Intimate Mechanism of Oxidative Addition to Zerovalent Palladium Complexes in the Presence of Halide Ions and Its Relevance to the Mechanism of Palladium-Catalyzed Nucleophilic Substitutions

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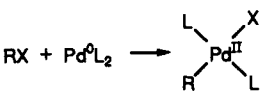
Abstract: The mechanism of oxidative addition of aryl halides to low-ligated zerovalent palladium species obtained by reduction of their divalent precursor complexes, $Pd^{II}Cl_2(PR_3)_2$, was investigated on the basis of ^{31}P NMR and electrochemistry. In strong contrast to usual expectations, it is shown that the reaction proceeds *via* a complex sequence of steps: (i) fast addition of the aryl halide to a halide ligated zerovalent palladium center, so as to afford a pentacoordinated anionic arylpalladium(II) center; (ii) a fast but reversible uphill elimination from the pentacoordinated anionic arylpalladium(II) center of a halide ion ligand, possibly through its substitution by a solvent ligand; (iii) rearrangement of this second short-lived intermediate into the thermodynamically stable *trans*-arylpalladium(II) product of the reaction. On the basis of this detailed mechanism, a new mechanism is proposed for the catalysis of nucleophilic substitutions by palladium complexes. In contrast to the catalytic cycles that are usually considered, this new catalytic cycle accounts for the well-used effects of halide ions as well as that of small metal cations and rationalizes their role in the overall efficiency of palladium-catalyzed nucleophilic substitutions.

Introduction

Zerovalent palladium complexes are efficient catalysts for a large number of fundamental organic synthetic reactions, such as nucleophilic aromatic and vinylic substitutions,[1] arylation of olefins,[2] *etc.* All these catalytic reactions are considered to proceed *via* chain cycles.[1-6] These cycles are initiated by oxidative addition of an organic halide or pseudohalide (noted RX in the following) to a low ligated zerovalent palladium complex, Pd^0L_2:[4]



(1)

Pd^0L_2 may be formed *in situ* by spontaneous endergonic deligation of stable zerovalent complex precursors, such as *e.g.* $Pd^0(PPh_3)_4$[7] or $Pd^0(dba)L_2$ generated from mixtures of $Pd^0(dba)_2$ and phosphines,[8] or by reduction of a stable divalent palladium complex, $Pd^{II}Y_2L_2$:

$$Pd^{II}Y_2L_2 \xrightarrow{\text{redn}} Pd^0L_2 + 2Y^- \quad (2)$$

In this latter case, the reducer is usually an organometallic species such as a Grignard reagent or an organometal,[1,9] most generally the nucleophile itself, or a phosphine when Y is an oxygen ligand such as acetate.[10] Also, this reduction can be performed electrochemically.[11]

The catalytic cycle is thought to proceed further through nucleophilic substitution of the halide or pseudohalide ion of the *trans*-σ-palladium(II) complex formed in eq 1,[3,5] followed by

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(1) For reviews, see: (a) Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669. (b) Negishi, E. I. *Acc. Chem. Res.* **1982**, *15*, 340. (c) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

(2) For reviews, see: (a) Heck, R. F. *Acc. Chem. Res.* **1979**, 12, 146. (b) Heck, R. F. *Org. React. (N.Y.)* **1982**, *27*, 345. (c) Heck, R. F. *Palladium in Organic Synthesis*; Academic Press: New York, 1985.

(3) The existence and validity of most of the supposed steps of these catalytic mechanisms have been established independently;[4-6] these steps have been characterized kinetically at several instances. However, and to the best of our knowledge, no study of a whole catalytic sequence has ever been reported for these reactions.

(4) For oxidative addition proposed as the rate determining step (r.d.s.): (a) Fauvarque, J. F.; Jutand, A. *Bull. Soc. Chim. Fr.* **1976**, 765. (b) Fauvarque, J. F.; Jutand, A. *J. Organomet. Chem.* **1977**, *132*, C17. (c) Fauvarque, J. F.; Jutand, A. *J. Organomet. Chem.* **1979**, *177*, 273. (d) Fauvarque, J. F.; Jutand, A. *J. Organomet. Chem.* **1981**, *209*, 109. For reviews on oxidative addition, see *e.g.*: (e) Collman, J. P. *Acc. Chem. Res.* **1968**, *1*, 136. (f) Collman, J. P.; Roper, W. R. *Adv. Organomet. Chem.* **1968**, *7*, 53. (g) Halpern, J. *Acc. Chem. Res.* **1970**, *3*, 386. (h) Tsuji, J. *Fortsch. Chem. Forschr.* **1972**, *28*, 41. (i) *Transition Metal Organometallics in Organic Synthesis*; Alper, M., Ed.; Academic Press: New York, 1976. (j) For a comprehensive discussion of the various mechanisms proposed for oxidative addition, see: Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978; Part I, Chapter 7, pp 156–183.

(5) For nucleophilic substitution as the r.d.s., see: (a) Negishi, E.; Takahashi, T.; Baba, S.; van Horn, D. E.; Okukado, N. *J. Am. Chem. Soc.* **1987**, *109*, 2393. (b) Farina, V.; Krishnan. B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.

(6) For reductive elimination proposed as the r.d.s., see: (a) Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933. (b) Loar, M.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4174. (c) Mravsky, A.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4182. (d) Ozawa, F.; Ito, T.; Nakamura, Y.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1868. (e) Tatsumi, K.; Nakamura, A.; Komiya, S.; Yamamoto, A.; Yamamoto, T. *J. Am. Chem. Soc.* **1984**, *106*, 8181.

(7) (a) Fitton, P.; McKeon, J. E. *Chem. Commun.* **1968**, 4. (b) Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287.

(8) For earliest use of $Pd^0(dba)_2$ with (a) monodentate ligands, see: Inoue, Y.; Hibi, T.; Satake, M.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1979**, 982. (b) With bidentate ligands, see: Fiaud, J. C.; Hibon de Gournay, A.; Larchevêque, M.; Kagan, H. B. *J. Organomet. Chem.* **1978**, *154*, 175. For a study of zerovalent species generated under these conditions, see: (c) Amatore, C.; Jutand, A.; Khalil, F.; M'Barki, M. A.; Mottier, L. *Organometallics* **1993**, *12*, 3168.

(9) For a study of zerovalent species generated under these conditions, see: Negishi, E. I.; Takahashi, T.; Akiyoshi, K. *J. Chem. Soc., Chem. Commun.* **1986**, 1338.

(10) For kinetic evidences of *in situ* generation of zerovalent palladium *via* $Pd^{II}(OAc)_2$ reduction by phosphines, see: (a) Amatore, C.; Jutand, A.; M'Barki, M. A. *Organometallics* **1992**, *11*, 3009. (b) Ozawa, F.; Kubo, A.; Hayashi, T. *Chem. Lett.* **1992**, 2177. For earliest applications of this method, see: (c) Yamane, T.: Kikukawa, K.; Takagi, M.; Matsuda, T. *Tetrahedron* **1973**, *29*, 955. (d) Dieck, H. A.; Heck, R. F. *J. Am. Chem. Soc.* **1974**, *96*, 1133.

(11) (a) Amatore, C.; Azzabi, M.; Jutand, A. *J. Am. Chem. Soc.* **1991**, *113*, 1670. (b) Amatore, C.; Azzabi, M.; Jutand, A. *J. Organomet. Chem.* **1989**, *363*, C41. (c) Amatore, C.; Azzabi, M.; Calas, P.; Jutand, A.; Lefrou, C.; Rollin, Y. *J. Electroanal. Chem.* **1990**, *288*, 45. (d) Amatore, C.; Azzabi, M.; Jutand, A. *J. Am. Chem. Soc.* **1991**, *113*, 8375.

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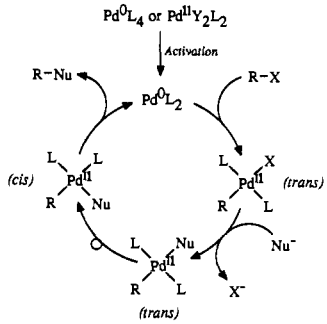
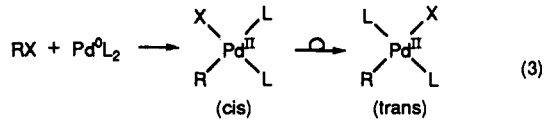
Scheme I



reductive elimination of the substituted product, R–Nu,[3,6] which regenerates the low-ligated zerovalent palladium intermediate, as summarized in Scheme I. Since reductive elimination may only proceed from *cis* complexes,[12,13] the thermodynamically stable *trans* derivative formed upon nucleophilic substitution must isomerize before this step may occur.[12-17] Similarly, since oxidative addition to zerovalent complexes has been established to proceed *via* a concerted insertion of the digonal Pd^0L_2 moiety into the RX σ-bond,[18] it is presumed that within the frame of Scheme I this reaction is a two-step sequence: oxidative addition[18] being followed by isomerization of the transient *cis* derivative[19] into the thermodynamically stable *trans* product:[7]



(3)

Therefore, whenever rationalized within the framework of Scheme I, catalysis of nucleophilic substitution must involve a series of isomerization reactions of divalent palladium complexes that occurs between its three basic steps: oxidative addition, ligand substitution, and reductive elimination. The *cis*-to-*trans* isomerization that should occur after the oxidative addition is thermodynamically favored.[7] It is thus expected to be rather fast. Conversely, the uphill *trans-to-cis* isomerization occurring before the reductive elimination is expected to be rather slow.[12-17] This should force both *cis* complexes to obey steady-state kinetic regimes. In agreement with both hypotheses and to the best of our knowledge, none of these *cis* intermediates have ever been characterized under real catalytic conditions, although their existence has been established independently in a few cases.[13,19]

(12) (i) *trans*-R–$M^{II}NuL_2$ complexes are stable *vis a vis* reductive elimination (M = Pd, Ni):[7] Parshall, G. W. *J. Am. Chem. Soc.* **1974**, *96*, 2360. However, under several experimental circumstances they may undergo reductive elimination *via* the supposed intermediacy of their *cis* isomers or of unidentified intermediates in which the two ligands to be eliminated are in *cis* positions.[13] These specific circumstances involve for example photochemical or thermal activation,[14] addition of a fifth ligand,[6a,15] or possibly chemical or electrochemical oxidation.[14,16] (ii) For several plausible mechanisms of *cis-trans* isomerization of square planar complexes, see *e.g.* refs 6d and 15 and: (a) Romeo, R.; Uguagriati, P.; Belluco, U. *J. Mol. Catal.* **1975(76)**, *1*, 325. (b) Komiya, S.; Albright, T. A.; Hoffmann, R.; Kochi, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 7255. (c) Anderson, G. D.; Cross, R. J. *Chem. Soc. Rev.* **1980**, *9*, 185. (d) Ozawa, F.; Yamamoto, T.; Yamamoto, A. *J. Organomet. Chem.* **1985**, *279*, 233.

(13) Some stable *cis* complexes have been prepared: for example *cis*-Me_2Ni^{II}(dppe) is stable up to 130 °C;[17] similarly, *cis*-Me_2Pd^{II}(dppe) has a rate constant of 5×10^{-7} s^{-1} for reductive elimination at 80 °C, while this rate is 1×10^{-3} s^{-1} at 60 °C for *cis*-$Me_2Pd^{II}(PPh_3)_2$.[6a]

(14) (a) Morrell, D. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1975**, *97*, 7262. (b) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 1634.

(15) Cross, R. J. *Chem. Soc. Rev.* **1984**, 197.

(16) Almemark, M.; Akermark, B. *J. Chem. Soc., Chem. Commun.* **1978**, 66.

(17) Green, M. L. H.; Smith, M. J. *J. Chem. Soc.* A **1971**, 639.

(18) (a) Fauvarque, J. F.; Pflüger, F.; Troupel, M. *J. Organomet. Chem.* **1981**, *208*, 419. (b) Amatore, C.; Pflüger, F. *Organometallics* **1990**, *9*, 2276.

(19) For a reported example of a fully characterized stable *cis*-R-$Pd^{II}X(PR_3)_2$ complex, see: Urata, H.; Tanaka, M.; Fuchikami, T. *Chem. Lett.* **1987**, 751.

Owing to these kinetic complications, all reported attempts to kinetically characterize the mechanism in Scheme I have dealt with individual segments of this cycle. Thus, independent kinetic studies, based on different systems, have been reported for oxidative addition,[4,18,20] nucleophilic substitution,[5] or reductive elimination.[6] As such they have provided support to the formulation of each step in Scheme I, yet without ever demonstrating that their *built-up* combination into that overall catalytic sequence is really operative. Conversely, there are several indications pointing out that the overall formulation may be incorrect at least under some circumstances. For example, the data reported in Table I establish that under several circumstances the kinetics of the whole catalytic chain may be faster than that of the sequence 'ligand substitution + reductive elimination' supposed to pertain to the same catalytic sequence.[4a-d] In this respect it is worthwhile to compare the results in the 6th and 7th entries of Table I: the reaction efficiency is much higher when Ph–$Pd^{II}I(PPh_3)_2$ is used catalytically (6th entry) than when it is used stoichiometrically (7th entry). Moreover under most circumstances, stoichiometric reactions between *trans*-σ-phenyl derivatives and nucleophiles in Table I[4a-d] (entries 2, 7, and 9) afford a significant yield (from 30 to 50%) of biphenyl, suggesting that decomposition or reduction of the *trans* intermediate may competitively occur. It is noteworthy that this side product is not observed for the corresponding catalytic systems (entries 1, 5, 6, and 8). Both observations lead to questions about the generality (if not at all the validity) of the formulation in Scheme I, since they clearly establish that the *trans*-R–$Pd^{II}XL_2$ derivative cannot be an intermediate of the chain reactions accounting for the catalytic substitutions reported in Table I.

Such observations, as well as others that are described and discussed hereafter, led us to reinvestigate the mechanism of oxidative addition to zerovalent palladium complexes, with the aim of identifying other possible intermediates that may be precursors to the stable *trans* complex and evaluating their potential role in the mechanism of palladium-catalyzed nucleophilic substitutions. For this, we took advantage of the feasible generation of *stoichiometric* amounts of low-ligated zerovalent palladium complexes *via* preparative or transient electrochemical reduction of their divalent precursors, $Pd^{II}X_2L_2$.[11] In the following we wish to present and discuss the results of these studies and discuss afterwards their possible relevance to the mechanism of palladium catalyzed nucleophilic substitutions.

Results

Oxidative Addition of PhI to Electrogenerated Low-Ligated Zerovalent Palladium Complexes, As Monitored by ^{31}P NMR. Two-electron preparative-scale reduction of millimolar solutions of $Pd^{II}Cl_2(PPh_3)_2$ affords stoichiometrically low-ligated zerovalent palladium complexes.[11] In the absence of intentionally added chloride ions, a single palladium(0) complex is obtained, which involves a ligation by a chloride ion:[11d]

$$Pd^{II}Cl_2(PPh_3)_2 + 2e \rightarrow Pd^0(PPh_3)_2Cl^- + Cl^- \quad (E^p = -1.00\ V) \quad (4)$$

Within the time scale of electrochemical methods, this species is in rapid equilibrium with its dimer and with its chloride ion adduct $Pd^0(PPh_3)_2Cl_2^{2-}$

$$2Pd^0(PPh_3)_2Cl^- \rightleftarrows [Pd^0(PPh_3)_2Cl]_2^{2-} \quad (K = 90\ M^{-1}) \quad (5)$$

$$Pd^0(PPh_3)_2Cl^- + Cl^- \rightleftarrows Pd^0(PPh_3)_2Cl_2^{2-} \quad (K' = 70\ M^{-1}) \quad (6)$$

as established previously in THF on the basis of ^{31}P NMR and kinetics.[11d] The three species could be kinetically characterized

(20) Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10*, 434 and references therein.

Table I. Comparison between Catalytic or Stoichiometric Nucleophilic Substitutions of Organic Halides Mediated by Palladium Complexes[a]

catalytic reaction: $MNu + RX \rightarrow R\text{–}Nu + MX$

stoichiometric reaction: $MNu + trans\text{-}R\text{–}Pd^{II}X(PPh_3)_2 \rightarrow R\text{–}Nu + MX + [Pd^0]$

		system			products (%)[b]		
entry	MNu	catalytic	stoichiometric	conditions	R–Nu	R-R	ref
1	MeMgBr	PhI + 2% Pd^0L_4		1 h, 65 °C	85	0	4a
2			$PhPd^{II}IL_2$	1 h, 65 °C	62	30	4a
3	PhMgBr	PhI + 2% Pd^0L_4		1 h, 65 °C	64	*c*	4a
4			$PhPd^{II}IL_2$	1 h, 65 °C	70	*c*	4a
5	$BrZnCH_2CO_2Et$	PhI + 10% Pd^0L_4		3 h, 45 °C	45	0	4b,c
6		PhI + 10% $PhPd^{II}IL_2$		3 h, 45 °C	90	0	4b,c
7			$PhPd^{II}IL_2$	4 h, 45 °C	43	34	4b,c
8	$BrZnCH_2CO_2Et$	PhBr + 10% Pd^0L_4		3 h, 45 °C	65	0	4b,c
9			$PhPd^{II}BrL_2$	4 h, 45 °C	53	48	4b,c
10	$BrZnCH_2CO_2Et$	PhCH:CHBr[d] + 10% Pd^0L_4		3 h, 45 °C	96	0	4d
11			$PhCH{:}CHPd^{II}BrL_2$[d]	3 h, 45 °C	34	0	4d
12	$PhCH_2MgBr$	MeI + 2% Pd^0L_4		1 h, 65 °C	79	0	4a
13			$MePd^{II}IL_2$	1 h, 65 °C	67	0	4a

[a] Catalyst $Pd^0(PPh_3)_4$ or *trans*-R–$Pd^{II}X(PPh_3)_2$, as indicated. Initial quantities of reactants are identical for each set of reactions to allow comparison. Data from ref 4a–d (solvent: entries 1–4, 12, and 13, THF; entries 5–11, methylal/HMPA, 1:1 v:v). [b] Missing yield corresponds to unconverted reactants. [c] R–R and R–Nu are identical (Ph–Ph). [d] *E*-isomers.

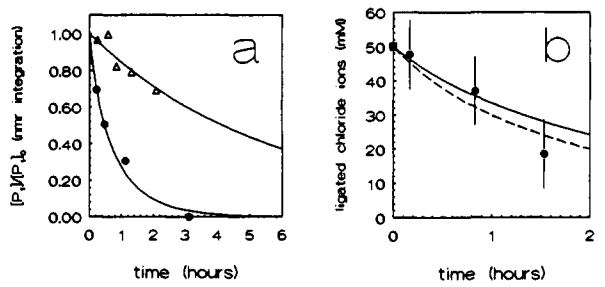


Figure 1. Variations of the concentration of the primary intermediate of oxidative addition (P_1) as a function of time as monitored by ^{31}P NMR (a) or by redox titration with $AgNO_3$ (b), at 20 °C. P_1 was generated by addition of PhI (10 equiv) to solutions of zerovalent palladium electrogenerated *via* a two-electron reduction of $Pd^{II}Cl_2(PPh_3)_2$ solutions of concentration C° in THF, 0.3 M nBu_4NBF_4. $C^\circ = 1.25 \times 10^{-2}$ M in part a or 5×10^{-2} M in part b. Filled circles feature data obtained in the absence of added chloride ions ($n = 0$); open triangles feature data obtained in the presence of added nBu_4NCl (0.125 M; $n = 10$). In part b the filled square at $t = 0$ indicates the value for 1 equiv of chloride ions. The solid lines are the theoretical predictions based on the rate law in eqs 30 and 31 with $k_2K_1 = k_2(k_1/k_{-1}) = 2.35 \times 10^{-2}$ Mh^{-1} (see text). The dashed line is the best fit of the data on the basis of the rate law in eqs 30 and 31 ($k_2K_1 = k_2(k_1/k_{-1}) = 3.1 \times 10^{-2}$ M h^{-1}).

and identified by their ^{31}P NMR singlets at 23.15 ($Pd^0(PPh_3)_2Cl_2^{2-}$), 25.22 ($Pd^0(PPh_3)_2Cl^-$), and 27.14 ($[Pd^0(PPh_3)_2Cl]_2^{2-}$) ppm *vs* H_3PO_4. The values of K and K' are of sufficient magnitudes for $Pd^0(PPh_3)_2Cl^-$ to be the major species present in solution for millimolar concentrations of palladium and in the absence of added chloride ions.[11d]

Immediately after addition of PhI (10 equiv) to an electrolyzed solution of $Pd^{II}Cl_2(PPh_3)_2$, 1.25 mM, the signals featuring the above species disappeared and were replaced by two sharp singlets at 33.47 (S_1) and 24.17 ppm (S_2). No other signal could be observed. The upfield singlet, S_2, is identical to that obtained in the spectrum of an authentic sample of *trans*-Ph–$Pd^{II}I(PPh_3)_2$ taken under identical conditions (24.17 ppm).[11b,d] Upon increasing time, the singlet S_1 decayed progressively while S_2 increased correspondingly (compare Figure 1a). It is noteworthy that at any reaction time the sum of the integrations of S_1 and S_2 remained almost constant,[21] being roughly equal to that observed for *trans*-Ph–$Pd^{II}I(PPh_3)_2$ alone at the same concentration. This suggests (i) that these two signals feature the resonance of all phosphines initially borne by the zerovalent palladium centers present in the solution at the end of electrolysis and (ii) that an unknown primary product of oxidative addition, P_1, observed at S_1 is slowly converted into the stable product of the reaction, *viz.* the *trans* derivative observed at S_2:

$$PhI + Pd^0(PPh_3)_2Cl^- \xrightarrow{\text{fast}} \underset{\text{(singlet } S_1)}{P_1} \quad (7)$$

$$P_1 \xrightarrow{\text{slow}} \underset{\text{(singlet } S_2)}{trans\text{-Ph–}Pd^{II}I(PPh_3)_2} \quad (8)$$

Because of the conservation of phosphine,[21] we know also that species P_1 must bear two phosphines that are chemically equivalent, since they give rise to a singlet signal (S_1).[22]

When the same experiments were performed in the presence of intentionally added chloride ions (nBu_4NCl), the same overall phenomena were observed. However, integrations for the singlet S_1 were larger upon increasing chloride ion concentrations, and its rate of decay concomitantly decreased (compare *e.g.* Figure 1a for 0 or 10 equiv of added nBu_4NCl). Conversely, performing the same experiment in the absence of added chloride ion, but in the presence of a stoichiometric amount of Na^+ (2 equiv of $NaBF_4$), resulted in the immediate observation of the singlet S_2, without any hint of the presence of the singlet S_1. An identical result was achieved when the reaction was performed in the presence of trace amounts—*viz.* 1% to 10% with respect to palladium—of triphenylphosphine. Both series of observations evidence that the presence of halide ions plays a significant role in the kinetics of the processes schematized in eqs 7 and 8: reaction 8 is extremely fast in the complete absence of chloride ions[23] and considerably slowed down in their presence. Also, reaction 8 can

(21) We suppose that relaxation times are comparable for the species observed at S_1 and S_2. Tentative checks of this hypothesis have been performed by varying the parameters of ^{31}P NMR signal acquisitions during repeated experiments (same number of acquisition scans, but with different time pauses between scans). The results could be considered as being identical within experimental reproducibility.

(22) Compare to ref 19, where a doublet of doublets is observed in ^{31}P NMR (δ 20.8 and 31.9 ppm, $J_{P\text{–}P}$ = 29 Hz; $CDCl_3$, PPh_3) for *cis*-R–$Pd^{II}I(PPh_3)_2$, R = 1,3-dimethyl-5-fluoro-6-iodouracil, being located almost symetrically around the singlet (δ 26.4 ppm) of the *trans* isomer.

(23) In THF, Na^+ ions (from $NaBF_4$) scavenge chloride ions *via* ion pairing and precipitation. Similarly when zerovalent palladium was electrogenerated in a divided cell equipped with a lithium sacrificial anode, P_1 underwent a faster transformation to the stable *trans* product. However such kinetics were highly irreproducible because they depended on the irreproducible amount of Li^+ cations migrating through the cell diaphragm.

be catalyzed by small quantities of phosphine.[6a,24] This latter result is to be compared to the fact that when PhI is reacted with $Pd^0(PPh_3)_4$ instead of low-ligated zerovalent palladium species, one observes an extremely fast formation of *trans*-Ph–$Pd^{II}I(PPh_3)_2$, as evidenced by the immediate appearance of its NMR singlet S_2, without any other observable signal.[11,18]

To conclude this section we wish to emphasize that the effect of chloride ions described above cannot be described in terms of an independent reaction between *trans*-Ph–$Pd^{II}I(PPh_3)_2$ and chloride ions occurring after reactions 7 and 8. This is indeed obvious from a strict thermodynamic point of view, since *trans*-Ph–$Pd^{II}I(PPh_3)_2$ is the final product of the oxidative addition even in the presence of large excesses of chloride ions.[11] This is also further confirmed by the fact that when an authentic sample of *trans*-Ph–$Pd^{II}I(PPh_3)_2$ was left in the presence of excesses of chloride ions, no modification of its resonance (singlet S_2) was observed, except for expected slight shifts due to changes of ionic strength.

Kinetics of Release of Chloride Ions during Oxidative Addition of PhI to Electrogenerated Chloride-Ligated Zerovalent Palladium Complexes, As Determined by Redox Titration. For millimolar concentrations of electrolyzed $Pd^{II}Cl_2(PPh_3)_2$, eq 4 predicts that 1 equivalent of chloride ion is released, while a second equivalent remains coordinated to the zerovalent palladium center.[11d] After completion of the overall process in eqs 7 and 8, this second equivalent is necessarily released, since the final product, Ph–$Pd^{II}I(PPh_3)_2$, does not bear any chloride ligand. Owing to the crucial role of chloride ions on the kinetics of formation of the latter (eq 8), evidenced by the above ^{31}P NMR study, it appeared of importance to decide whether the second equivalent of chloride ion is released upon the initial stage (*viz.* eq 7) or during the second stage (*viz.* eq 8) of the overall oxidative addition.

A series of solutions of electrogenerated low-ligated zerovalent palladium complexes prepared by two-electron electrolysis of $Pd^{II}Cl_2(PPh_3)_2$ (0.055 M) were mixed with PhI (10 equiv) and left to react during different times, after which they were potentiometrically titrated with $AgNO_3$. When the titration was performed immediately after the mixing, the titration curve presented two titration waves, each one corresponding to 1 equiv of silver nitrate per palladium. When the titration was performed after increasing reaction times, the number of silver nitrate equivalents necessary to titrate the first wave decreased, and that required to titrate the second wave increased correspondingly, so that their sum remained constant at 2 equiv. When the reaction time exceeded a few hours, only the second titration wave was observed and required 2 equiv of $AgNO_3$. Independent calibration of the titration procedure with nBu_4NCl and nBu_4NI showed that the second wave corresponded to free chloride ions. The first wave corresponded to a species with a larger affinity for Ag^+ ions than that of free chloride ions but a lesser affinity than that of free iodide ions. Also, independent experiments showed that the iodide ligand of *trans*-Ph–$Pd^{II}I(PPh_3)_2$ could not be titrated by $AgNO_3$.

From this we deduce that the variation with the time of the number of equivalents required to titrate the second wave represents the kinetics of release of free chloride ions in the solution, from 1 equiv at initial time to 2 equiv at large reaction times. In other words, the complement to two of the $AgNO_3$ equivalents required for titration of the second wave (compare Figure 1b) represents the variations with time of a species containing a ligated chloride ion. Comparison of these variations to those observed for species P_1, during the above NMR study (compare Figure 1a), suggests that both variations feature the kinetics of conversion of the same species into the thermodynamically stable *trans* derivative (eq 8).

(24) This result is in agreement with proposed isomerization mechanisms of square planar complexes.[12ii,6a] It is however noteworthy that in ref 19 addition of phosphine results in the opposite effect.

Because of the conservation of the number of equivalents (*viz.* 2) of silver nitrate required to titrate both waves, it is inferred that the first wave corresponded to the titration of palladium-ligated halide ions. Therefore the variation of their concentration with time (identical to those in Figure 1b) reflected also the variations with time of the concentration of species P_1. However it is doubtful that this wave corresponded to the titration of ligated chloride ions, because it necessarily features a titration that is thermodynamically more favorable than that of free chloride ions. On the other hand, independent calibrations with free iodide ions (nBu_4NI) had shown that this first wave featured a titration more difficult than that of free iodide ions. We are thus inclined to rationalize these results by considering that the species P_1 contains a chloride ligand and also an iodide one. The iodide ligand should be preferentially titrated (first titration wave) by reaction of P_1 with $AgNO_3$ to afford a species containing a chloride ligand impossible to titrate. Conversely the conversion of P_1 into Ph-$Pd^{II}I(PPh_3)_2$ generates a free chloride ion that may be titrated at the second wave together with the first equivalent of chloride ion released upon electrolysis of $Pd^{II}Cl_2(PPh_3)_2$. We are therefore able to substantiate further the process schematized above in eqs7 and 8

$$PhI + Pd^0(PPh_3)_2Cl^- \xrightarrow{fast} \mathcal{L}Pd(PPh_3)_2ICl^- \quad (9)$$
(P_1, singlet S_1)

$$\mathcal{L}Pd(PPh_3)_2ICl^- \xrightarrow{slow} \textit{trans}\text{-Ph–}Pd^{II}I(PPh_3) + Cl^- \quad (10)$$
(singlet S_2)

$$\mathcal{L}Pd(PPh_3)_2ICl^- + Ag^+ \rightarrow AgI(\downarrow) + \mathcal{L}Pd(PPh_3)_2Cl$$
(first titration wave) (11)

$$Cl^- + Ag^+ \rightarrow AgCl(\downarrow) \text{ (second titration wave)} \quad (12)$$

where $\mathcal{L}$ represents any other possible ligand of P_1 not yet identified at this stage of the study (*vide infra*). Note that the above rationalization supposes that the halide ligands in $\mathcal{L}Pd(PPh_3)_2Cl$ (*viz.* Cl^-) and in *trans*-Ph–$Pd^{II}I(PPh_3)_2$ (*viz.* I^-) cannot be displaced by $AgNO_3$. An independent check of this hypothesis is obviously impossible for the unknown $\mathcal{L}Pd(PPh_3)_2Cl$ species but was performed for *trans*-Ph–$Pd^{II}I(PPh_3)_2$, as described above. Also, it was checked that when *trans*-Ph–$Pd^{II}I(PPh_3)_2$ is titrated in the presence of chloride ions (1 or 2 equiv of nBu_4NCl), one observes only the titration curve of the corresponding amount of free chloride ions. This confirms independently our above result based on NMR that our observations are not related to any interference between chloride ions and *trans*-Ph–$Pd^{II}I(PPh_3)_2$.

Oxidative Addition of PhI to Electrogenerated Low-Ligated Zerovalent Palladium Complexes, As Monitored by Cyclic Voltammetry at Short Time Scales. The above methods of investigation have allowed several important conclusions to be drawn on the reactivity and structure of the intermediate P_1. However, their use for precise and quantitative kinetics is rather difficult. Indeed, because of the long acquisition times in NMR or of the intrinsic duration of titration procedures, the kinetic variations presented in Figure 1a and b have only a qualitative nature.

In particular, the region corresponding to short times could not be explored kinetically by NMR. Indeed, with this method, the first investigation point corresponds roughly to 15–20 min after the preparation of the solution, a time at which a significant fraction of P_1 has already been converted into *trans*-Ph–$Pd^{II}I(PPh_3)_2$.

Cyclic voltammetry provides an easy way to explore kinetically such initial stages of a reaction. Upon scanning the electrode potential negatively, zerovalent palladium centers may be created

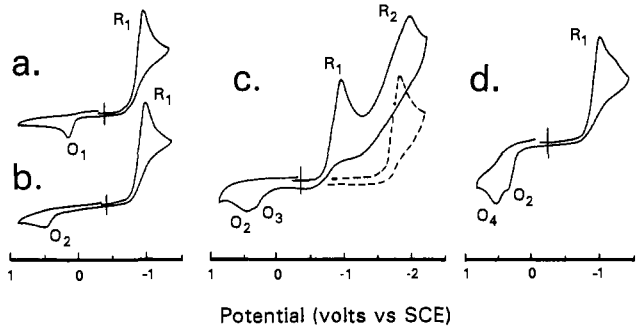
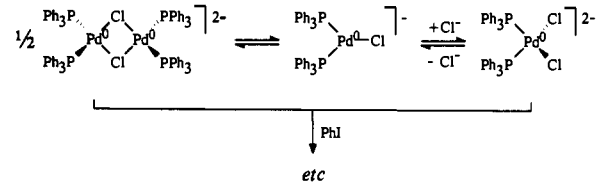


Figure 2. Cyclic voltammetry of $Pd^{II}Cl_2(PPh_3)_2$, 2 mM in THF, 0.3 M nBu_4NBF_4, alone (a) or in the presence of PhI, 10 equiv (b, d) or 1 equiv (c). In part c, the reduction of an authentic sample of *trans*-Ph–$Pd^{II}I(PPh_3)_2$, 2 mM, under identical conditions is shown as the dashed voltammogram. In part d, the voltammogram was performed as in (b) except for the addition of nBu_4NCl, 4 mM (2 equiv) to the solution. Gold disk electrode (diameter 0.5 mm); scan rate, v = 0.2 V s^{-1}; 20 °C.

by reduction of $Pd^{II}Cl_2(PPh_3)_2$ (eq 4) in the presence of PhI and the resulting electroactive products monitored almost immediately either by pursuing the scan negatively (reducible products) or by inverting the scan direction (oxidizable products). Appropriate selection of the potential scan rate, v, allows us to determine the time scale of investigation.[11] However, because of the interference of convective effects at long times,[25] the method, as described just above, cannot be used for reaction times that exceed a few seconds. Voltammetry may nevertheless be used to explore larger time scales, but then only as an analytical tool.[18b] Bulk reactive solutions may be prepared as described above for NMR studies, and the evolution of the electroactive products and intermediates can be monitored as a function of time by cyclic voltammetric investigation of these solutions at selected times. We wish to describe hereafter the results of these two approaches. The present section deals with the short-time one, in which cyclic voltammetry is used simultaneously to create the conditions of the reaction and investigate its progress.

In the absence of PhI or added halide ions, reduction of $Pd^{II}Cl_2(PPh_3)_2$ occurs *via* an overall two-electron process featured by the reduction wave R_1 (E^p = –1.0 V*vs* SCE at v = 0.2 Vs^{-1}) represented in Figure 2a.[11] Upon scan reversal the overall two-electron oxidation of the zerovalent palladium centers created at R_1 (eqs 4–6) is detected at the oxidation wave O_1 (E^p = 0.1 V*vs* SCE at v = 0.2 Vs^{-1}).[11,26] For the same scan rate, but in the presence of PhI (10 equiv), wave R_1 remains unchanged; however, wave O_1 is no longer observed (Figure 2b), showing that all zerovalent palladium centers created at R_1 have been consumed by reaction with PhI within the time required to scan the electrode potential between waves R_1 and O_1. As reported previously,[11] shortening this time scale by increasing the scan rate allows us to recover progressively wave O_1 at its full magnitude. This allowed the complete kinetic characterization of the primary stages of the reaction of PhI with electrogenerated zerovalent palladium centers, represented in Scheme II.[11]

Scheme II



However, the nature of the primary product of oxidative addition (*viz.* P_1), leading ultimately (eqs 9 and10) to the stable *trans*-Ph–$Pd^{II}I(PPh_3)_2$ derivative, could not be fully established in our previous work.[11] P_1 is detected electrochemically by a double signature: a two-electron oxidation wave, O_2 (E^p = 0.405 V*vs* SCE at v = 0.2 Vs^{-1}),[27] observed upon scan reversal (Figure 2b), and a broad two-electron reduction wave, R_2 (E^p = –2.0 V*vs* SCE at v = 0.2 Vs^{-1}), observed when the reductive scan is extended negatively (Figure 2c). When cyclic voltammetry is used to monitor the fate of the reaction product(s) over longer time scales (*vide infra*), these two waves are still present although they have smaller current intensities; no other waves, except for those of chloride ion oxidation or of *trans*-Ph–$Pd^{II}I(PPh_3)_2$ reduction, are observable. Since we know from the above NMR investigation that only one intermediate (P_1) is observable on the way to *trans*-Ph–$Pd^{II}I(PPh_3)_2$, we are led to the conclusion that these waves feature respectively the oxidation and the reduction of an identical intermediate, *viz.* P_1.

Let us first focus on the reduction wave R_2. This wave is observed within the same potential range where the reduction of an authentic sample of *trans*-Ph–$Pd^{II}I(PPh_3)_2$ occurs (compare Figure 2c).[29] However, on the one hand we know from the above study that this latter species is not yet formed in stoichiometric amounts within the time scale considered here, and on the other hand wave R_2 is much broader than that featuring the reduction of the stable *trans* derivative. Moreover no oxidation wave could be observed for an authentic sample of *trans*-Ph–$Pd^{II}I(PPh_3)_2$,

(25) (a) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods*; Wiley and Sons: New York, 1980. (b) A CE mechanism should result in a broadening of wave R_2, as noted experimentally. Moreover, wave R_2 is a catalytic wave because Pd(0) formed by an initial two-electron reduction reacts with PhI to produce again the oxidative addition complex reducible at R_2. Under the conditions of Figure 2c, this results in an apparent broader and larger reduction wave than expected for a simple two-electron wave (for a similar situation, see: Amatore, C.; Jutand, A. *Organometallics* **1988**, *7*, 2203). This phenomenon is however modest in Figure 2c because only 1 equiv of PhI is used. The catalytic current increase arises only because diffusion of PhI occurs with a larger diffusion coefficient than that of palladium-centered species.

(26) Note that oxidation wave O_1 is smaller than reduction wave R_1, although both feature processes involving an identical number of electrons (2) exchanged per molecule.[11] This happens because a significant fraction of the product(s) formed at R_1 and oxidized at O_1 is lost by diffusion toward the solution bulk[25] while the potential is scanned between waves R_1 and O_1. This can be accounted for on a quantitative basis by mathematical treatment of diffusion equations.[25]

(27) (a) In ref 11a, a vinylic analog of P_1 was detected in ^{31}P NMR and electrochemically *via* its two-electron oxidation wave and was tentatively supposed to be the *cis*-vinylpalladium(II) intermediate according to the classical mechanism of oxidative addition in eq 3. Indeed, authentic samples of *trans* derivatives do not give rise to any oxidation wave, whereas some *cis*-constrained square planar complexes (*cis*-R–MX(L–L), L–L = dppe, M = Ni,[28] Pd[29]) may be oxidized: for example, *cis*-Ph–$Pd^{II}I$(dppe) is oxidized at 1.1 V *vs* SCE (E^p at 0.2 V s^{-1}),[11a] whereas *trans*-Ph–$Pd^{II}I(PPh_3)_2$ is not oxidizable before the solvent discharge.[29] In view of the present study, where P_1 is shown to be a chloride-ligated palladium(II) center (*vide infra et* eqs10, 16, 20, 21, and 32), its oxidation may tentatively be ascribed to a CE sequence[25] through which the oxidation of ligated halide ions liberated reversibly by P_1 (*vide infra et* eqs 16, 21, and 32) occurs. Within such an interpretation, and taking into account that free chloride ions are oxidized at a more positive potential (wave O_4 in Figure 2d) than that at which oxidation of P_1 occurs, while free iodide ions are oxidized at a less positive potential (wave O_3 in Figure 2c), it would appear that under these circumstances iodide ions are liberated instead of chloride ones. Such a formulation would then be consistent with the observation that iodide ions ligated to P_1 are selectively titrated by $AgNO_3$ (eq 11). However, this interpretation must be discarded, since it would require wave O_2 to involve a one-electron ($I^- - e \rightarrow {}^1/_2I_2$) or a two-third of an electron ($3I^- - 2e \rightarrow I_3^-$) process, while it corresponds to a two-electron process. Therefore one is led to the conclusion that wave O_2 necessarily features the two-electron oxidation of a palladium(II) center, possibly mediated by its halide ligands *via* an inner-sphere mechanism. (b) All our attempts to characterize an oxidized palladium species resulting from this oxidation either voltammetrically or by preparative electrolysis failed. Yet, in conjunction with the formation of a transient cationic Pd species is the fact that the free chloride oxidation wave (O_4) is not apparent on the voltammogram when no chloride ion is added to the solution (compare *e.g.* Figure 2b to Figure 2d), although we know, on the basis of the chloride ion titration experiment (Figure 1b), that 1 equiv of chloride ion is present under these conditions. We then conclude that the oxidized palladium center formed at wave O_2 scavenges the free chloride ion equivalent. (c) This latter point is in complete agreement with the fact that the peak potential of wave O_2 depends on the chloride ion concentration, being less positive in the presence of added chloride ions (compare wave O_2 in Figure 2b and 2d), showing that chloride ions are involved in the kinetic control of two-electron oxidation wave O_2. For a similar situation involving the two-electron oxidation of a zerovalent palladium center, see Figure 4a in ref 11d.

(28) Amatore, C.; Jutand, A. Quoted in footnote 25b.

(29) Amatore, C.; Jutand, A; Khalil. F.; Nielsen, M. F. *J. Am. Chem. Soc.* **1992**, *114*, 7076.

either in the absence or in the presence of chloride ions. All these facts establish that wave R_2 is not due to the reduction of the *trans* compound but to reduction of P_1 that must therefore be closely related. This close relationship is further confirmed by the identity of the reduction products of P_1 with those of the *trans*-Ph–$Pd^{II}I(PPh_3)_2$ derivative (eq 13):[29]

$$trans\text{-Ph–}Pd^{II}I(PPh_3)_2 + 2e \rightarrow Ph\text{–}Pd^0(PPh_3)_2^- + I^- \quad (13)$$

Oxidation of iodide ions produced upon the reduction at R_2 is observed at wave O_3 (E^p = 0.34 V*vs* SCE at v = 0.2 Vs^{-1}) that is observed upon scan reversal as illustrated in Figure 2c. Similarly, the oxidation of the anionic zerovalent phenylpalladium center, Ph–$Pd^0(PPh_3)_2^-$,[29] may be observed at shorter time scales (E^p = –0.61 V*vs* SCE at v = 200 Vs^{-1}).[30] In addition, as shown in Figure 2c, the diffusional plateau of wave O_2 is rather ill-defined when recorded after the reduction at R_2 has been performed. This stems from two factors: (i) the reduction at R_2 partially depletes the concentration of P_1 in the diffusion layer, giving rise to a smaller oxidation current at O_2, and (ii) the same reduction gives rise to another species oxidizable at a potential slightly positive to wave O_2 (wave O_4; E^p = 0.59 V*vs* SCE at v = 0.2 Vs^{-1}). Both factors result in a poor definition of wave O_2 and in its broadening under these circumstances. Addition of an authentic sample of chloride ions (nBu_4NCl, 2 equiv), as illustrated in Figure 2d, allows us to show that the additional oxidation wave O_4 corresponds to the oxidation of free chloride ions. We may then describe the overall reduction occurring at R_2 by the following balanced equation

$$P_1 + 2e \rightarrow Ph\text{–}Pd^0(PPh_3)_2^- + I^- + Cl^- \quad (14)$$

which agrees with our above formulation (*vide* eqs 9 and 10) and states in addition that P_1 contains a phenyl ligand (*viz.* $\mathcal{L} = C_6H_5$ in eqs 9 and 10).

The presence of a phenyl ligand in P_1 is further confirmed by the variations of the oxidation peak potential of wave O_2 when different organic halides are used instead of PhI:

$$Pd^{II}Cl_2(PR_3)_2 + 2e \xrightarrow{ArX} P_1 \quad (15)$$

These variations reported in Table II demonstrate a strong dependence of $E^p_{O_2}$ on the nature of the aryl moiety, Ar,[31] or on that of the halide substituent, X, of the organic halide, as well as on that of the phosphine ligand of the palladium(II) precursor complex. From these results and the above ones obtained by means of NMR or titration studies, we are led to consider that the minimal structure for the primary intermediate P_1, formed in eq 15, which accounts for all observations is Ar–$Pd^{II}X(PR_3)_2Cl^-$, *i.e.* implies a pentacoordination of the palladium(II) center.[32]

On the basis of this result, it appears puzzling that P_1 and the final product of the reaction, *viz.* the *trans*-Ph–$Pd^{II}I(PPh_3)_2$ derivative, appear to be reducible at very close potentials. Indeed P_1, as described above, is expected to be reducible at more negative potentials than *trans*-Ph–$Pd^{II}I(PPh_3)_2$, because of a Coulombic repulsion due to the negative charge. This agrees with the respective peak positions, as shown in Figure 2c. However, this seems inconsistent with the fact that the foot of the broad wave R_2 is observed in the same potential range where *trans*-Ph–$Pd^{II}I(PPh_3)_2$ is reduced. This objection can be turned down by assuming that one halide ligand may rapidly decoordinate through a rapid uphill equilibrium. Indeed, within the time scale considered here, P_1 could be stable in the bulk solution but oppositely be unstable at the electrode surface because of the reduction of the palladium(II) moiety formed by deligation of the halide ligand. This should result in a continuous displacement of the dissociation equilibrium, that is to the apparent overall reduction of P_1 *via* the following CE sequence[25]

$$Ph\text{–}Pd^{II}X(PPh_3)_2Cl^- \rightleftarrows \{Pd^{II}\} + (Cl^- \text{ or } I^-) \quad (C) \quad (16)$$

$$\{Pd^{II}\} + 2e \rightarrow Ph\text{–}Pd^0(PPh_3)_2^- + (I^- \text{ or } Cl^-) \quad (E) \quad (17)$$

whose balanced equation is identical to that given above in eq 14. It must be emphasized that the species labeled {Pd^{II}} in eqs 16 and 17 cannot be the *trans*-phenylpalladium(II) complex, because we know from above that the latter is stable in the presence of chloride ions. Such a tentative rationalization will be further corroborated in the following.

To conclude this section, we wish to mention the results of the two following experiments that confirm independently our above NMR observations. When voltammetry of $Pd^{II}Cl_2(PPh_3)_2$ is performed in the presence of PhI (eq 15), either in the presence of stoichiometric amounts of sodium cation (2 equiv of $NaBF_4$) or in the presence of catalytic quantities of triphenylphosphine (1–10%), wave R_1 is not affected but the oxidation wave O_2 is no longer observed. It is noteworthy that under such circumstances, wave R_2 is still present but is better defined, being then identical to that observed for an authentic sample of *trans*-Ph–$Pd^{II}I(PPh_3)_2$.[29] Therefore, the presence of catalytic amounts of

Table II. Oxidation Peak Potentials (Wave O_2) of the Primary Intermediate (P_1) of the Oxidative Addition of Aryl Halides (ArX) to Zerovalent Palladium Complexes Electrogenerated by Reduction of Divalent Palladium Complexes ($Pd^{II}Cl_2(PR_3)_2$)[a,b]

ArX		$Pd^{II}Cl_2(PR_3)_2$	
Ar	X	R	E^p (V)[a]
C_6H_5	I	C_6H_5	0.405
	I	*n*-C_4H_9	0.555
	Br	*n*-C_4H_9	0.315
p-CH_3–C_6H_4	I	C_6H_5	0.500
	I	*n*-C_4H_9	0.615
	Br	*n*-C_4H_9	0.460
p-CH_3O–C_6H_4	I	C_6H_5	0.395
	I	*n*-C_4H_9	0.650
	Br	*n*-C_4H_9	0.300
2-C_4H_3S[c]	I	C_6H_5	0.380
	Br	C_6H_5	0.475

[a] In V *vs* SCE, as determined at a gold disk electrode (0.5-mm diameter) in THF, 0.3 M nBu_4NBF_4. Scan rate 0.2 V s^{-1}. 25 °C. [b] Initial concentrations: $Pd^{II}Cl_2(PR_3)_2$, 2 mM; ArX, 20 mM. [c] 2-Thienyl.

(30) (a) The lifetime of Ph–$Pd^0(PPh_3)_2^-$ is extremely short under our conditions.[29] In order to perform this experiment one must use an unsymmetrical potential scan. P_1 is electrogenerated[11] and reduced simultaneously during a potential step of 1-s duration performed on the plateau of wave R_2; Ph–$Pd^0(PPh_3)_2^-$ is detected during a rapid potential scan (v > 10 V s^{-1})[29] performed toward positive potentials immediately after the end of the negative potential step. Also an unsymmetrical scan with a slow forward scan (v < 1 Vs^{-1})[11] toward negative potentials could have been used to generate P_1, instead of a potential step. (b) Within a larger time scale (as *e.g.* in Figure 2c) Ph–$Pd^0(PPh_3)_2^-$ decomposes to afford a benzene σ-anion, that is protonated to PhH, and a $Pd^0(PPh_3)_2$ moiety.[29] The latter undergoes a rapid oxidative addition with PhI that diffuses toward the electrode while the potential is scanned back. Thus no signature due to Ph–$Pd^0(PPh_3)_2^-$ (or to its follow-up products) may be observed in Figure 2c.

(31) Due to its electrochemical irreversibility, the peak potential of the two-electron oxidation wave O_2 features both thermodynamic ($E°$) and kinetic (rate constants of electron transfer, k_s, and of follow-up chemical reactions, k) parameters.[25a] Its unsystematic variations as a function of Ar or of X (I, Br) may then result from competition between these effects.

(32) (a) Pentacoordinated palladium(II) complexes are supposed intermediates in isomerization mechanisms of square planar complexes.[12,6a,15] Some have also been characterized kinetically[11a] or been isolated; see *e.g.*: Albano, V. G.; Castellari, C.; Cucciolito, M. E.; Panunzi, A.; Vitagliano, A. *Organometallics* **1990**, *9*, 1269 and references therein. Pentacoordinated palladium(II) complexes are also supposed intermediates in the substitution step.[5b] (b) In eqs 20, 32, and 33 and Scheme III we indicate for simplicity only one possible structure for P_1 and P_2. Other trigonal bipyramidal structures, as well as square pyramidal ones,[15] are obviously possible provided they respect the chemical equivalence of the two phosphine ligands if they are not labile within the NMR time scale. Conversely if these trigonal bipyramidal and/or square pyramidal structures are sufficiently labile, they may all be represented and be involved in fast fluxional equilibria (as suggested in the mechanism of isomerization of square planar complexes; see *e.g.* ref 15, pp 199–200), so as to afford a single ^{31}P NMR signal.

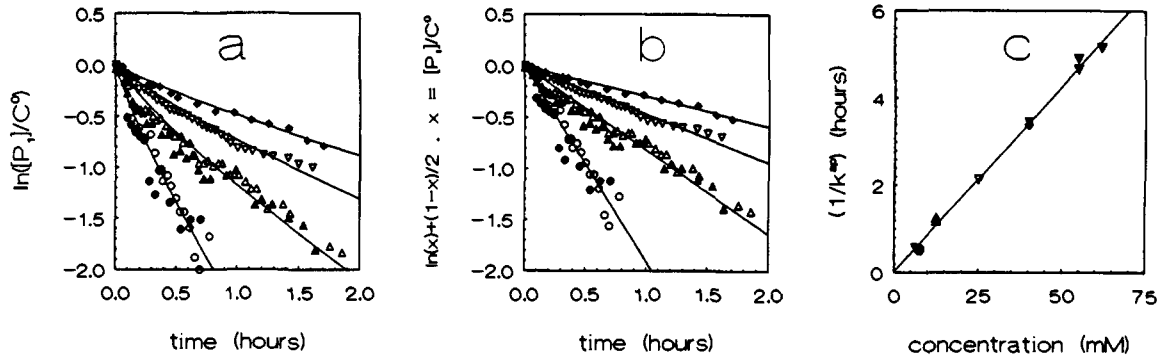


Figure 3. Variations of the concentration of the primary intermediate of oxidative addition (P_1) as a function of time as monitored by steady state voltammetry (eq 18). Gold disk ultramicroelectrode (diameter 25 μm); scan rate, $v = 0.02$ V s^{-1}; 20 °C. P_1 was generated by addition of PhI (10 equiv) to solutions of zerovalent palladium electrogenerated *via* a two-electron reduction of $Pd^{II}Cl_2(PPh_3)_2$ solutions of concentration $C°$ in THF, 0.3 M nBu_4NBF_4, in the absence of added chloride ions. (a) First-order-kinetics plot of data as a function of time. (b) Plot of the data shown in part a according to the rate law in eq 30. (c) Variations of the apparent rate constant k^{ap} (eqs 30 and 31) with $C°$. In parts a and b, $C° = 7.5$ (○, ●), 12.5 (△, ▲), 25 (▽), and 40 (◆) mM. Solid curves in part a or solid lines in part b correspond to eq 30 with $k^{ap} = 1.9$ (○, ●), 0.82 (△, ▲), 0.47 (▽), and 0.294 (◆) h^{-1}. Correlation coefficients of linear regressions: in part b, $r = 0.950$ (○, ●), 0.984 (△, ▲), 0.992 (▽), and 0.995 (◆); in part c, $r = 0.998$.

phosphine or the scavenging of chloride ions by sodium cations[23] results in a considerable increase in the rate of formation of *trans*-Ph–$Pd^{II}I(PPh_3)_2$.

Oxidative Addition of PhI to Electrogenerated Low-Ligated Zerovalent Palladium Complexes, As Monitored by Cyclic Voltammetry at Long Time Scales. As explained above, cyclic voltammetry *per se* allows only the exploration of short time scales, *viz.* under a few seconds. However, the time variations of the voltammograms of solutions of zerovalent palladium (prepared by two-electron reduction of $Pd^{II}Cl_2(PPh_3)_2$) after their reaction with ArX, allow us to investigate the kinetics of the reaction in eq 10 over longer times. In the previous section we have identified that the primary intermediate of oxidative addition, P_1, gives rise to two electrochemical signatures: an oxidation wave (O_2) and a reduction wave (R_2). Because wave R_2 overlaps with the reduction wave of the final product of the reaction, *trans*-Ph–$Pd^{II}I(PPh_3)_2$, the kinetics of decay of P_1 cannot be followed by monitoring the variations of this wave. Conversely, since *trans*-Ph–$Pd^{II}I(PPh_3)_2$ does not give any oxidation wave,[29] the kinetics of P_1 decay can be monitored by the variations of the peak current of wave O_2 as a function of time. Because of a partial contribution of chloride ion oxidation at the peak potential of wave O_2 (compare Figure 2d), the concentration of P_1 at time t, $[P_1]_t$, is not strictly proportional to the current, $(i_{O_2})_t$, measured at wave O_2 for this time. However, it can easily be deduced (see Experimental Section) that at any time t

$$[P_1]_t/C° = [(i_{O_2})_t - (i_{O_2})_\infty]/[i(i_{O_2})_0 - (i_{O_2})_\infty] \quad (18)$$

where $(i_{O_2})_0$ and $(i_{O_2})_\infty$ are the values of i_{O_2} at zero and infinite time, respectively, and $C°$ is the initial concentration of the electrolyzed divalent palladium complex. Equation 18 is valid when plateau currents of wave O_2 in steady-state voltammetry at ultramicroelectrodes are used instead of currents measured with transient voltammetry. Steady-state voltammetry led to better accuracies in $[P_1]_t/C°$ determinations and was therefore used for measurements of the data reported hereafter.

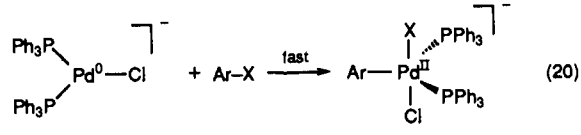
The variations of $\ln([P_1]_t/C°)$ *vs* time are represented in Figure 3a for different values of the initial palladium concentration $C°$. It is easily deduced from these variations that the observed kinetics are quite complex, a result that agrees with our previous qualitative observations based on NMR. The plots of $\ln([P_1]_t/C°)$ *vs* time become linear for large conversions, evidencing that the kinetic regime featuring the conversion of P_1 into *trans*-Ph–$Pd^{II}I(PPh_3)_2$ approaches then a pseudo-first-order law:

$$d[P_1]/dt \xrightarrow[t \to \infty]{} -k[P_1] \quad (19)$$

It is also noteworthy that the rate of conversion, *viz.* k, decreases with the initial concentration $C°$ (compare Figure 3a) in a fashion reminiscent of that noted above (see Figure 1a) upon increasing the chloride ion concentration.

Discussion

Mechanism of Oxidative Addition to Low-Ligated Zerovalent Palladium Complexes in the Presence of Halide Ions. The above results have established that oxidative addition of aryl halides to electrogenerated zerovalent palladium complexes proceeds to the corresponding *trans*-Ar–$Pd^{II}X(PPh_3)_2$ derivatives. However the final product of the reaction is formed through the intermediacy of an unknown transient species termed P_1, whose formation occurs within a few tenths of a second, as reported previously.[11d] On the basis of cyclic voltammetry, halide titration experiments, and ^{31}P NMR investigations, it has been shown that the minimal chemical structure to be considered to describe the properties of P_1 is Ar–$Pd^{II}(PPh_3)_2XCl^-$, where the two phosphines are chemically equivalent. To account for these facts, one may then propose that P_1 consists of a pentacoordinated anionic palladium(II) species with two chemically equivalent phosphine ligands or represents a series of pentacoordinated intermediates involved in rapid fluxional equilibia, so that a single phosphorus NMR is observed.[32a] This is schematized in eq 20, using one possible structure among all those possible:[32b]



(20)

This (or these) pentacoordinated intermediate(s) evolve(s) over a few hours to afford ultimately the *trans* derivative and a chloride ion. Although this evolution occurs *via* a complex kinetic law, no other intermediate could be detected either by NMR or by cyclic voltammetry. This evidences that if such other intermediate exists it must follow a kinetic steady-state regime. On the other hand, we know that an increase of the chloride ion concentration decreases severely the conversion rate, although the stability of the final product of the reaction (*viz. trans*-Ar–$Pd^{II}X(PPh_3)_2$) is not affected by the presence of a large excesses of chloride ions. The simplest mechanism that reconciles all the above facts consists in considering that P_1 is involved in a rapid uphill equilibrium that affords a second intermediate P_2 and a chloride ion. A subsequent first-order reorganization of P_2 would ultimately afford the *trans* derivative:[33]

(33) Note that eq 21 is identical to eq 16, with $P_2 = \{Pd^{II}\}$.

$$\mathrm{Ar\text{-}Pd^{II}(PPh_3)_2XCl^-} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{P_2} + \mathrm{Cl^-} \qquad (K_1 = k_1/k_{-1} \ll 1\ \mathrm{mM}) \quad (21)$$

$$\mathrm{P_2} \xrightarrow{k_2} \textit{trans}\text{-Ar-Pd}^{\mathrm{II}}\mathrm{X(PPh_3)_2} \quad (22)$$

Assuming that P_2 obeys a steady-state kinetic law (*vide supra*) affords the following rate law for the overall conversion of P_1 into the *trans* arylpalladium(II) complex

$$\mathrm{d[P_1]}/\mathrm{d}t = -k^*[\mathrm{P_1}] \quad (23)$$

where

$$k^* = k_1k_2/(k_2 + k_{-1}[\mathrm{Cl^-}]) \quad (24)$$

is a time-dependent pseudo-rate constant, since the concentration in chloride ions varies with time. However, at long reaction times, this latter concentration tends toward $(2 + n)C^\circ$, where n is the number of equivalents of chloride ions intentionally added to the solution. In agreement with the above experimental observations (compare eq 19), the kinetics of conversion then approaches a first-order law (eq 23) with $k^* \rightarrow k$, such as

$$k = k_1/[1 + (k_{-1}/k_2)(2 + n)C^\circ] \quad (25)$$

For shorter reaction times, the general kinetic law in eqs 23 and 24 has to be considered. From the conservation law of chloride ions

$$[\mathrm{Cl^-}] = (2 + n)C^\circ - [\mathrm{P_1}] \quad (26)$$

one obtains

$$\mathrm{d[P_1]}/\mathrm{d}t = -k_1k_2[\mathrm{P_1}]/\{k_2 + (2 + n)k_{-1}C^\circ - k_{-1}[\mathrm{P_1}]\} \quad (27)$$

whose integration yields readily

$$\ln([\mathrm{P_1}]/C^\circ) + \epsilon(1 - [\mathrm{P_1}]/C^\circ) = -kt \quad (28)$$

where

$$\epsilon = k_{-1}C^\circ/[k_2 + (2 + n)k_{-1}C^\circ] \quad (29)$$

and k is identical to that defined in eq 25.

The data reported in Figure 3a were obtained in the absence of added chloride ion ($n = 0$). Double parameter regression analysis (compare ref 34, for a similar rate law and description of the method used) of these data afforded values of ϵ that were close to 0.5, within the experimental accuracy of their determination ($\epsilon = 0.5 \pm 0.1$). Moreover no systematic deviation from the mean value at 0.5 could be observed upon concentration changes. This implies that in eq 29 the term $(2 + n)k_{-1}C^\circ$ dominates over k_2, so that $\epsilon \approx 0.5$. This establishes in turn that the reverse reaction 21 is much faster than reaction 22, eq 21 acting then as a rapid pre-equilibrium followed by eq 22 acting as the rate-determining step of the process. Under these conditions eq 28 simplifies into

$$\ln([\mathrm{P_1}]/C^\circ) + (1 - [\mathrm{P_1}]/C^\circ)/(2 + n) = -k^{\mathrm{ap}}t \quad (30)$$

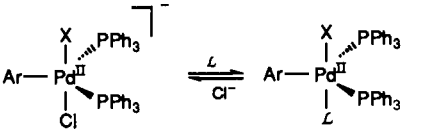
with

$$k^{\mathrm{ap}} = k_1k_2/(2 + n)k_{-1}C^\circ = k_2K_1/(2 + n)C^\circ \ll k_2 \quad (31)$$

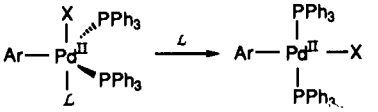
Figure 3b presents the results of the regression analysis of the data in Figure 3a on the basis of the rate law in eq 30. The ensuing values of k^{ap} are plotted as a function of the concentration in Figure 3c, together with other k^{ap} values also determined by cyclic voltammetry ($n = 0$).[35] As expected from the formulation in eq 31, it is seen that the reciprocal of k^{ap} linearly correlates with C°. The fact that a zero intercept is obtained further confirms that $(2 + n)k_{-1}C^\circ \gg k_2$; indeed if this inequality was not satisfied, k^{ap} would obey a law identical to that in eq 25, with $k^{\mathrm{ap}} = k$, that predicts a positive intercept.

The slope of the correlation line in Figure 3c affords $k_2K_1 = k_2(k_1/k_{-1}) = 2.35 \times 10^{-2}$ M h^{-1}. From this value and the rate law in eqs 30 and 31, the variations of the concentration $[P_1]$ as a function of time can be evaluated under conditions that differ significantly from those considered in Figure 3. Such predicted variations shown for example by the solid curves in Figure 1 are in reasonable agreement with the data obtained under the conditions of the ^{31}P NMR or titration studies.

All the above data obtained by NMR, titration, or cyclic voltammetry are thus consistent with the description of the conversion of P_1 into the stable *trans*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$ derivative along the sequence of reactions 21 and 22. This sequence involves an endergonic intermediate, P_2 , that is involved in a fast equilibrium with P_1 , and may spontaneously yield *trans*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$. P_2 could not be observed spectroscopically or voltammetrically because of its extremely small concentration. The formulation in eq 21 tends to imply that this second intermediate is a tetraligated palladium(II) species, *i.e.* an isomer of the *trans* product, namely the *cis*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$ derivative. Because pentacoordinated complexes such as P_1 are considered to be intermediates in *cis-trans* isomerizations,[15] a direct conversion (such as in eq 22) of P_2 into the *trans*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$ product is highly doubtful. Also, pentacoordinated intermediates such as P_1 are considered to be thermodynamically unstable[15] *vis a vis cis* or *trans* tetracoordinated species, in opposition to the uphill nature of eq 21. It is then doubtful that P_2 may consist of a *cis*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$. We are thus inclined to consider that P_2 is not a tetraligated species, but that reaction 21 is actually a reversible substitution of a chloride ligand by a solvent molecule. Deligation of this weak solvent ligand would then afford the *trans*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$ product. This is shown in eqs 32 and 33 by considering one of the possible structures[32] for P_1 ($\mathcal{L}$ = THF):



(32)



(33)

Without spectroscopic evidences to allow a structural characterization of P_2, it is impossible to confirm this hypothesis. However, it is interesting to parallel it with the effect noted in the presence of catalytic amounts of phosphine. Indeed we know from our previous studies that, in the presence of chloride ions, the addition of a few percent of triphenylphosphine does not change the initial step of oxidative addition.[11d] Therefore P_1 remains the initial product of the reaction. However, we have shown above that under these conditions P_1 is no longer observable even in fast cyclic voltammetric experiments. This implies that the rate of conversion of P_1 into *trans*-Ph-Pd$^{\mathrm{II}}$I(PPh$_3$)$_2$ is dramatically increased by the presence of catalytic amounts of triphenylphosphine. Such an effect may easily be rationalized within the formulation used in eqs 32 and 33 by considering that in the

(34) See Experimental Section, pp 7480–7481, in: Schlesener, C. J.; Amatore, C.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7472.

(35) All kinetics monitored by cyclic voltammetry were performed in the absence of intentionally added chloride ions ($n = 0$) because oxidation of these latter interfere with the determination of the peak current of wave O_2 (*vide supra et* eq 18).

presence of catalytic amounts of phosphine the role of the solvent is played by a phosphine ($\mathcal{L}$ = PPh_3). This would amount to stabilization the uphill intermediate P_2 and therefore to an increase in the overall rate of formation of the *trans*-Ph–$Pd^{II}I(PPh_3)_2$ product.

Effect of Intentionally Added Sodium Ions. The addition of 2 equiv of $NaBF_4$ to the solution results also in a dramatic increase of the rate of formation of the stable *trans*-Ph–$Pd^{II}I(PPh_3)_2$ derivative. This increase exceeds a factor 10 000, since under these conditions P_1 could not be observed even on the voltammetric time scale. The reasons for such an increased rate may be multiple. On the basis of Negishi's results,[9] it is expected that the chloride-ligated zerovalent palladium species ion pairs with sodium ions when those are present before the oxidative addition occurs. The resulting new reagent may then undergo oxidative addition by PhI through a different reaction path leading directly to the *trans* derivative without the intermediate formation of P_1. Alternatively, oxidative addition to this reagent may still proceed through the sequence described here, yet leading to an intermediate akin to P_1 but involving ion pairing with sodium ions. Conversion of such a species into P_2 is expected to be thermodynamically favored because the elimination of a tight [Na^+, Cl^-] ion pair should stabilize the right-hand side of reaction 32 and prevent the backward reaction from occurring.[23] We know from the above study that, already in the absence of sodium ions, reactions 32 (in both directions) and 33 are intrinsically fast, although the whole conversion is slow because reaction 32 is uphill and equilibrated. Therefore, favoring its thermodynamics and preventing its backward reaction from occurring should result in a dramatic increase of the rate of the overall conversion.

It is almost impossible to decide between these two possibilities on the basis of the short time scale voltammetric experiments. Indeed, in these experiments, sodium ions are necessarily present in the solution before zerovalent palladium centers are electrogenerated. However, in the ^{31}P NMR experiments or when cyclic voltammetry is used as a monitoring device, PhI was introduced in the solution prior to $NaBF_4$. Oxidative addition, a fast reaction, then proceeds within less than a second[11b] in the absence of sodium ions and necessarily affords P_1 as established above. The immediate disappearance of P_1 upon addition of $NaBF_4$ (2 equiv) to the resulting solutions is therefore strong evidence that the second alternative discussed above occurs efficiently under these conditions.[36]

Relevance of the Mechanism in Eqs 20, 32, and 33 to the Mechanism of Palladium-Catalyzed Nucleophilic Substitutions. As summarized in Scheme I, catalysis of nucleophilic substitutions by palladium complexes is considered to proceed along three successive steps: (i) oxidative addition of the organic halide or pseudohalide to a zerovalent low-ligated palladium species;[4] (ii) nucleophilic substitution of the halide or pseudohalide ligand at the palladium(II) center formed in step i;[5] (iii) reductive elimination of the organic substituted moiety from the palladium(II) center formed in step ii,[6] to afford the low-ligated zerovalent palladium center necessary for step i to occur. Some of these three steps may actually involve pre- or postisomerization reactions as discussed in the Introduction. However, for our purpose here, a three-step decomposition is sufficient. It is noteworthy that the catalytic centers that propagate this sequence, *viz.* Pd^0L_2 (step i),*trans*-R–$Pd^{II}XL_2$ (step ii), and *trans*-R–$Pd^{II}NuL_2$ (step iii), have considerably different energies. Thus, even under the most favorable conditions, that is when the relative concentrations of these three species approach their equilibrium values, the concentration of the most unstable one, Pd^0L_2, is almost negligible, the palladium catalyst being mainly "stored" under the form of the two other species. On strict thermodynamic grounds there is nothing to object to such a situation, since the energy balance for one cycle is imposed by the substitution reaction alone: the energy used to effect the uphill reductive elimination (step iii) is brought back by the medium to which it was released upon the downhill oxidative addition (step i). However, from a kinetic point of view the situation in Scheme I is highly disadvantageous. Indeed, the rate of a catalytic cycle being necessarily less than that of any of its constitutive reactions, the rate of the cycle in Scheme I is smaller than the effective rate of the oxidative addition in step i

$$\text{rate} = -d[RX]/dt = d[RNu]/dt \leq k_{ox.ad}[RX][Pd^0L_2] = (k_{ox.ad}\kappa_{Pd})[RX][Pd] \xrightarrow{\kappa_{Pd} \to 0} 0 \quad (34)$$

where $k_{ox.ad}$ is the rate constant of oxidative addition, [Pd], the overall concentration in palladium centers, and κ_{Pd} the fraction of palladium being under the form of Pd^0L_2. The value of $k_{ox.ad}$ is necessarily limited because of the bimolecular nature of the oxidative addition.[37] It is thus understood that the occurrence in Scheme I of palladium(II) intermediates that are much more stable than the zerovalent one considerably slows down the rate of the catalytic sequence, because this makes κ_{Pd} vanishingly small. Note that, although not usually explained as above, this is the basic principle of action of nondestructive inhibitors in chemical or enzymatic catalysis: on strict thermodynamic grounds they should result in no effect at all,[38] yet they may impede a catalytic sequence by making the concentration of active centers too small for obtaining a significant rate of conversion.

It should then be understood that although each of the steps in Scheme I may exist individually and may have been characterized alone at several instances,[1-6] their association as in Scheme I to describe an effective catalytic sequence is somewhat unlikely on kinetic grounds. A more efficient sequence would be one where the zerovalent species would be partially stabilized whereas the divalent intermediates would be destabilized, so that the palladium catalyst would be distributed almost equally. This is exactly what happens in the sequence of reactions 20 and 32 that have been identified in this work. Indeed, if one replaces the ligand $\mathcal{L}$ in equation 32 by a nucleophile, Nu^-,[39a] or an olefin,[39b] it is seen that equation 32 is a surrogate to nucleophilic substitution at the palladium(II) center of Scheme I or consists in the olefinic preactivation step in the Heck reaction. Moreover, such a ligand exchange is expected to be extremely fast since reaction 32 was shown to act as a rapid pre-equilibrium in the sequence of reactions 32 and 33. It is also noted that since the energetic difference between the pentacoordinated palladium(II) species formed in equation 32 ($\mathcal{L}$ = Nu^-) and the halide-stabilized $Pd^0XL_2^-$ center is necessarily less than that between the stable *trans*-R–$Pd^{II}XL_2$ and the much more unstable low-ligated Pd^0L_2 species, such a reductive elimination is favored thermodynamically *vis a vis* that invoked in Scheme I. On the basis of these considerations,[41] the catalytic sequence represented in Scheme III appears as a much more efficient alternate to that usually considered to describe the

(36) However, this does not imply that the first alternative cannot operate when sodium ions are initially present.

(37) $k_{ox.ad}$ is necessarily smaller than the diffusion limit.

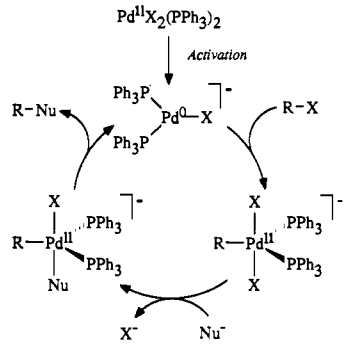
(38) Since they involve reversible reactions. In other words the situation is akin to that encountered here for the two *trans*-palladium(II) complexes in Scheme I.

(39) (a) Similarly, the nucleophile could replace the chloride ligand recoordination in the backward eq 32. The occurrence of one of these two processes depends on the associative or dissociative (interchange)[40] nature of the substitution. (b) In the Heck reaction, the role of the fifth ligand (*viz.* $\mathcal{L}$ in P_2, and eqs 32 and 33, Nu in Scheme III) may be played by the olefin moiety. The pentacoordinated intermediates would then closely ressemble those isolated by Albano *et al.* (reference given in footnote 32a).

(40) See, *e.g.*: Langford, C. H.; Gray, H. B. *Ligand Substitution Processes*; W. A. Benjamin, New York, 1965.

(41) Furthermore, the fluxional lability of pentacoordinated species is considered to be extremely high,[15] these species acting as uphill intermediates in the isomerization of square planar complexes. The organic and nucleophilic ligands have easily adequate relative positions for reductive elimination.

Scheme III



mechanism of palladium-catalyzed nucleophilic substitutions under conditions where free halide ions are present.[42]

It is noteworthy that the formation of the stable *trans*-arylpalladium(II) species *via* eq 33, that is an essential step of the mechanism of Scheme I, represents a side reaction for the mechanism in Scheme III. Because reductive elimination from this species is feasible,[6] this reaction is not a dead-end route; yet, it decreases the efficiency of the overall catalysis by diverting part of the palladium catalyst from the more efficient cycle in Scheme III. These predictions are in full agreement with the results reported in Table I.

For simplicity, in Scheme III we have considered that the halide or pseudohalide ions originating from the divalent palladium precursor, the organic halide, or those added to the reaction medium are identical. Under practical experimental conditions the three anions may differ and the sequence in Scheme III is then most certainly complicated by halide-exchange reactions that may take place between two of the steps considered in Scheme III.[39] Similarly, under our conditions tetrabutylammonium cations are the only cationic species present in the medium, except when $NaBF_4$ was added to the solution. Such large ions are expected to introduce only small perturbations in Scheme III *via* ion-pairing effects. However, when reduction of the divalent palladium(II) catalyst precursor is performed by a Grignard reagent, an organometal, *etc.*, and/or when the nucleophile consists of such species,[1,9] ion-pairing effects are expected to be involved in the catalytic mechanism. A first consequence will imply a fine tuning of the halide or pseudohalide ions interchange mechanisms discussed above, because of selective ion pairing. Ion pairing is also expected to affect the chemical reactivity of the three anionic palladium species considered in Scheme III. For example, Negishi *et al.* have proposed that reduction of a dihalide palladium(II) complex $Pd^{II}X_2L_2$ by Grignard or organometallic reagents, RM, resulted in the formation of $[Pd^0L_2(XM)_n]_m$ species ($n = 1, 2$; $m \geq 1$?).[9] This earlier conclusion based upon NMR studies was further substantiated (see Scheme II) by a minute kinetic investigation of the reaction performed on the basis of electrochemical data.[11b,d] It was thus shown that addition of $LiClO_4$ to a solution of $Pd^0L_2Cl^-$ electrochemically generated in the presence of NBu_4BF_4 resulted as expected in an increased rate of oxidative addition by iodobenzene.[11d] However, such ion pairing affected only modestly the reactivity of halide-ligated zerovalent palladium species, the overall rate being only twice that determined in the absence of added Li^+ cations. Our present observation that the presence of stoichiometric amounts of $NaBF_4$ increases considerably the rate of formation of the *trans*-arylpalladium(II) shows that ion-pairing effects play a much more important role on the fate of the primary products of oxidative addition. This suggests that the relative involvement of the mechanisms in Schemes I and III may be finely adjusted by addition to the reaction medium of Lewis acids or of small cations (*e.g.* from groups Ia or IIa) associated with large anions. Indeed, because of selective ion pairing with halide ions, the presence of free small cations should favor the catalytic mechanism in Scheme I, resulting in an overall decrease of the reaction efficiency (compare *e.g.* Table I in ref 1b: Li^+ and $Na^+ \ll MgBr^+ < ZnCl^+$). In agreement with numerous reports,[42] the presence of chloride ions associated with large cations (*viz.* NR_4Cl) is predicted to have opposite consequences. Indeed, they are expected to favor Scheme III (or its analogs for the Heck reaction)[39b] because they stabilize halide-ligated zerovalent or divalent palladium-centered complexes.[11d] In nucleophilic substitutions, they may also have an additional positive role based on their ability to confiscate small metal cations (those generated by the nucleophile upon reaction of its organic anion) by preferential ion pairing. The effect of an addition of chloride ions associated to small cations (*viz.* LiCl, *etc.*)[42a,b] is however difficult to predict for what concerns the relative importance of the mechanisms in Schemes I and III. Yet, in any case they should help to stabilize the zerovalent palladium centers.[9,11b]

Finally, on the basis of our observation that the presence of substoichiometric amounts of phosphine also greatly accelerate the rate of formation of the *trans*-arylpalladium(II) derivative, it is inferred that the presence of more than 2 equiv of phosphine ligand per palladium center should result in a trend for the catalytic reaction to proceed *via* the intermediacy of this latter derivative, *viz.* to prefer the slower mechanism in Scheme I. An example of this situation is given by the comparison of entries 5 and 6 in Table 1, where it is seen that, for the same amount of catalyst, the system using Pd^0L_4 is much slower than the other.[43]

(42) Following an initial report by T. Jeffery (Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287) tetraalkylammonium halides have been frequently used to facilitate difficult palladium catalyzed nucleophilic substitutions; see, *e.g.*: (a) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033. (b) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478. (c) Andersson, C. M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 2112. (d) Friess, B.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1988**, *29*, 4089. (e) Karabellas, K.; Hallberg, A. *J. Org. Chem.* **1989**, *54*, 1773. (f) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581. (g) Arcadi, A.; Cacchi, S.; Marinelli, F.; Morera, E.; Ortar, G. *Tetrahedron* **1990**, *46*, 7151. The presence of halide ions and particularly of chloride ions appears also to be crucial to the success of the Heck reaction under several circumstances: (h) Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667. (i) Grigg, R.; Sridharan, B.; Stevenson, P.; Worakun, T. *J. Chem. Soc., Chem. Commun.* **1986**, 1697. (j) Jeffery, T. *Synthesis* **1987**, 70. (k) Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1987**, *28*, 3039. (l) Larock, R. C.; Babu, S. *Tetrahedron Lett.* **1987**, *28*, 5291. (m) Larock, R. C.; Baker, B. E. *Tetrahedron Lett.* **1988**, *29*, 905. (n) Larock, R. C.; Song. H.; Baker, B. E.; Gong, W. H. *Tetrahedron Lett.* **1988**, *29*, 2919. (o) Larock, R. C.; Stinn, D. E. *Tetrahedron Lett.* **1988**, *29*, 4687. (p) Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, *44*, 2033. (q) Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, *44*, 2049. (r) Burns, B.; Grigg, R.; Sridharan, V.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4325. (s) Burns, B.; Grigg, R.; Ratananukui, P.; Sridharan, V.; Stevenson, P.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4329. (t) Jeffery, T. *Synth. Commun.* **1988**, *18*, 77. (u) Larock, R. C.; Johnson, P. L. *J. Chem. Soc., Chem. Commun.* **1989**, 1368. (v) Hoffmann, H. M. R.; Schmidt, B.; Wolff, S. *Tetrahedron* **1989**, *45*, 6113. (w) Larock, R. C.; Gong, W. H.; Baker, B. E. *Tetrahedron Lett.* **1989**, *30*, 2603. (x) Amorese, A.; Arcadi, A.; Bernocchi, E.; Cacchi, S.; Cerrini, S.; Fedeli, W.; Ortar, G. *Tetrahedron* **1989**, *45*, 813. (y) Grigg, R.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S. *Tetrahedron* **1989**, *45*, 3557. (z) Carlström, A. S.; Frejd, T. *Synthesis* **1989**, 2049. (aa) Larock, R. C.; Berrios-Pena, N.; Narayanan, K. *J. Org. Chem.* **1990**, *55*, 3447. (bb) Larock, R. C.; Fried, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 5882. (cc) Lawsky, A.; Reiser, O.; de Meijere, A. *Synlett* **1990**, 405. (dd) Andersson, C. M.; Larsson, J.; Hallberg, A. *J. Org. Chem.* **1990**, *55*, 5757. (ee) Arcadi, A.; Bernocchi, E.; Cacchi, S.; Marinelli, F. *Synlett* **1991**, 27. (ff) Grigg, R.; Markandu, J. *Tetrahedron Lett.* **1991**, *32*, 279. (gg) Arcadi, A.; Cacchi, S.; Delmastro, M.; Marinelli, F. *Synlett* **1991**, 407. (hh) Arcadi, A.; Cacchi, S.; Delmastro, M.; Marinelli, F. *Synlett* **1991**, 409. (ii) Larock, R. C.; Kuo, M. Y. *Tetrahedron Lett.* **1991**, *32*, 569. (jj) Carlstroem, A. S.; Frejd, T. *J. Chem. Soc., Chem. Commun.* **1991**, 1216. (kk) Grigg, R.; Coulter, R. *Tetrahedron Lett.* **1991**, *32*, 1359. (ll) Jeffery, T. *Tetrahedron Lett.* **1991**, *32*, 2121. (mm) Grigg, R.; Sukirthalingam, S.; Sridharan, V. *Tetrahedron Lett.* **1991**, *32*, 2545. (nn) Grigg, R.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* **1991**, *32*, 3855. (oo) Arcadi, A.; Bernocchi, E.; Cacchi, S.; Marinelli, F. *Tetrahedron* **1991**, *47*, 1525. (pp) Carlstroem, A. S.; Frejd, T. *J. Org. Chem.* **1991**, *56*, 1289. (qq) Larock, R. C.; Berrios-Pena, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615. (rr) Larock, R. C.; Lu, Y. D.; Bain, A. C.; Russell, C. E. *J. Org. Chem.* **1991**, *56*, 4589. (ss) Larock, R. C.; Yum, E. K. *J. Am. Chem. Soc.* **1991**, *113*, 6689. (tt) Larock, R. C.; Lee, N. H. *J. Am. Chem. Soc.* **1991**, *113*, 7815. (uu) Carlstroem, A. S.; Frejd, T. *Acta Chem. Scand.* **1992**, *46*, 163. (vv) Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. R. *J. Org. Chem.* **1992**, *57*, 976.

(43) Use of Pd^0L_4 results also in a diminished rate of oxidative addition.[11d,18]

Conclusion

The mechanism of oxidative addition of iodobenzene to zerovalent palladium species generated by reduction of their divalent precursor complexes has been investigated. The reaction proceeds *via* a three-step mechanism: A first step involves a rapid addition of iodobenzene to the halide-stabilized zerovalent palladium species. The pentacoordinated divalent palladium species thus formed is in rapid uphill equilibrium with another palladium(II)-centered species that slowly affords the stable *trans*-arylpalladium(II) product of the reaction.

The occurrence of this mechanism suggests that when free halide ions are available, the cycle in Scheme I that is classically used to describe the mechanism of palladium-catalyzed nucleophilic substitution may be overrun by a faster catalytic cycle (Scheme III) involving halide-ligated palladium species. Most of the predictions or conclusions on reactivity of catalytic systems and conditions that could be drawn out on the basis of Scheme I remain obviously valid for Scheme III. In addition, the mechanism in Scheme III accounts for several other important factors such as the increased efficiency of these catalytic systems in the presence of halide ions.[42] Similarly, the mechanism in Scheme III explains the fact that several nucleophilic substitution reactions proceed faster in the presence of catalytic palladium than when the reaction is performed stoichiometrically using the *trans*-R–$Pd^{II}XL_2$ complex. Indeed, within the framework of Scheme III, this species is no longer an essential intermediate of the catalytic sequence, as in Scheme I, but is a side product that deviates some of the catalyst from the fast cycle in Scheme III to the slower cycle in Scheme I.

Experimental Section

Chemicals. THF (Janssen) was stored over potassium hydroxide for 24 h and distilled from a sodium benzophenone solution under an argon atmosphere before use. It was transferred to the cells according to standard Schlenk procedures. nBu_4NBF_4 was obtained from the hydrogen sulfate salt (Janssen), by treatment with $NaBF_4$ (Janssen) in water, and was further recrystallized from ethyl acetate/petroleum ether, dried under vacuum, and stored under argon before use. nBu_4NCl and nBu_4NI were commercial (Janssen); they were dried by melting under vacuum and stored under argon before use. Palladium complexes (starting materials and products) were synthesized according to published procedures.[7,11,29]

^{31}P NMR spectra were recorded in THF on a Bruker 162-MHz spectrometer using H_3PO_4 as an external reference.

Electrochemical Setup and Electrochemical Procedures. Cyclic voltammetry and chronoamperometry were performed as described in previous works of this group.[11] Electrodes consisted of gold disks of 0.5-mm or 25-μm diameter that were selected as a function of scan rate. A home-built potentiostat equipped with positive feedback for ohmic-drop compensation was used.[44] The reference electrode was an SCE (Tacussel) separated from the solution by a bridge (3 mL) filled with a 0.3 M nBu_4NBF_4 solution in THF, identical with that used in the cell. All potentials given here refer to this reference electrode. All the experiments reported here were performed at 20 °C (Lauda RC20 thermostat). All data were stored using a Nicolet 391 digital oscilloscope and transferred to a PC-386 (Amstrad) for treatment and presentation of the results.

Electron consumptions in transient electrochemistry were determined following a method previously described that combines the use of classical working electrodes and ultramicroelectrodes.[11c] Other electrochemical procedures including preparation of stock solutions of electrogenerated zerovalent palladium complexes were identical with those previously described.[11d]

Silver nitrate titrations were performed according to classical procedures with a silver electrode (Tacussel) and a TS-4N Tacussel pH meter-titrimeter. PhI was added to a solution (30 mL) of electrogenerated zerovalent palladium (*vide infra*). Aliquots (1 mL) were taken at selected times, poured into 30 mL of acidic water (H_2SO_4, 0.1 N), and titrated with aqueous $AgNO_3$, 1 mM. Threshold potentials were determined and compared to those measured upon independent calibrations using authentic samples of nBu_4NI and nBu_4NCl.

Description of Typical Procedure for Electrogeneration of Low-Ligated Zerovalent Palladium for Kinetic Measurements. Electrolysis of $Pd^{II}Cl_2(PPh_3)_2$ at a selected concentration in 30 mL of THF, 0.3 M nBu_4NBF_4, was performed in a divided cell.[11] Electrolysis was interrupted after the consumption of two Faradays permole, and the concentration of zerovalent palladium was checked to be identical to that of the initial divalent palladium complex, based on the peak current of its oxidation wave in cyclic voltammetry (wave O_1 in Figure 2a). PhI (10 equiv) was then added, and it was checked by cyclic voltammetry that the zerovalent palladium was totally consumed and replaced by the primary intermediate P_1. $NaBF_4$ (2 equiv) or PPh_3 (1–10%) were then possibly added (see text). Aliquots of these solutions were taken for ^{31}P NMR (2 mL) or titration (1 mL) experiments. For monitoring the decay of P_1 by cyclic voltammetry, a gold ultramicroelectrode (25-μm diameter) was inserted into the catholyte of the cell and steady-state voltammetry[45] of the solution was performed at selected time intervals over the potential range –0.4 to +1 V *vs* SCE. Because of the presence of wave O_4 (compare Figure 2d), the current plateau of wave O_2 was not perfectly resolved. Measurements were therefore performed at a constant potential corresponding to that of the inflection point between the two waves.

Derivation of Eq 18. The current measured at the potential of wave O_2 is the sum of two contributions: one is due to the product of interest (P_1) and the other to free chloride ions. One has therefore at any selected potential[25]

$$i_{O_2} = \alpha[P_1] + \beta[Cl^-]$$

where α and β are two unknown factors independent of time. On the other hand, the conservation law for chloride ions is written as

$$[Cl^-] = (2 + n)C^\circ - [P_1]$$

where C° is the initial concentration of $Pd^{II}Cl_2(PPh_3)_2$ and n the number of equivalents of $nNBu_4Cl$ added to the solution. It then follows that at any time t

$$(i_{O_2})_t = (\alpha - \beta)[P_1]_t + (2 + n)\beta C^\circ$$

Since $[P_1]_\infty = 0$, one has $(i_{O_2})_\infty = (2 + n)\beta C^\circ$, from which one obtains

$$[(i_{O_2})_t - (i_{O_2})_\infty] = (\alpha - \beta)[P_1]_t$$

Introducing $[P_1]_0 = C^\circ$ eliminates the unknown factor $(\alpha - \beta)$, which affords finally eq 18.

$$[P_1]_t/C^\circ = [(i_{O_2})_t - (i_{O_2})_\infty]/[(i_{O_2})_0 - (i_{O_2})_\infty]$$

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