *via* aliphatic C−H bond activation or when the steric hindrance affects the planarity of the imine in an important way. The activation of aliphatic C−H bonds has been achieved for *endo* six-membered metallacycles only when the alternative aromatic C−H bond activation would produce a four-membered *exo* compound; no activation of aliphatic C−H bonds to form *exo* five-membered complexes has been observed. The reactions have been monitored kinetically at different temperatures and pressures in order to establish the mechanism through which these spontaneous reactions occur. Three different sets of activation parameters are apparent from the results obtained: those related to the benzylamines and propylamine ($\Delta H^{\ddagger} = +45/+67$ kJ mol^{-1}, $\Delta S^{\ddagger} = -100/-180$ J K^{-1} mol^{-1}, $\Delta V^{\ddagger} = -11/-17$ cm^3 mol^{-1}), those related to the aniline derivatives ($\Delta H^{\ddagger} = +66/+75$ kJ mol^{-1}, $\Delta S^{\ddagger} = -96/-123$ J K^{-1} mol^{-1}, $\Delta V^{\ddagger} = -21/-25$ cm^3 mol^{-1}), and finally those related to the imines producing aliphatic bond activation ($\Delta H^{\ddagger} = +48/+49$ kJ mol^{-1}, $\Delta S^{\ddagger} = -167/-177$ J K^{-1} mol^{-1}, $\Delta V^{\ddagger} = -20/-24$ cm^3 mol^{-1}). The results are interpreted as the formation of a highly ordered four-center transition state, involving the C−H and Pd−O(acetato) bonds, which is found to be very sensitive to the flexibility and steric hindrance of the imine ligands and very insensitive to electronic changes of the C−H bonds.

Introduction

Cyclometalation reactions on Pd(II) complexes have been throughly studied by a number of research groups.[1] The synthesis of cyclopalladated complexes is a field of great interest as a consequence of their applications, for example, in organic synthesis[2] or in the design of new metallomesogenes[3] or antitumor drugs.[4] Optically active cyclopalladated derivatives have also been used for the enantiomeric excess determination[5] and optical resolution of amines and phosphines.[6]

The number of these studies dealing with kinetic−mechanistic information is limited.[7] Very little information is available about the nature of the species existing in these reaction solutions; even the nature of the starting material, palladium acetate, is rather unclear.[8] Although it is generally assumed that cyclopalladated compounds maintain their dimeric structure in solution, it has been shown recently that acetone is able to break the bridge of the cyclopalladated complex $[Pd(\mu\text{-}Br)(C_6H_4CH(Me)NH_2)]_2$, producing mononuclear species.[9]

Our interests have been centered in studies of this type of reaction on iminic ligands[10] as well as in the mechanisms operating in organometallic reactions involving the activation of C−H bonds on Pt(II) and

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[1] (a) Bruce, M. I. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 73. (b) Newkome, G. R.; Puckett, W. E.; Gupta, W. K.; Kiefer, G. E. *Chem. Rev.* **1986**, *86*, 451. (c) Omae, I. *Coord. Chem. Rev.* **1988**, *83*, 137. (d) Dunina, V. V.; Zalevskaya, O. A.; Potatov, V. M. *Russ. Chem. Rev. (Engl. Transl.)* **1988**, *57*, 250. (e) Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403.

[2] (a) Ryabov, A. D. *Synthesis* **1985**, 233. (b) Pfeffer, M. *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 567.

[3] Thompson, N. J.; Serrano, J. L.; Baena, M. J.; Espinet, P. *Chem. Eur. J.* **1996**, *2*, 214.

[4] (a) Navarro-Ranninger, C.; López-Solera, I.; Pérez, J. M.; Masaguer, J. R.; Alonso, C. *Appl. Organomet. Chem.* **1993**, *7*, 57. (b) Navarro-Ranninger, C.; López-Solera, I.; González, V. M.; Pérez, J. M.; Alvarez-Valdés, A.; Martín, A.; Raithby, P. R.; Masaguer, J. R.; Alonso, C. *Inorg. Chem.* **1996**, *35*, 5181.

[5] (a) Chooi, S. Y. M.; Leung, P. H.; Lim, C. C.; Mok, K. F.; Quek, G. H.; Sim, K. Y.; Tan, M. K. *Tetrahedron: Asymmetry* **1992**, *3*, 529. (b) Kyba, E. P.; Rines, S. P. *J. Org. Chem.* **1982**, *47*, 4800. (c) Albert, J.; Granell, J.; Muller, G.; Sainz, D.; Font-Bardia, M.; Solans, X. *Tetrahedron: Asymmetry* **1995**, *6*, 325.

[6] (a) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743. (b) Gabbitas, N.; Salem, G.; Sterns, M.; Willis, A. C. *J. Chem. Soc., Dalton Trans.* **1993**, 3271. (c) Chooi, S. Y. M.; Siah, S. Y.; Leung, P. H.; Mok, K. F. *Inorg. Chem.* **1993**, *32*, 4812. (d) Gladiali, S.; Dore, A.; Fabbri, D.; De Lucchi, O.; Manassero, M. *Tetrahedron: Asymmetry* **1994**, *5*, 511. (e) Pabel, M.; Willis, A. C.; Wild, S. B. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1835. (f) Barclay, C. E.; Deeble, G.; Doyle, R. J.; Elix, S. A.; Salem, G.; Jones, T. L.; Wild, S. B.; Willis, A. C. *J. Chem. Soc., Dalton Trans.* **1995**, 57.

[7] (a) Ryabov, A. D.; Sakodinskaya, I. K.; Yatsimirski, A. K. *J. Chem. Soc., Dalton Trans.* **1985**, 2629. (b) Ryabov, A. D.; Yatsimirski, A. K. *Inorg. Chem.* **1984**, *23*, 789. (c) Ryabov, A. D. *Inorg. Chem.* **1987**, *26*, 1252.

[8] Romm, I. P.; Kravtsova, S. V.; Perepelkova, T. I.; Petrov, E. S.; Kalinovski, I. O.; Buslaeva, T. M. *Russ. J. Coord. Chem. (Engl. Transl.)* **1995**, *21*, 740.

[9] Vicente, J.; Saura-Llamas, I.; Jones, P. G. *J. Chem. Soc., Dalton Trans.* **1993**, 3619.

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dinuclear Rh(II) complexes.[11] The final goal of these investigations is the study of the importance of the relative influence of steric and electronic factors that could tune the reactivity and thermodynamic preferences of the reactions involved in different processes.[12]

$$\text{palladium acetate} + \underset{\mathbf{X}}{\mathrm{RC_6H_4CH{=}NR'H}} \rightarrow \underset{\mathbf{1x},\ endo}{[\mathrm{Pd}(\mu\text{-}\mathrm{CH_3CO_2})(\mathrm{RC_6H_3CH{=}NR'H})]_2} + \underset{\mathbf{2x},\ exo}{[\mathrm{Pd}(\mu\text{-}\mathrm{CH_3CO_2})(\mathrm{R'N{=}CHC_6H_4R})]_2}$$

In this paper we report the preparation and kinetic study of the influence of temperature and pressure on the reaction of cyclometalation of a wide variety of imines, **X** (Chart 1), by palladium acetate. The imines are suitable ligands to study cyclometalation reactions, since they can undergo metalation on different carbon atoms (polyfunctional ligands); consequently, they have been selected to allow comparison of the metalation of aromatic *versus* aliphatic carbon atoms. The electronic and steric influence of the substituents in the process and the importance of the size (five- or six-membered) and nature of the metallacycle formed (*endo*, **1x**, *versus exo*, **2x**; see above)[13] have also been looked into. The reactions have been carried out in toluene, a poor coordinating solvent, to ensure the existence of the dimeric forms of both starting material and cyclometalated final complexes. The important differences in kinetic, and thermal and pressure activation parameters detected are associated with the flexibility of the iminic ligands and to the formation of an initial species that produces a lag time in the increase of the absorbance accompanying the cyclometalation reaction.

Results and Discussion

Compounds. The reaction of palladium acetate with imines **A**–**N** (Chart 1) in toluene at 60 °C was studied. When this reaction was carried out with imines **A**–**F**, the *endo* five-membered metallacycles **1a**–**f** were obtained, by metalation of the $C_{aromatic}$–H bond (Scheme 1); these compounds have a dinuclear acetato-bridged structure. The presence, on the aromatic ring to be metalated, of substituents with important differences in their electronic characteristics does not seem to affect the process. In contrast, the influence of the steric effects in the process is clearly observed. Thus, although imine **E** could afford two different *endo* five-membered metallacycles, under the experimental conditions studied only the metalation of the less hindered $C_{aromatic}$–H bond was achieved.

Benzylidenebenzylamines **I**, **J**, and **L** can undergo the metalation on different aromatic carbon atoms to afford five-membered *endo* or *exo* metallacycles; in all cases the *endo* metallacycles have been selectively obtained. These results confirm the strong tendency of these N-donor ligands to form endocyclic derivatives.[10,14] Again, although imine **L**, containing a nitro substituent, could afford two different five-membered *endo* metallacycles (similarly to imine **E**), only metalation of the less hindered bond has been observed. The cyclopalladation reaction of imine **K** produced a reaction mixture with a very complex ^{1}H NMR spectrum. Reaction of the solid thus obtained with PPh_3 and LiBr affords the mononuclear compounds [Pd(*C*–*N*)Br(PPh_3)] which can be separated and identified as the *endo* and *exo* palladacycles **3k** and **4k**, respectively (Scheme 2). Formation of the exocyclic compound with this imine can be explained by the presence of a nitro group in the 2-position of the benzylidenic ring that hinders a planar disposition of the iminic moiety and this aromatic ring. Consequently, the formation of the four-center transition state (see below) leading to compound **1k** is less favored and the *exo* complex **2k** is also obtained. Even so, the *endo* compound, **1k**, can be obtained in much better yields when the reaction is performed under more severe conditions or in protic solvent.

Imines **M** and **N** can produce both five-membered *exo* metallacycles by activation of a $C_{aromatic}$–H bond and six-membered *endo* metallacycles by activation of a $C_{aliphatic}$–H bond. Although it is widely accepted that a strong tendency exists to form five-membered metallacycles *via* preferential activation of aromatic over aliphatic C–H bonds,[1] some exceptions are known.[14b,15] Under the reaction conditions of this work, the five-membered *exo* metallacycles **2m,n** are selectively obtained (Scheme 3). The six-membered *endo* metallacycles produced by activation of a $C_{aliphatic}$–H bond were only obtained from imines **G** and **H** (Scheme 4). Activation of a $C_{aromatic}$–H bond would form, in these cases, unusual four-membered metallacycles.[1]

The previously described compounds **1b**,**f**,**g**,**i**,**j** and **2m**,**n** had been characterized by comparison of their ^{1}H NMR spectra with those published.[10b,e,14] The metalation compounds of imines **G**, **M**, and **N** have already been described, but their dimeric acetato-bridged compounds were not characterized.[10b,14b]

All new compounds were characterized by elemental analysis, IR, and ^{1}H NMR. The acetato bands appear at *ca.* 1580 and 1420 cm^{-1} in the IR spectra of compounds **1x** and **2x**, indicating that the ligand is in a bridging position.[16] In the ^{1}H NMR spectra, the acetato CH_3 signal appears as a singlet, in accord with a *trans*

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[10] (a) Albert, J.; Ceder, R. M.; Gómez, M.; Granell, J.; Sales, J.; Solans, X. *Organometallics* **1990**, *9*, 1405. (b) Albert, J.; Ceder, R. M.; Gómez, M.; Granell, J.; Sales, J. *Organometallics* **1992**, *11*, 1536. (c) Albert, J.; Granell, J.; Moragas, R.; Sales, J.; Font-Bardia, M.; Solans, X. *J. Organomet. Chem.* **1995**, *494*, 95. (d) Albert, J.; Granell, J.; Sales, J.; Font-Bardia, M.; Solans, X. *Organometallics* **1995**, *14*, 1393. (e) Granell, J.; Sainz, D.; Sales, J.; Solans, X.; Font-Altaba, M. *J. Chem. Soc., Dalton Trans.* **1986**, 1785.

[11] (a) Crespo, M.; Martinez, M.; Sales, J. *Organometallics* **1992**, *11*, 1288. (b) Crespo, M.; Martinez, M.; Sales, J. *Organometallics* **1993**, *12*, 4297. (c) González, G.; Lahuerta, P.; Martinez, M.; Sanau, M.; Peris, E. *J. Chem. Soc., Dalton Trans.* **1994**, 545. (d) Estevan, F.; Lahuerta, P.; Peris, E.; Ubeda, M. A.; García-Granda, S.; Gómez-Beltrán, F.; Pérez Carreño, E.; González, G.; Martinez, M. *Inorg. Chim. Acta* **1994**, *218*, 189. (e) Estevan, F.; González, G.; Lahuerta, P.; Martinez, M.; Peris, E.; van Eldik, R. *J. Chem. Soc., Dalton Trans.* **1996**, 1045.

[12] (a) Crespo, M.; Martinez, M.; Sales, J. *J. Chem. Soc., Chem. Commun.* **1992**, 822. (b) Schmülling, M.; Ryabov, A. D.; van Eldik, R. *J. Chem. Soc., Chem. Commun.* **1992**, 1609. (c) González, G.; Moullet, B.; Martinez, M.; Merbach, A. E. *Inorg. Chem.* **1994**, *33*, 2330. (d) González, G.; Martinez, M.; Rodriguez, E. *J. Chem. Soc., Dalton Trans.* **1995**, 891.

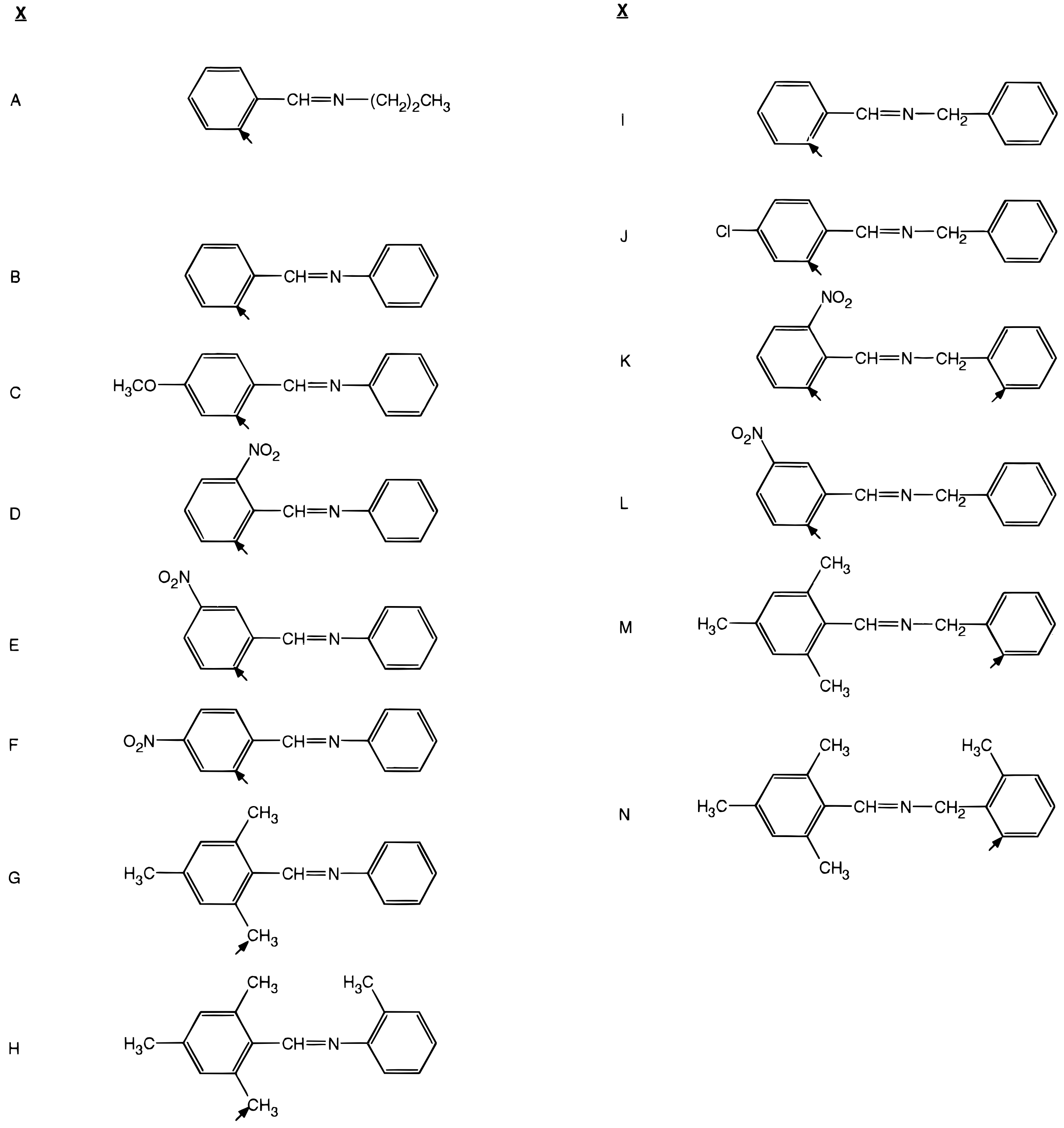
[13] An imine cyclometalated compound is considered endocyclic when the C=N bond is contained in the metallacycle.

[14] Albert, J.; Granell, J.; Sales, J. *J. Organomet. Chem.* **1984**, *273*, 393. (b) Albert, J.; Granell, J.; Sales, J.; Solans, X.; Font, M. *Organometallics* **1986**, *5*, 2567.

[15] (a) Alsters, P. L.; Engel, P. F.; Hogerheide, M. P.; Copjin, M.; Spek, A. L.; van Koten, G. *Organometallics* **1993**, *12*, 1831. (b) De Munno, G.; Ghedini, M.; Neve, F. *Inorg. Chim. Acta* **1995**, *239*, 155.

[16] Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 3rd ed.; Wiley: New York, 1978; p 232.

Chart 1[a]



[a] Arrows indicate the activated position.

arrangement of the C−N ligands relative to the $\{Pd_2(\mu\text{-}O_2CCH_3)_2\}$ fragment. The signal corresponding to the CH_2 protons of the benzylamine derivatives appears as two doublets (spin system AB), as expected for a dimeric acetato-bridged open-book structure (folded), already found by X-ray diffraction studies for some cyclopalladated acetato-bridged dimers.[17] The aromatic and methinic proton signals for the ^1H NMR spectra of these compounds show that all imines, except **K**, afford selectively the *endo* metallacyclic complexes. The proton NMR spectrum of the solid obtained after reaction of this imine and palladium acetate is very complex, and its reaction with PPh_3 was studied in order to determine its nature (Scheme 2). The aromatic region in the proton NMR spectra of the derived compounds **3k** and **4k** (that could be separated as pure solids by their different solubilities in acetone and dichloromethane), provides conclusive evidence of the palladation position, allowing the identification of these complexes as the *endo* and *exo* metallacycles, respectively. The aromatic protons of the palladated ring in both compounds appear shifted to high field, indicating a *cis* arrangement of the

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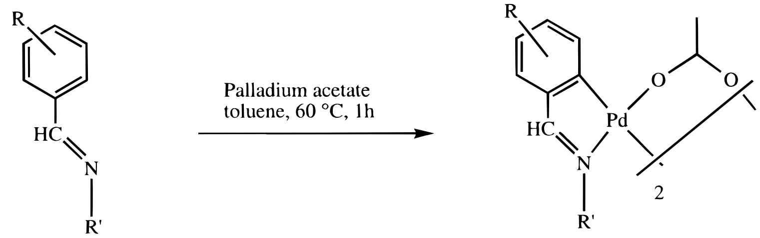
[17] (a) Albinati, A.; Pregosin, P. S.; Ruedi, R. *Helv. Chim. Acta* **1985**, *68*, 2046. (b) Selbin, J.; Abboud, K.; Watkins, S. F.; Gutiérrez, M. A.; Fronczek, F. R. *J. Organomet. Chem.* **1983**, *241*, 259. (c) Balavoine, G.; Clinet, J. C.; Zerbib, P.; Boubeukur, K. *J. Organomet. Chem.* **1990**, *389*, 259. (d) García-Ruano, J. L.; López-Solera, I.; Massaguer, J. R.; Navarro-Ranninger, C.; Rodríguez, J. H.; Martínez-Carrera, S. *Organometallics* **1992**, *11*, 3013.

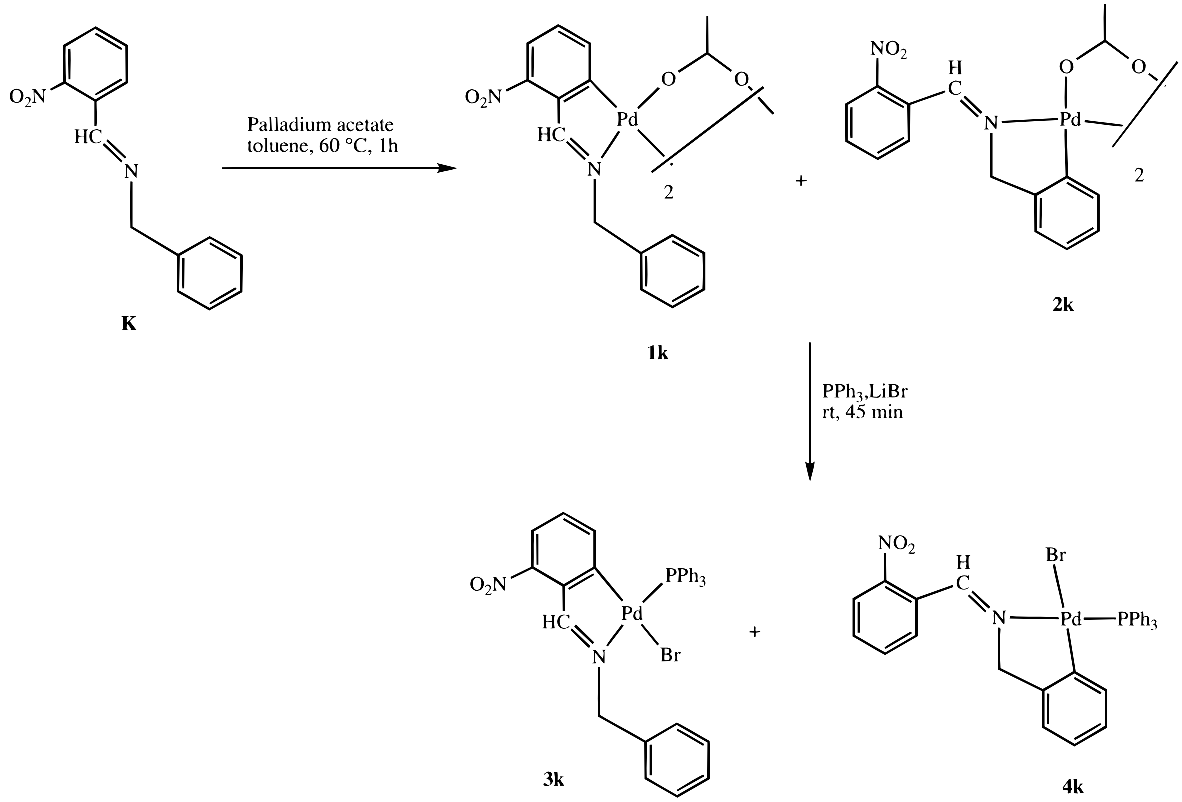
Scheme 1



A, R= H, R'= $CH_2CH_2CH_3$
B, R= H, R'= Ph
C, R= 4-MeO, R'= Ph
D, R= 2-NO_2, R'= Ph
E, R= 3-NO_2, R'= Ph
F, R= 4-NO_2, R'= Ph
I, R= H, R'= CH_2Ph
J, R= 4-Cl, R'= CH_2Ph
L, R= 3-NO_2, R'= CH_2Ph

1a, R= H, R'= $CH_2CH_2CH_3$
1b, R= H, R'= Ph
1c, R= 4-MeO, R'= Ph
1d, R= 2-NO_2, R'= Ph
1e, R= 3-NO_2, R'= Ph
1f, R= 4-NO_2, R'= Ph
1i, R= H, R'= CH_2Ph
1j, R= 4-Cl, R'= CH_2Ph
1l, R= 3-NO_2, R'= CH_2Ph

Scheme 2

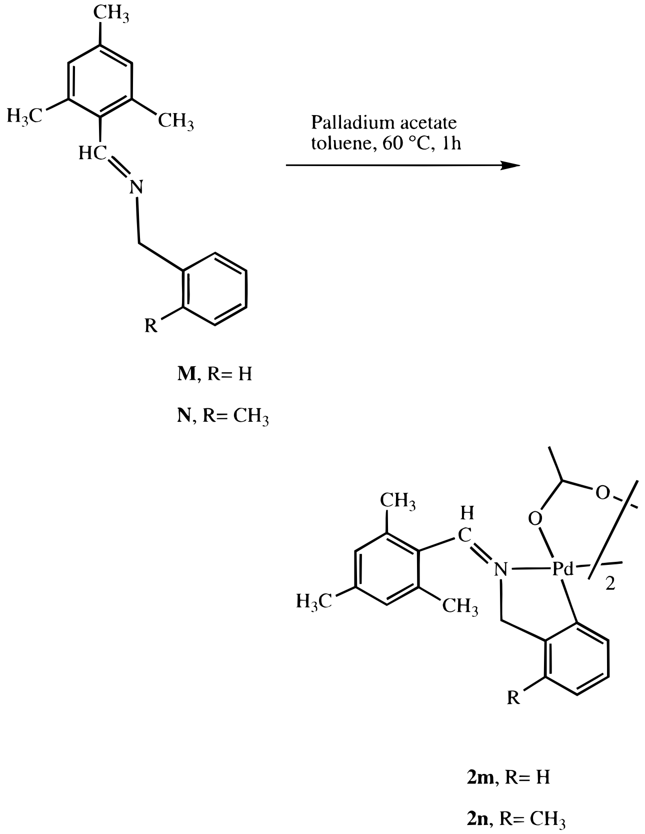


phosphine and the metalated carbon atom.[10b] Furthermore, the methinic proton signal of **3k** appears shifted to high field (relative to that of the free imine) and coupled with the phosphorus atom, $^4J(PH) = 8.2$ Hz, in good agreement with an endocyclic structure.[10a] In contrast, the same proton signal for **4k** appears shifted to low field, in good agreement with an exocyclic structure with the imine in the *Z* form relative to the C=N bond.[10a]

Kinetics. The cyclometalation reaction of palladium acetate with the different imines in toluene solution has been studied under second-order conditions ([Pd]/[imine] = 0.7–1.3) to avoid the formation of the insoluble bis(imine) complexes $[Pd(CH_3COO)_2(imine)_2]$. The reactions were followed spectrophotometrically, and the absorbance *versus* time traces were derived at the wavelength where larger differences were detected. After the appearance of a lag time in the increase of the absorbance accompanying the reaction, strongly dependent on the nature of the imine used, in all cases a monophasic first-order behavior was observed. Monitoring of the overall reaction at the appropriate intervals by ^1H NMR spectroscopy agrees with the second reaction being the intramolecular cyclometalation (C–H bond activation) and the initiation period being the formation of a non-organometallic coordination compound (see below).

Overall, the coordination of the imine to the dimeric

Scheme 3



Scheme 4

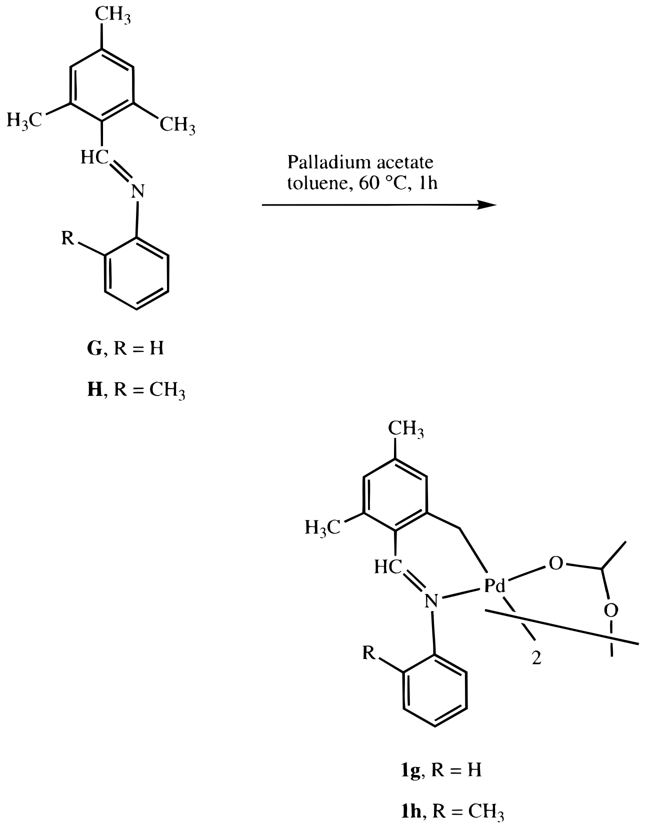
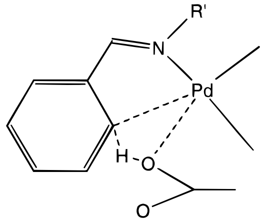


Table 1. Kinetic and Activation Parameters for the Cyclometalation Reactions of Palladium Acetate with the Imines Indicated in Chart 1 in Toluene Solution

imine X	metalated compd	10^4k^{323}, s^{-1}	$\Delta H^{\ddagger}$, kJ mol^{-1}	$\Delta S^{\ddagger}$, J K^{-1} mol^{-1}	$\Delta V^{\ddagger}$, $cm^3\ mol^{-1}$ (T/K)
A	**1a**	4.7	63 ± 5	−115 ± 16	−12 ± 3 (318)
B	**1b**	1.4	71 ± 6	−102 ± 18	−23 ± 3 (343)
C	**1c**	1.2	73 ± 10	−97 ± 30	−24 ± 5 (323)
D	**1d**	1.3^a	66 ± 10	−123 ± 33	−23 ± 4 (343)
E	**1e**	1.6^a	67 ± 12	−113 ± 36	−21 ± 2 (343)
F	**1f**	0.58	75 ± 18	−96 ± 50	−25 ± 2 (343)
G	**1g**	4.7	48 ± 3	−167 ± 9	−24 ± 3 (333)
H	**1h**	0.59	49 ± 11	−177 ± 33	−20 ± 1 (343)
I	**1i**	5.9	52 ± 3	−150 ± 10	−15 ± 2 (323)
J	**1j**	3.8	65 ± 1	−110 ± 2	−12 ± 1 (333)
K	**1k** + **2k**	5.5^b	46 ± 4	−168 ± 13	−11 ± 1 (323)
L	**1l**	3.3^a	45 ± 2	−180 ± 6	−15 ± 4 (323)
M	**2m**	7.0	67 ± 5	−100 ± 15	−12 ± 1 (323)
N	**2n**	9.2^a	62 ± 2	−120 ± 9	−17 ± 1 (323)

[a] A statistical factor of 2 has been applied. [b] A statistical factor of 1.1 has been applied according to the [**1k**]/[**2k**] = 2.5 ratio determined under these conditions.

Chart 2



palladium center is comparatively fast in relation to the cyclometalation reaction, as expected. The reaction observed, and monitored in this work, corresponds solely to the C−H bond activation on the already coordinated imine. All the values found for the observed rate constants, k_{obs}, for the systems studied as a function of imine, temperature, and pressure are available on request. From these observed rate constants, the first-order constants at 298 K, thermal activation parameters, and activation volumes collected in Table 1 are derived. The values for both the enthalpy and entropy of activation, as well as those for the activation volume, are within the range of values observed for other C−H bond activations *via* electrophilic substitution in the absence of added acids.[1e,11c−e] The values determined for $\Delta V^{\ddagger}$ are slightly less negative than those found for these reactions, indicating a less crowded arrangement of the transition state. The results agree with the presence of a highly ordered transition state such as that shown in Chart 2, where the neighboring terminal acetato group acts as a proton acceptor to produce acetic acid as a leaving group.[11c−e] Nevertheless, important differences, strongly dependent on the nature of the cyclometalating imine involved, are observed. Although other interpretations are also possible, such as those involving oxidative addition processes, for these types of reactions the existence of the transition state depicted in Chart 2 is fairly well-established.

As indicated above, the cyclometalation reaction of palladium acetate with the imines **X**, depicted in Chart 1, produces in all cases the clean *endo* (**1x**) or *exo* (**2x**) corresponding compounds; a mixture of both isomers is detected in the final reaction mixture with imine **K**. As for the changes in the UV−vis spectra, they are much more complex; in all cases small initial changes in the spectra are followed by further important and larger variations. These initially small changes became much more pronounced, with the imines having larger cone angles around the donor N atom and less basic character (the aniline derivatives **B**−**H**). In these cases a lag time in the increase of the absorbance *versus* time traces becomes evident. Workup of the systems at these reaction times produces the precipitation of the very insoluble *bis*(imine) compounds;[23] these complexes are also detected in the UV−vis cells when concentrations are on the high side. For the alkyl- and benzylamine derivatives (**A**, **I**−**N**), these initial variations were of very little importance.

Palladium acetate is a trinuclear compound in the solid state, with all the acetato groups acting as bridging ligands;[18] nevertheless, the ^{1}H NMR spectrum of a saturated solution of palladium acetate in C_6D_6 shows four singlets.[19] The high-field signals can be assigned to terminal acetato ligands and the low-field signals to bridging acetato ligands.[20] The relaxation time, T_1, values of these signals confirm this assignment; the high-field signals have small T_1 values, which is in agreement with their higher mobility. When the spectra were recorded at lower palladium acetate concentrations, new signals were observed, their number increasing with the dilution of the sample, suggesting that the formation of solvato complexes with palladium acetate occurs in solution. In this way trinuclear and dinuclear species with terminal acetato ligands can be present in the solution medium. It has been shown that the addition of Lewis bases, as amines or phosphines, to benzene solutions of palladium acetate affords, when an excess of ligand is added, the mononuclear coordination compounds $[Pd(CH_3COO)_2L_2]$.[8]

As a consequence of all the aforementioned facts, the cyclopalladation of imines in toluene can be proposed as the following: once the formation of imine−palladium coordination compounds, containing terminal and bridging acetato ligands, has taken place, the electrophilic attack of the metal atom at the C−H bond with elimination of acetic acid occurs, producing the final dinuclear cyclopalladated derivatives.

From the data in Table 1, it can be seen that important differences occur in kinetic and activation parameters for all the series of imines used. With respect to the bond activation, first-order rate constants of benzylamine derivatives **I**−**N** are found to be higher than those of the aniline derivatives **B**−**H**. No important or meaningful differences are found between the formation of *endo* or *exo* metallacycles (for example **1i** *versus* **2m**) for the group of benzylamine derivatives used, **I**−**N**; the same applies for the substituents on the aromatic ring.

Even more important is to note that, despite the fact that for compounds **1g** and **1h** an aliphatic C−H activation has taken place to produce a six-membered *endo* metallacycle, no significant changes in the values of *k* are detected in relation to the other aniline derivatives. Finally, imine **A** seems to react at a rate equivalent to that for the less hindered benzylamine derivatives, **I**−**N**.

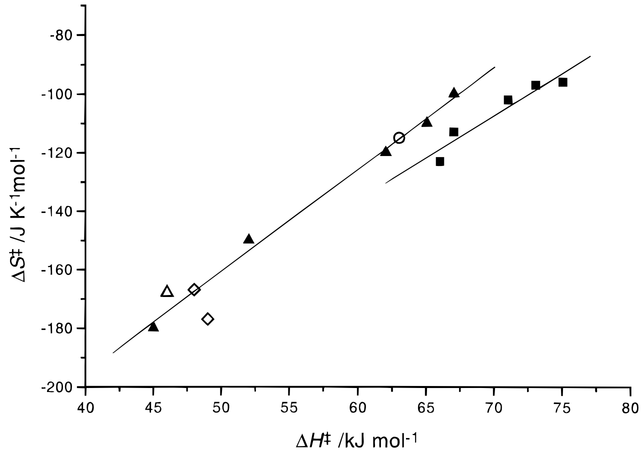


Figure 1. Isokinetic plot for the cyclometalation reactions in toluene solution of the imines indicated in Chart 1: (■) aniline derivatives; (▲) benzylamine derivatives; (○) propylamine derivative; (△) imine **K**; (◇) imines **G** and **H**. Empty points have not been used for the regression.

With respect to thermal activation parameters, $\Delta H^‡$ and $\Delta S^‡$, the pattern in Figure 1 is rather significant. Although no trends are clearly observed in Table 1, Figure 1 indicates that three separate sets of thermal activation parameters must be considered: those related to the benzylamine derivatives (including the benzylidenepropylamine **A**), those related to the aniline derivatives, and finally those related to the imines **G** and **H**, which produce the activation of $C_{aliphatic}$−H bonds.

In general it can be concluded that for the more sterically hindered imines (the aniline derivatives) enthalpies of activation are, as a whole, larger, due to the fact that the important space reorganization on going to the transition state cannot take place as easily (less negative $\Delta S^‡$ values). The values obtained for imine **K** cannot be considered, because two different compounds are produced; nevertheless, the fact that no differences for imines **M** and **N** (producing *exo* derivatives) have been detected made us assume that the activation parameters could be considered in the same lot. Much more dramatic differences are observed for the formation of the *endo* six-membered metallacycles *via* aliphatic C−H bond activation in imines **G** and **H**. In these reactions the entropy values are much more negative and are accompanied by very low activation entropy values; it seems clear that, although thermodynamic factors predict that these six-membered metallacycles with $C_{aliphatic}$−palladium bonds are less stable,[1] the kinetic information agrees with the fact that the easier approach of the C−H bond to the Pd center in the four-center transition state (Chart 2) results in a much smaller enthalpy value. The flexibility of the imine can also explain the values obtained for the activation volumes; for all the benzylamine derivatives $\Delta V^‡$ values are in the range −11 to −17 cm^3 mol^{-1}, while those from aniline are in the range −20 to −25 cm^3 mol^{-1}. Again it is important to note that the benzylidenepropylamine is included in the first group, its flexibility being very close to the benzylidenebenzylamines.

In summary, as found for similar systems, no important mechanistic differences exist in cyclometalation

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[18] (a) Skapski, A. C.; Smart, M. L. *J. Chem. Soc., Chem. Commun.* **1970**, 658. (b) Cotton, F. A.; Han, S. *Rev. Chim. Miner.* **1983**, *20*, 496. (c) Mawby, A.; Pringle, G. E. *J. Inorg. Nucl. Chem.* **1971**, *33*, 1989. (d) Cotton, F. A.; Han, S. *Rev. Chim. Miner.* **1985**, *22*, 277.

[19] Values of δ (T_1) for a saturated solution of palladium acetate in C_6D_6: 1.60 ppm (1.31 s), 1.53 ppm (1.32 s), 1.49 ppm (1.22 s), and 1.48 ppm (1.24 s).

[20] Albert, J.; Granell, J.; Moragas, R.; Font-Bardia, M.; Solans, X. *J. Organomet. Chem.* **1996**, *522*, 59.

[21] (a) Spitzer, M.; Gartig, F.; van Eldik, R. *Rev. Sci. Instrum.* **1988**, *59*, 2092. (b) Fleischman, F. K.; Conze, E. G.; Stranks, D. R.; Kelm, H. *Rev. Sci. Instrum.* **1977**, *99*, 1427.

reactions *via* electrophilic substitution that can be related to substituents on the phenyl rings to be activated. Furthermore, our results in this work also show that *endo* or *exo* activation does not seem to produce differences in the mechanism or activation parameters, as found for Pt(II) oxidative-addition cyclometalations.[11a,b,12a] Only the steric backbone of the imine systems studied seems to be important in the values found for kinetic and activation parameters, once the basicity of the imines has had its effect in the previous coordination step; cyclometalation reactions for dinuclear Rh(II) systems have also shown the same effects.[11c,e] Finally, it is clear from our data that formation of five- or six-membered metallacycles *via* aromatic or aliphatic C−H activation produces some differences that are not those traditionally established from a thermodynamic point of view.

Experimental Section

Instruments and Materials. ^{1}H and ^{31}P{^{1}H} NMR spectra were recorded on Varian XL-200 (200 MHz) and Bruker DRX-250 (101.26 MHz) spectrometers, respectively. Chemical shifts (in ppm) were measured relative to $SiMe_4$ for ^{1}H and to 85% H_3PO_4 for ^{31}P spectra; the solvent used was $CDCl_3$. IR spectra were recorded as KBr pellets on a Nicolet 520 FT-IR spectrometer. Microanalyses were performed by the Institut de Química Bio-Orgànica de Barcelona (CSIC) and by the Serveis Científico-Tècnics de la Universitat de Barcelona. All UV−vis spectra were recorded on a HP8452A diode array instrument and on a Beckman UV5420 instrument equipped with the high-pressure cell already described.[11]

Toluene and diethyl ether were dried over sodium−benzophenone and distilled before use. The imines were prepared according to procedures described in the literature.[22]

Compounds. The acetato-bridged cyclometalated *endo* compounds **1b**,**f**,**g**,**i**,**j** and the *exo* compounds **2m**,**n** have been characterized previously.[10b,e,14] Originally they were prepared from palladium acetate and the corresponding imine in acetic acid solution; in the present work, all have been prepared in toluene solution at 60 °C over 1 h, in good yields.

Compounds **1a**,**c**−**e**,**h**,**l** were all prepared in the same way. To a suspension of palladium acetate (0.22 g, 1×10^{-3} mol) in 20 cm^3 of toluene was added a solution of imine (1×10^{-3} mol: for **A**, 0.15 g; for **C**, 0.21 g; for **D**, 0.23 g; for **E**, 0.23 g; for **H**, 0.24 g; for **L**, 0.24 g) in 10 cm^3 of the same solvent; the mixture was then kept at 60 °C for 1 h and concentrated under reduced pressure to *ca.* 2 cm^3. After addition of 10 cm^3 of diethyl ether, a yellow solid was obtained, which was purified by SiO_2 column chromatography using $CHCl_3$/MeOH (90/10) as eluent.

Characterization data are as follows.

1a: yield 55%. Anal. Found (calcd) for $C_{24}H_{30}N_2O_4Pd_2$: C, 46.1 (46.25); H, 4.9 (4.85); N, 4.6 (4.49). ^{1}H NMR (δ, ppm): 7.95−7.15 (m, 10H, *HC*=N, *aromatic*), 3.20 (m, 4H, *CH$_2$*N), 2.20−1.95 (m, 10H, *CH$_2$*, *CH$_3$*COO), 0.85 (m, 6H, *CH$_3$*).

1c: yield 50%. Anal. Found (calcd) for $C_{32}H_{30}N_2O_6Pd_2$: C, 51.6 (51.15); H, 3.9 (4.02); N, 3.8 (3.73). ^{1}H NMR (δ, ppm): 7.60 (s, 2H, *HC*=N), 7.15−7.05 (m, 8H, *aromatic*), 6.85−6.75 (m, 4H, *aromatic*), 6.60 (dd, J_{HH} = 7.5, 2.2 Hz, 2H, *aromatic*), 6.05 (d, J_{HH} = 2.2 Hz, 2H, *aromatic*), 3.60 (s, 6H, *CH$_3$*O), 2.10 (s, 6H, *CH$_3$*COO).

1d: yield 30%. Anal. Found (calcd) for $C_{30}H_{24}N_4O_8Pd_2$: C, 46.0 (46.12); H, 3.0 (3.10); N, 7.0 (7.17). ^{1}H NMR (δ, ppm): 8.55 (s, 2H, *HC*=N), 7.90 (d, J_{HH} = 7.6 Hz, 2H, *aromatic*), 7.30−7.15 (m, 6H, *aromatic*), 7.10 (d, J_{HH} = 7.6 Hz, 2H, *aromatic*), 7.05 (t, J_{HH} = 7.6 Hz, 2H, *aromatic*), 6.90−6.80 (m, 4H, *aromatic*), 1.84 (s, 6H, *CH$_3$*COO).

1e: yield 20%. Anal. Found (calcd) for $C_{30}H_{24}N_4O_8Pd_2$: C, 46.3 (46.12); H, 3.2 (3.10); N, 6.9 (7.17). ^{1}H NMR (δ, ppm): 8.10 (d, J_{HH} = 2.1 Hz, 2H, *aromatic*), 7.87 (s, 2H, *HC*=N), 7.75 (dd, J_{HH} = 7.5, 2.1 Hz, 2H, *aromatic*), 7.30 (d, J_{HH} = 7.5 Hz, 2H, *aromatic*), 7.20−7.10 (m, 6H, *aromatic*), 6.85−6.70 (m, 4H, *aromatic*), 1.92 (s, 6H, *CH$_3$*COO).

1h: yield 45%. Anal. Found (calcd) for $C_{38}H_{42}N_2O_4Pd_2$: C, 56.9 (56.80); H, 5.1 (5.27); N, 3.2 (3.49). ^{1}H NMR (δ, ppm; $CDCl_3$ + py-d_5): 7.90 (s, 1H, *HC*=N), 7.20−6.50 (m, 6H, *aromatic*), 2.90 (s, 2H, *CH$_2$*−Pd), 2.70 (s, 3H, *CH$_3$*), 2.25 (s, 3H, *CH$_3$*), 1.80 (s, 3H, *CH$_3$*), 1.70 (s, 3H, *CH$_3$*).

1l: yield 50%. Anal. Found (calcd) for $C_{32}H_{28}N_4O_8Pd_2$: C, 46.9 (47.48); H, 3.4 (3.48); N, 6.8 (6.92). ^{1}H NMR (δ, ppm): 8.0−7.80 (m, 4H, *HC*=N, *aromatic*), 7.40 (dd, J_{HH} = 7.6, 2.2 Hz, 2H, *aromatic*), 7.20−7.10 (m, 8H, *aromatic*), 6.85−6.70 (m, 4H, *aromatic*), 4.65 (d, 2H, J_{HH} = 17.2 Hz, C*H$_2$*N), 4.15 (d, 2H, J_{HH} = 17.2 Hz, C*H$_2$*N), 2.25 (s, 6H, *CH$_3$*COO).

Compounds 1k, 3k, and 4k. 1k. To a suspension of palladium acetate (0.22 g, 1×10^{-3} mol) in 20 cm^3 of acetic acid was added a solution of imine **K** (0.24 g, 1×10^{-3} mol) in 10 cm^3 of the same solvent. The mixture was brought to reflux for 45 min and then concentrated under reduced pressure. After addition of diethyl ether, a yellow solid was obtained, which was purified by SiO_2 column chromatography.

3k. A 0.25×10^{-3} mol (0.20 g) amount of **1k** was treated with PPh_3 (0.13 g, 0.50×10^{-3} mol) and LiBr (43×10^{-3} g, 0.5×10^{-3} mol) in acetone solution at room temperature for 45 min, and the mixture was then filtered. The solution was concentrated *in vacuo*, and the solid obtained after addition of diethyl ether was recrystallized from $CHCl_3$ to give **3k**.

4k. A 0.25×10^{-3} mol amount of the solid obtained when imine **K** was treated with $Pd(AcO)_2$ in toluene at 60 °C for 1 h, which is a mixture of the *endo* and *exo* metallacycles **1k** and **2k**, was treated with PPh_3 (0.13 g, 0.50×10^{-3} mol) and LiBr (43×10^{-3} g, 0.5×10^{-3} mol) in CH_2Cl_2 at room temperature for 45 min. The solid formed was filtered, washed with diethyl ether, and recrystallized from chloroform and diethyl ether to afford **4k**.

Characterization data are as follows.

1k: yield 40%. Anal. Found (calcd) for $C_{32}H_{28}N_4O_8Pd_2$: C, 47.8 (47.48); H, 3.6 (3.48); N, 6.8 (6.92). ^{1}H NMR (δ, ppm): 8.10 (s, 2H, *HC*=N), 7.90 (dd, J_{HH} = 7.5, 2.1 Hz, 2H, *aromatic*), 7.55 (dd, J_{HH} = 7.5, 2.1 Hz, 2H, *aromatic*), 7.20−7.10 (m, 8H, *aromatic*), 7.05−6.90 (m, 4H, *aromatic*), 4.55 (d, 2H, J_{HH} = 17.2 Hz, C*H$_2$*N), 4.00 (d, 2H, J_{HH} = 17.2 Hz, C*H$_2$*N), 2.20 (s, 6H, *CH$_3$*COO).

3k: yield 50%. Anal. Found (calcd) for $C_{32}H_{26}N_2BrO_2Pd$: C, 55.8 (55.88); H, 3.8 (3.81); N, 4.0 (4.07). ^{1}H NMR (δ, ppm): 8.60 (d, J_{HP} = 8.2 Hz, 1H, *HC*=N), 7.70−7.50 (m, 6H, *aromatic*), 7.40−7.20 (m, 14H, *aromatic*), 6.75 (t, J_{HH} = 7.2 Hz, 1H, *aromatic*), 6.70−6.50 (m, 2H, *aromatic*), 5.0 (s, 2H, C*H$_2$*N).

4k: yield 20%. Anal. Found (calcd) for $C_{32}H_{26}N_2BrO_2Pd$: C, 55.5 (55.88); H, 3.6 (3.81); N, 4.2 (4.07). ^{1}H NMR: (δ, ppm): 9.15 (d, J_{HP} = 12.4 Hz, 1H, *HC*=N), 8.20 (m, 2H, *aromatic*), 7.70−7.50 (m, 6H, *aromatic*), 7.40−7.20 (m, 11H, *aromatic*), 7.10 (d, J_{HH} = 7.1 Hz, 1H, *aromatic*), 6.90 (t, J_{HH} = 7.1 Hz, 1H, *aromatic*), 6.45 (t, J_{HH} = 7.1 Hz, 1H, *aromatic*), 6.25 (t, J_{HH} = J_{HP} = 7.1 Hz, 1H, *aromatic*), 5.40 (s, 2H, C*H$_2$*N).

Kinetic Measurements. 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 and/or decrease of absorbance was observed. No

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[22] Bigelow, L. A.; Eatrough, H. In *Organic Syntheses*; Blatt, A. H., Ed.; Wiley: New York, 1994; Vol. 1, p 80.

[23] For imine **M** the compound has been isolated and characterized. To a suspension of 1×10^{-3} mol of palladium acetate in 20 cm^3 of toluene was added a solution of the imine (2.0×10^{-3} mol in 10 cm^3 of the same solvent) at room temperature. After it was stirred for 30 min, the mixture was filtered, and the solid was washed with toluene and diethyl ether and dried under reduced pressure. Yield: 0.68 g (94%). Anal. Calcd for $C_{40}H_{48}N_2O_4Pd$: C, 66.06; H, 6.65; N, 3.85. Found: C, 66.14; H, 6.60; N, 3.92.

dependence of the values on the selected wavelengths was detected, as expected for reactions where a good retention of isosbestic points is observed. The general kinetic technique is that previously described.[11,12] Solutions for the kinetic runs were prepared by dissolving the calculated amounts of the compounds (palladium acetate and imine) in toluene. In all cases no dependence on the concentration of palladium acetate or imine was detected, and a [Pd]/[imine] ratio within the 0.7−1.3 range was maintained to ensure the nonappearance of the well-known insoluble [Pd($CH_3COO)_2$(imine)$_2$] species.[8]

For runs at elevated pressure, a previously described pressurizing system and high-pressure cell were used.[21] In these cases the absorbance *versus* time traces were recorded on a Beckman UV5420 instrument at a fixed wavelength chosen from the atmospheric pressure experiments. Rate constants were derived from exponential least-squares fitting by the standard routines. Least-squares 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 fitting programs commercially available.

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