Mechanism of Aryl Chloride Oxidative Addition to Chelated Palladium(0) Complexes

Moshe Portnoy and David Milstein*

Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot 76100, Israel

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The mechanism of oxidative addition of aryl chlorides to $Pd(dippp)_2$ (**1**) has been studied in depth. ^{31}P NMR monitoring of the reaction of **1** with chlorobenzene in dioxane reveals that *cis*-(dippp)Pd(Ph)Cl (**2**) and *trans*-(η^1-dippp)$_2$Pd(Ph)Cl (**3**) are formed in parallel pathways and are also in equilibrium with each other, **2** being favored both kinetically and thermodynamically. The reaction is first order in chlorobenzene and approximately first order in Pd(0), the deviation resulting from a parallel equilibrium between **1** and the binuclear complex (dippp)Pd(μ-dippp)-Pd(dippp). Strong rate retardation by added dippp is observed, the reaction being approximately reciprocal first order in dippp. **1** undergoes reversible dissociation of dippp, followed by rate-determining oxidative addition of chlorobenzene to the 14-electron complex (dippp)Pd (**5**), whose existence was demonstrated directly by inversion transfer NMR experiments using (dippp)-$PdP^iPr_2{}^nBu$. The trans complex **3** is formed directly from the 14-electron complex (η^1-dippp)$_2$-Pd. Rate constants for oxidative addition of substituted aryl chlorides show an excellent fit to the Hammet σ^- constants, $\rho = +5.2$, whereas the fit to σ is poor. Activation parameters of $\Delta H^{\ddagger}_{obs} = 28 \pm 3$ kcal/mol and $\Delta S^{\ddagger}_{obs} = -2 \pm 8$ eu were measured; since $\Delta S^{\ddagger}_{obs} = \Delta S^{\circ}_{diss} + \Delta S^{\ddagger}_{OA}$ and $\Delta S^{\circ}_{diss} \gg 0$, then $\Delta S^{\ddagger}_{OA}$, $\ll 0$. These observations taken together provide strong evidence for an S_NAr-type charged transition state, probably stabilized by partial chloride coordination.

Introduction

Preparation of various aromatic compounds from aryl halides is an important part of modern organic synthetic chemistry.[1] A wide scope of palladium-catalyzed functionalization reactions has been developed for aryl bromides and iodides.[2,3] Unfortunately, aryl chlorides are much less reactive in such processes. Obviously, extending the scope of aryl halide functionalization to the chloro analogues is of great interest for synthetic laboratory and industrial chemistry.

In the past few years, we have reported successful Pd-catalyzed carbonylation, formylation and reduction of chloroarenes to yield amides, esters, acids,[4a] aldehydes,[4b] and arenes.[4c] The reactions exhibit high yields, and a large variety of functional groups are tolerated. The catalyst utilized in this series of processes is (dippp)Pd-(η^1-dippp) (**1**) [dippp = 1,3-bis(diisopropylphosphino)-propane], a trigonal unsaturated Pd(0) complex. The catalytic processes exhibit a strong dependence on the ligands utilized for the catalyst. Ligands very similar to dippp, such as dippb or dippe, form a less efficient catalyst (in the case of formylation, they are absolutely inefficient). Ligands differing more significantly from dippp in their electronic, steric, and chelating properties usually fail to form an active catalyst. Other catalytic systems for aryl chloride carbonylation under different conditions have also been recently reported.[5]

We found that the catalytic cycles mentioned above[4] proceed through a common rate-determining step—oxidative addition of the chloroarene to a Pd(0) complex. Investigation of this step can provide us with the reason for the uniqueness of the observed processes and for the superiority of the dippp complexes over other Pd(0) phosphine complexes. We have observed that even under CO pressure, the CO-free complex **1** is present in the reaction mixture[6] and it is active toward the oxidative addition of PhCl, while the CO-coordinated species are not. Therefore, we concentrated our efforts on the mechanistic investigation of the reaction of **1** with chloroarenes and have compared it with reactions of Pd(0) complexes of various other phosphine ligands with chlorobenzene. The results of the mechanistic studies are reported in this work, while comparative studies are summarized in the preceding article.[7]

The oxidative addition of haloarenes to d^{10} metal phosphine complexes has been a topic of much interest[8] because of its relevance to many important catalytic processes. In systems involving Ni(0) phosphine complexes, a concerted mechanism[9] involving a three-centered transition state, as well as an electron transfer mechanism[10] proceeding through an ion pair intermediate, consisting

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[1] March, J. *Advanced Organic Chemistry*; John Wiley & Sons: New York, 1985.

[2] Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: London, 1985; pp 184–195, 223–227, 276–287, 348–362, 415–418.

[3] Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: Berlin, 1980; pp 137–146.

[4] (a) Ben-David, Y.; Portnoy, M.; Milstein, D. *J. Am. Chem. Soc.* **1989**, *111*, 8742. (b) Ben-David, Y.; Portnoy, M.; Milstein, D. *J. Chem. Soc., Chem. Commun.* **1989**, 1816. (c) Ben-David, Y.; Gozin, M.; Portnoy, M.; Milstein, D. *J. Mol. Catal.* **1992**, *73*, 173.

[5] (a) Huser, M.; Youinou, M.-T.; Osborn, J. A. *Angew Chem., Int. Ed. Engl.* **1989**, *28*, 1386. (b) Dufaud, V.; Thivolle-Cazat, J.; Basset, J.-M. *J. Chem. Soc., Chem. Commun.* **1990**, 426. (c) Dufaud, V.; Thivolle-Cazat, J.; Basset, J.-M.; Mathiew, R.; Jaud, Z.; Waissermann, J. *Organometallics* **1991**, *10*, 4005. (d) Grushin, V. V.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1992**, 611.

[6] Portnoy, M.; Milstein, D. Unpublished.

[7] Portnoy, M.; Milstein, D. *Organometallics*, preceding article in this issue.

[8] (a) Stille, J. K.; Lau, K. S. J. *Acc. Chem. Res.* **1977**, *10*, 434. (b) Koshi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press, New York, 1978; pp 168–173 (see also references therein). (c) Parshall, G. W. *J. Am. Chem. Soc.* **1974**, *96*, 2360.

[9] (a) Fahey, D. R. *J. Am. Chem. Soc.* **1970**, *92*, 402. (b) Fahey, D. R.; Mahan, J. E. *J. Am. Chem. Soc.* **1977**, *99*, 2501. (c) Foa, M.; Cassar, L. *J. Chem. Soc., Dalton Trans.* **1975**, 2572.

[10] (a) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 6319. (b) Reference 9b.

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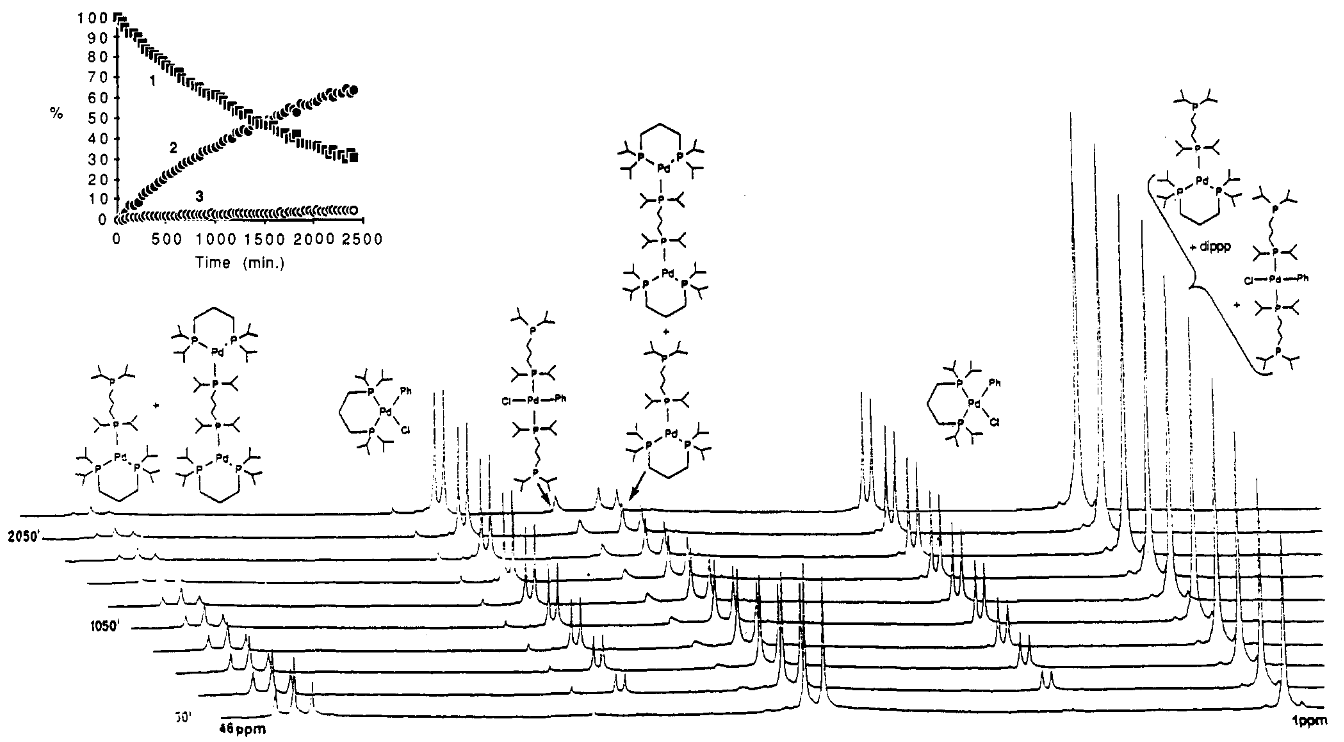


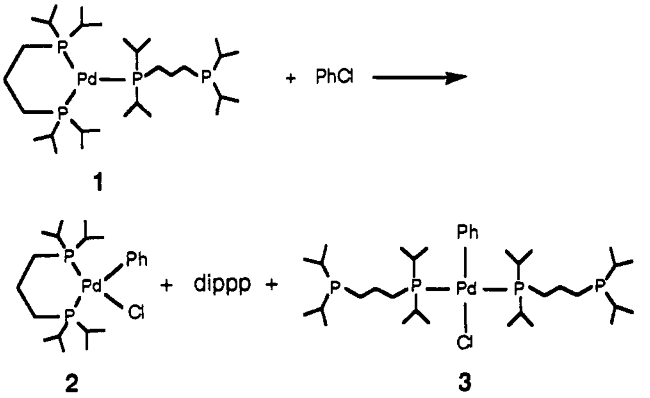
Figure 1. Reaction progress in a typical experiment, a 73 mM solution of 1 in dioxane reacted with a 10-fold excess of PhCl at 50 °C: (a) ^{31}P{^{1}H} NMR follow-up; (b, inset) reaction mixture composition as a function of time.

of an aromatic anion radical and Ni(I) complex, were suggested. The only reaction explored till now that dealt with a Pd(0) complex was oxidative addition of haloarenes (mainly iodoarenes) to Pd(PPh$_3$)$_4$.[11] In all cases, the 14-electron Pd(PPh$_3$)$_2$ complex was found to be involved in the oxidative addition process. Pathways proceeding through neutral[11a] and charged[11b,c] transition states were proposed. However, none of the reported studies, to our knowledge, dealt with addition of nonactivated chloroarenes to Pd(0). Similarly, none of the studies had mechanistically explored oxidative addition of haloarene to complexes of electron-rich *chelating* ligands.

In light of these facts, we have embarked on a mechanistic investigation aimed at understanding the nature of this important organotransition metal transformation. The attractiveness of aryl chlorides as starting materials for the preparation of various aromatic substances, combined with their relative inertness, makes the thorough study of their oxidative addition to metal centers necessary and potentially very beneficial.

Results and Discussion

a. Reaction of Pd(dippp)$_2$ with PhCl. The complex Pd(dippp)$_2$ reacts with a variety of aryl chlorides in various solvents. For example, the reaction of Pd(dippp)$_2$ with a 10-fold excess of PhCl in dioxane at 90 °C is accompanied by a yellow color loss and is completed in ca. 2 h (eq 1). Three products are observed by ^{31}P{^{1}H} NMR of the reaction mixture at the end of the reaction. Two doublets at 11.2 and 29.0 ppm belong to *cis*-(dippp)Pd(Ph)Cl (**2**), ca. 93% yield, reported in the preceding article.[7] The free dippp ligand appears as a singlet at 2.6 ppm. **3** (7% yield) appears as a small singlet at 24.5 ppm (P coordinated to Pd) accompanied by a singlet at 1.9 ppm (free P).[12] The analogous complexes *trans*-(P^{i}Pr$_2$^{n}Bu)$_2$Pd(Ph)Cl and *trans*-(η^1-dippb)$_2$Pd(Ph)Cl exhibit singlet peaks in ^{31}P{^{1}H} NMR at 24.6 and 24.3 ppm, respectively.[7] ^{13}C{^{1}H} NMR of the reaction mixture exhibits a small broad singlet at 150.8, assigned to C$_{ipso}$ of **3** in analogy with *trans*-(η^1-dippb)$_2$-Pd(Ph)Cl in which C$_{ipso}$ appears as a broad singlet at 152.6 ppm. The most important piece of evidence for the identification of **3** was supplied by a reaction of pure *cis*-(dippp)Pd(Ph)Cl with a slight excess of dippp. ^{31}P NMR of the reaction mixture revealed that, while most of the starting material remained unchanged, a singlet at 24.5 ppm appeared, pointing unequivocally at *trans*-(η^1-dippp)$_2$-Pd(Ph)Cl as the reaction product and indicating the existence of equilibrium (2). This is also supported by ^{31}P NMR monitoring of the mixture of products, which resulted from the reaction of 1 with 4-MeC(O)C$_6$H$_4$Cl (after the reaction was completed), which showed that the ratio between the three species, dippp, *cis*-(dippp)Pd(4-MeC-



(1)

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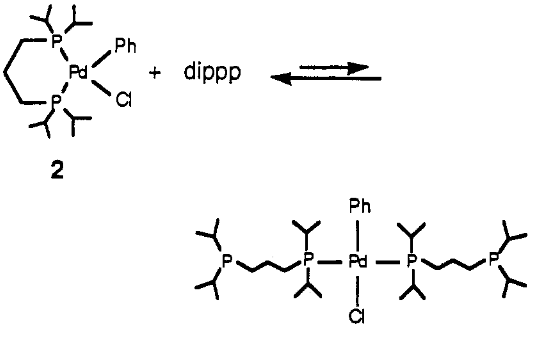
(11) (a) Amatore, C.; Pfluger, F. *Organometallics* **1990**, *9*, 2276. (b) Fauvarque, J.-F.; Pfluger, F.; Troupel, M. *J. Organomet. Chem.* **1971**, *28*, 287. (c) Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287.

(12) Formation of binuclear *trans,trans*-(Ph)Pd(Cl)(μ-dippp)$_2$Pd(Ph)-Cl, as well as oligomeric products, cannot be excluded. However, formation of 3 is more likely in the presence of excess dippp.



2

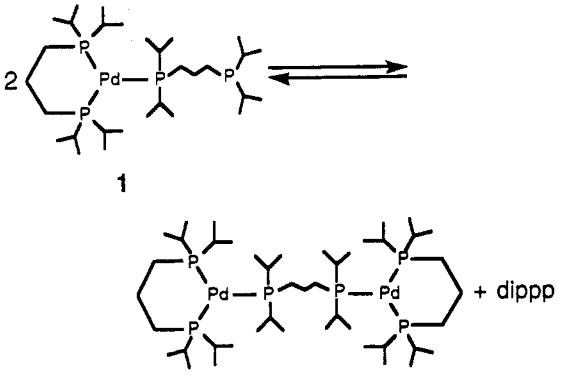
3

(2)

(O)C$_6$H$_4$)Cl and *trans*-(η^1-dippp)$_2$Pd(4-MeC(O)C$_6$H$_4$)Cl remained unchanged (hourly spectra were taken at 60 °C for 8 h).

b. Kinetics and Mechanism. ^{31}P{^{1}H} NMR provided a useful tool for measuring the oxidative addition kinetics. As may be seen in Figure 1a, reaction of 1 with chlorobenzene is accompanied by the growth of the doublets assigned to *cis*-(dippp)Pd(Ph)Cl and of the singlet due to *trans*-(η^1-dippp)$_2$Pd(Ph)Cl, while the signals of Pd(dippp)$_2$ constantly decrease.[13] The well-separated signals enable accurate determination of the reaction mixture composition (Figure 1b). Our solvent of choice is dioxane, because of the following reasons. The rate of the reaction is sensitive to the polarity of the solvent and follows the order hexane < dioxane ≈ THF < DMF. The solubility of Pd(dippp)$_2$ in DMF is limited, while protic solvents, such as methanol, protonate the Pd(0) complex.[14] Low boiling solvents, like THF and acetone, were not suitable for the temperature range of our kinetic measurements (30–70 °C).

Reaction 1 does not follow simple kinetics. While it is first order in the chloroarene (Figure 2), it is only approximately first order in Pd(0) and approximately reciprocal first order in dippp. We believe that deviation from simple kinetics is caused by equilibrium (3) of the zerovalent palladium in solution.[7]



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4

(3)

To explain the influence of equilibrium (3) on the reaction kinetics more clearly, we will refer to the central part of the mechanism—formation of the major product 2 (the framed part of Figure 3).

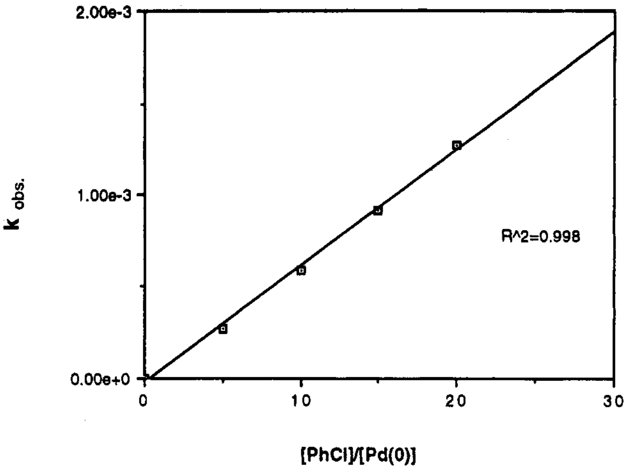
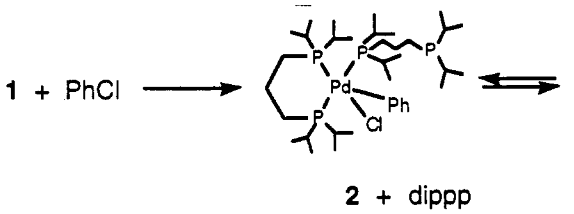


Figure 2. Dependence of k°_{obs} on the ratio [PhCl]/[Pd(0)]. In each experiment, $[Pd(0)]_{start}$ = 0.073 M.

As established by several reports, oxidative addition of aryl iodides to Pd(0) complexes proceeds through an unsaturated 14-electron Pd(0) intermediate.[11] Involvement of such an intermediate in the oxidative addition of chlorobenzene to Pd(dippp)$_2$ fits our observation of strong retardation of the reaction rate by added dippp.

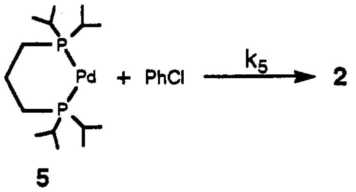
A mechanism inolving direct oxidative addition of PhCl to the 16-electron complex 1, followed by ligand dissociation (eq 4) can be excluded, on the basis of the following



(4)

reasoning. If the oxidative addition step of mechanism 4 is slower than ligand dissociation, additions of excess ligand should not affect the reaction rate (addition of excess dippp to 1 does not lead to formation of a saturated complex in any detectable amount). On the other hand, if one assumes that ligand dissociation from the saturated complex is rate-determining, then this pentacoordinate intermediate should be observable; we have not observed an intermediate in any of our kinetic experiments, nor have we been able to generate it by addition of dippp to the oxidative addition product.

The most plausible 14-electron intermediate in the formation of 2 is Pd(dippp) (5). Equilibrium (3) is most likely to proceed through this intermediate, and the existence of 5 was proven by an inversion transfer NMR experiment, as will be described below. The rate-determining step of complex 2 formation is the irreversible oxidative addition of PhCl to 5, since a dissociation-controlled reaction should not be very sensitive to the ligand addition.



5

(5)

Therefore, the approximate kinetic law for the formation

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(13) Under the experimental conditions, free ligand is inseparable on the NMR scale from the signal of the free phosphine "arm" of 1. This explains the growth of the broad singlet at ca. 2 ppm during the reaction course.

(14) Portnoy, M.; Milstein, D. To be published.

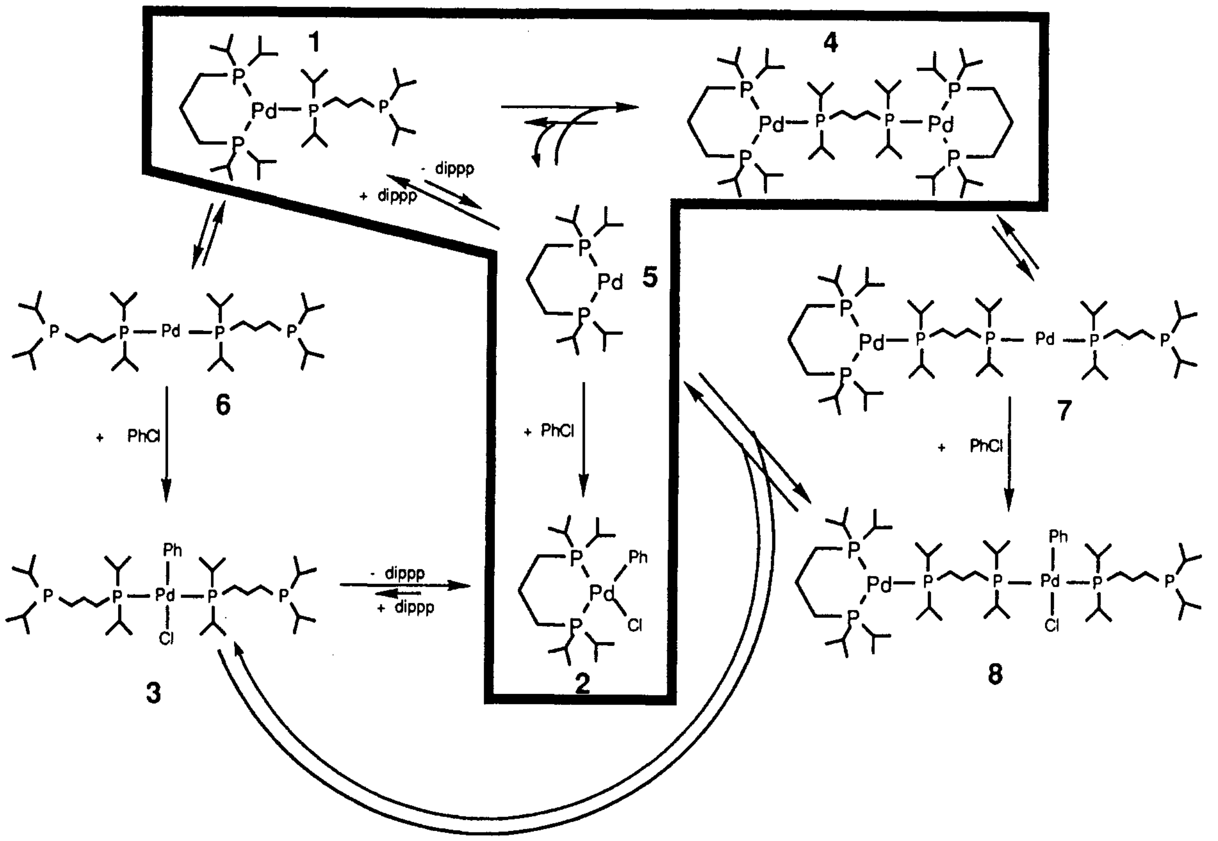

Figure 3. Proposed mechanism of reaction 1.

of 2 is $v = k_5[\mathrm{PhCl}][\mathbf{5}]$ (I).[15] The steady-state concentration of **5**, taking into consideration eq 5 and the preequilibria (6) and (7), is given by (II).

$$\mathbf{1} \underset{k_{-6}}{\overset{k_6}{\rightleftarrows}} \mathbf{5} + \text{dippp} \qquad K_6 = k_6/k_{-6} \tag{6}$$

$$\mathbf{4} \underset{k_{-7}}{\overset{k_7}{\rightleftarrows}} \mathbf{1} + \mathbf{5} \qquad K_7 = k_7/k_{-7} \tag{7}$$

$$[\mathbf{5}] = (k_6[\mathbf{1}] + k_7[\mathbf{4}])/(k_{-6}[\text{dippp}] + k_{-7}[\mathbf{1}] + k_5[\text{PhCl}]) \quad \text{(II)}$$

The term $k_5[\mathrm{PhCl}]$ should be very small compared to the two other terms in the denominator and can, therefore, be ignored. One can easily see that combination of equilibria (6) and (7) leads to equilibrium (3). The equilibrium constant K_3 is, therefore, given by K_6/K_7. The concentration of **4**, thus, can be easily obtained as $(K_6/K_7)([\mathbf{1}]^2/[\text{dippp}])$. Substituting this into the simplified version of eq II gives[16] $[\mathbf{5}] = K_6[\mathbf{1}]/[\text{dippp}]$ (III). Therefore, one can see that $v = k_5[\mathrm{PhCl}]K_6[\mathbf{1}]/[\text{dippp}]$ (IV) or, expressing [**1**] through [**4**], $v = k_5[\mathrm{PhCl}](K_6K_7[\mathbf{4}]/[\text{dippp}])^{1/2}$ or $v = k_5[\mathrm{PhCl}]K_7[\mathbf{4}]/[\mathbf{1}]$.

Thus, the reaction rate is proportional to the term [**1**]/[dippp] and to the term [**4**]/[**1**]. Unfortunately, the ratio between **1** and the total amount of zerovalent palladium is not constant during the reaction and the same is true for **4**. Therefore, the reaction rate is not proportional to the total zerovalent palladium and the reaction is not strictly first order in Pd(0). We cannot prove experimentally whether the reaction is first order in **1** or **4**, since their $^{31}\mathrm{P}\{^1\mathrm{H}\}$ NMR patterns are inseparable under the reaction conditions.[7] However, the obedience of the reaction, in its early stage, to first-order kinetics in zerovalent palladium is quite good, since the ratios $[\mathbf{1}]/[\mathrm{Pd(0)_{total}}]$ and $[\mathbf{4}]/[\mathrm{Pd(0)_{total}}]$ are not changed dramatically during this stage of the reaction.

According to eq IV, the rate is inversely proportional to dippp concentration and the reaction should be reciprocal first order in the free ligand. However, the $^{31}\mathrm{P}\{^1\mathrm{H}\}$ NMR signal of the free dippp is inseparable, under the reaction conditions, from the signal of the free "arm" in $\mathrm{Pd(dippp)_2}$. Therefore, precise evaluation of the free ligand concentration in the reaction mixture at $t = 0$ is impossible. This fact, we believe, is the cause of the imperfection in the determination of the reaction order in dippp.

Additional mechanistic pathways, leading to the trans complex **3**, that were ignored in the discussion till now are presented in Figure 3. The 14-electron intermediates **6** and **7** were not observed, but there are several facts supporting their existence. Chelate ring opening in Pd(0) complexes of dippp is one of two possible explanations for the major differences in the dynamic behavior of the complexes **1** and **4** in solution.[7] In addition, analogous intermediates are necessary to explain the fact that the trans product is formed faster than the cis in the case of dippb.[7] Linear intermediates L–Pd–L are involved in various oxidative additions to Pd(0) complexes of monodentate ligands.[17] Stable complexes of this type were

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[15] Assuming $v = \mathrm{d}[\mathbf{2}]/\mathrm{d}t = k_5[\mathrm{PhCl}][\mathbf{5}]$, we neglect equilibrium (2), which does not contribute significantly to $\mathrm{d}[\mathbf{2}]/\mathrm{d}t$, according to our observations.

[16] Simplified by ignoring the term $k_5[\mathrm{PhCl}]$, as explained in the text.

[17] (a) Reference 11. (b) Di Bugno, C.; Pasquali, M.; Leoni, P.; Sabatino, P.; Braga, D. *Inorg. Chem.* **1989**, *28*, 1390. (c) Urata, H.; Suzuki, H.; Moro-oka, Y.; Ikawa, T. *J. Organomet. Chem.* **1989**, *364*, 235. (d) Otsuka, S. *J. Organomet. Chem.* **1980**, *200*, 191.

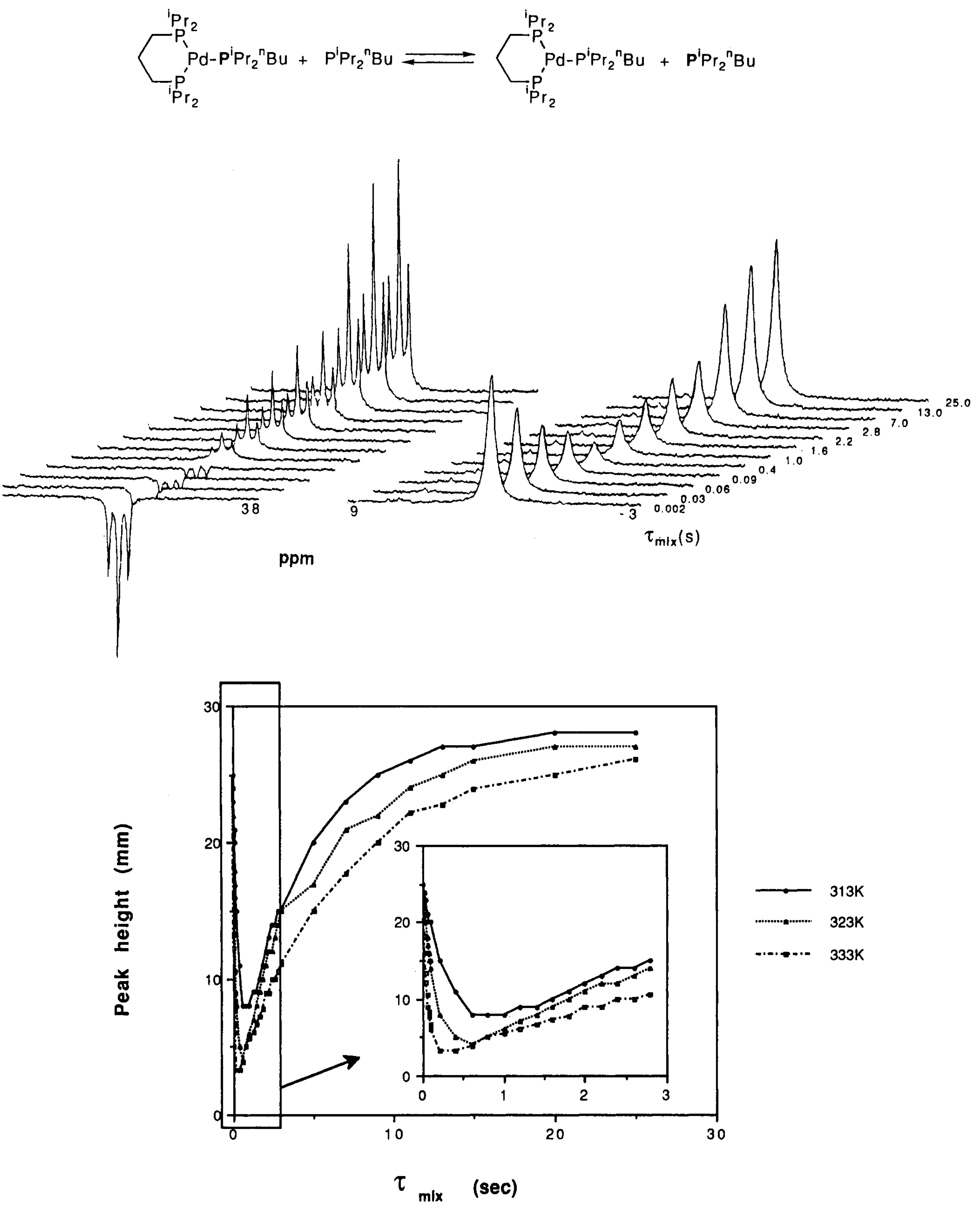

Figure 4. Inversion transfer experiment for a 1:1 mixture of 9 and P^{i}Pr$_2$^{n}Bu in dioxane: (a) as was monitored by ^{31}P{^{1}H} NMR at 60 °C; (b) free ligand signal intensity as a function of the mixing time.

prepared for more bulky ligands,[18] and we have also observed such a species in solution for L = P^{i}Pr$_2$^{n}Bu,[7] a monodentate analogue of dippp. The formation of the binuclear Pd(II)/Pd(0) complex 8 is supported by the observation that, at the beginning of the reaction, two small and very close singlets appear at 24.5 ppm. As the reaction proceeds, one of them grows significantly (**3**) and the other (**8**) decreases until it disappears completely.

The complete mechanism of the reaction contains the equilibrium (2) as well (Figure 3). This equilibrium is slower than the overall direct formation of **2** and **3**, through

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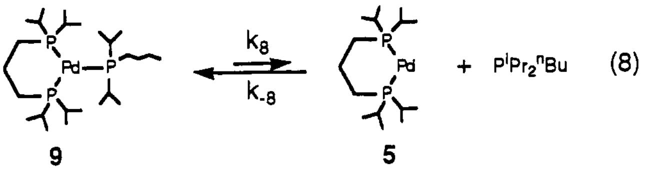
[18] (a) Kuran, W.; Musco, A. *Inorg. Chim. Acta* **1975**, *12*, 187. (b) Otsuka, S.; Yoshida, T.; Matsumoto, M.; Nakatsu, K. *J. Am. Chem. Soc.* **1976**, *98*, 5850.

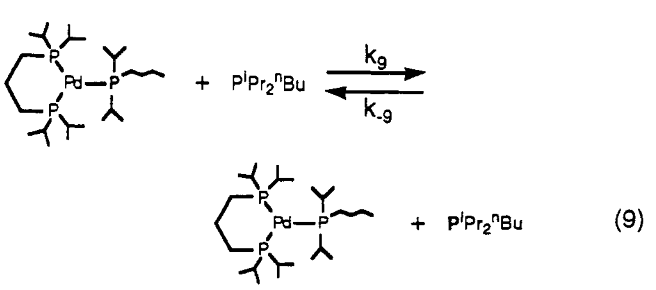
their 14-electron precursors, as one can conclude by analogy with the reaction of (dippb)Pb(μ-dippb)Pd(dippb) with PhCl.[7] Thus, the complex *cis*-(dippp)Pd(Ph)Cl (**2**) is preferable to *trans*-(η^1-dippp)$_2$Pd(Ph)Cl (**3**) not only thermodynamically but also kinetically (**2** is formed faster than **3** before the equilibrium between them has time to act in any direction). This kinetic preference may be a result of the following two reasons: (a) the concentration of the 14-electron intermediate **5** is higher than the sum of the concentrations of **6** and **7**; (b) the rate of oxidative addition of PhCl to **5** is higher than that to **6** and **7**. While we do not have information about the first possibility, the second is justified on theoretical grounds. Upon the decrease of the P–M–P angle in MP$_2$ complexes (M = Pt or Pd, P = phosphine ligand), the nucleophilicity of the complex increases.[19] As a result, the reactivity of the chelated 14-electron d^{10} complex Pd(dippp) (**5**) toward oxidative addition is superior to that of the nonchelated 14-electron complex (η^1-dippp)$_2$Pd (**6**).

c. Inversion Transfer Experiment. The existence of the equilibrium leading to the formation of **5** was directly demonstrated by an inversion transfer ^{31}P NMR experiment. The complex (dippp)PdP^{i}Pr$_2$^{n}Bu (**9**) was used in this series of experiments instead of Pd(dippp)$_2$ itself. The monodentate ligand, P^{i}Pr$_2$^{n}Bu possesses steric and electronic properties very similar to those of dippp[20] but lacks its chelating and bridging abilities. The replacement of one molecule of dippp in complex **1** by a molecule of P^{i}Pr$_2$^{n}Bu prevents equilibrium (3) as well as dynamic behavior.[7] The equilibrium (8) is expected to be very similar to equilibrium (6).



(8)

The inversion transfer experiment is not able to detect the equilibrium (8), unless there is a sufficient amount of free ligand. Since the free ligand, produced by dissociation of pure **9**, is present in a solution of this complex in amounts undetectable by NMR, 1 equiv of P^{i}Pr$_2$^{n}Bu was added. The ligand exchange process is thus formulated as (9).



(9)

Table I. Pseudo-First and -Second-Order Rate Constants for Eq 9, As Calculated from the Inversion Transfer Experiments

T (°C)	k_f (s^{-1})	k_b (s^{-1})	k_9 (L·mol^{-1}·s^{-1})	k_{-9} (L·mol^{-1}·s^{-1})
40	1.34(±0.20)	1.25(±0.18)	18.6(±3.6)	17.4(±3.2)
50	3.27(±0.14)	3.17(±0.14)	45(±4)	44(±4)
60	7.98(±0.18)	7.95(±0.19)	111(±7)	110(±7)

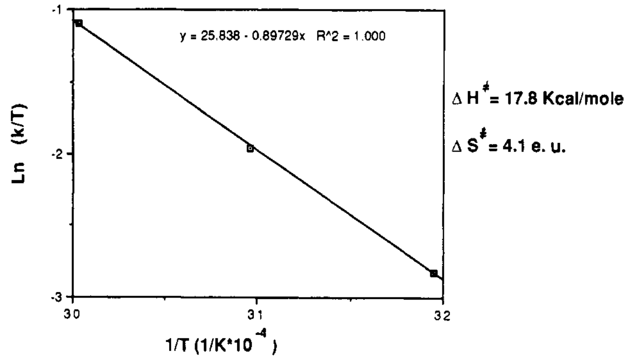
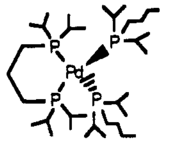


Figure 5. Eyring plot for k_{forward} of ligand exchange according to (9), [P^{i}Pr$_2$^{n}Bu] = 0.072 M.

Selective inversion of the triplet assigned to the coordinated ligand P^{i}Pr$_2$^{n}Bu results, after an appropriate evolution time, in a significant change in the intensity of the singlet assigned to the free ligand (Figure 4), proving the existence of chemical exchange between the coordinated and the free ligand. However, a dissociative exchange, as represented by equilibrium (8), is not the only possibility and an associative pathway through an 18-electron intermediate **10** may also be operative. Since neither **5** nor **10** are observable on the NMR scale, one way to distinguish between the two possible ligand exchange pathways is through the entropy of activation. The structure of the transition state in the associative pathway should be similar to the tetracoordinate intermediate **10**. Therefore, similar entropies would be expected, and the $\Delta S^{\ddagger}$ for the whole process will be large and negative. In the dissociative pathway, the composition of the transition state should be similar to that of the starting complex **9** (the transition-state complex will contain Pd, dippp, and P^{i}Pr$_2$^{n}Bu). Therefore, it is likely that their entropies are similar and a small (and probably positive) $\Delta S^{\ddagger}$ would be expected for the whole process.



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Inversion transfer experiments were performed at various temperatures in the range 40–60 °C. Employing T_1 values for the free ligand, measured independently by a common inversion-recovery technique, k_{forward} and k_{backward} (forward means coordinated ligand into free ligand, and backward is vice versa) were calculated. The kinetic rates obtained by the inversion transfer technique are first-order constants. Therefore, $k_f = k_9$[P^{i}Pr$_2$^{n}Bu], $k_b = k_{-9}[\mathbf{9}] = k_9[\mathbf{9}]$. The calculated kinetic constants, summarized in Table I, lead to an Eyring plot (Figure 5) which gives a $\Delta S^{\ddagger}$ value of 4.1 ± 0.1 eu, indicating that the dissociative pathway is operative. However, some small contribution of the associative pathway to the ligand exchange process cannot be excluded. The dissociative ligand exchange pathway confirms the existence of equilibria (6)–(8).

d. Rate-Determining Step and Its Transition State. The rate-determining role of the oxidative addition step in the reaction of chloroarenes with Pd(0) complexes of

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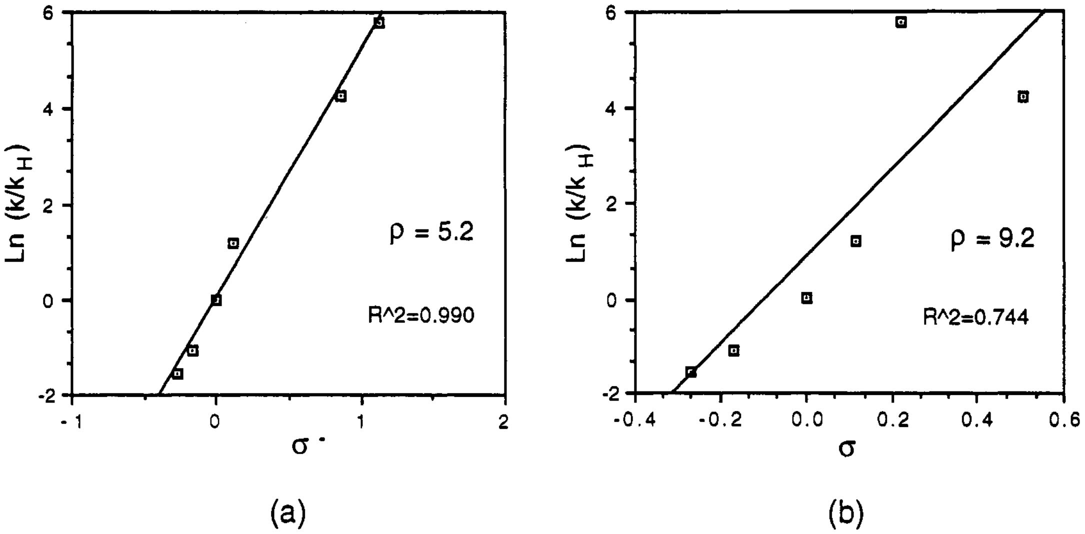
(19) Reference 17d.

(20) It is obvious that the cone angle of P^{i}Pr$_2$^{n}Bu must be very similar to that of P^{i}Pr$_2$(CH$_2$)$_3$P^{i}Pr$_2$. Regarding the basicity, we can assume the similarity on the basis of pK_a's for dppp and PPh$_2$Me observed by Angelici: Sowa, J. R., Jr.; Angelici, R. J. *Inorg. Chem.* **1991**, *30*, 3534.



(a) (b)

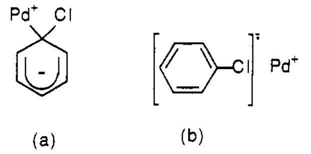
Figure 6. Hammett correlation of the observed initial pseudo-first-order rate constant k°_{obs} (a) to σ^- constants, (b) to σ constants (for $[1]_{st}$ = 0.073 M, $[ArCl]_{st}$ = 0.73 M, dioxane, 60 °C).

Table II. Pseudo-First-Order Rate Constants for Reactions of 1 (73 mM) with RC_6H_4Cl (730 mM) in Dioxane at 58 °C

R	k_{obs} (min^{-1})	R	k_{obs} (min^{-1})
4-OMe	1.58×10^{-4}	3-OMe	2.44×10^{-3}
4-Me	2.50×10^{-4}	4-C(O)Me	5.29×10^{-2}
H	7.42×10^{-4}	4-C(O)H	2.44×10^{-1}

dippp is further supported by a series of experiments evaluating the Hammett ρ value and the thermodynamic parameters of activation. The rate constants for formation of the *cis* product were measured at 58 °C for a series of substituted chlorobenzenes (Table II). Whereas correlation based on regular Hammett σ constants is poor (Figure 6b), use of σ^- Hammett constants for substituents with strong electron-withdrawing resonance effects improves the correlation dramatically (Figure 6a).[21]

A highly positive value of ρ = +5.2 is obtained, meaning that the substituents have a very strong electronic effect on the transition state. Such a substituent effect is likely to indicate a charged transition state.[22] The σ^- values give a better correlation than normal σ values whenever direct conjugation of a pair of electrons at the reaction site with the substituent is possible.[23] Two charge-bearing transition states were suggested in the past for the reaction of Ni(0), Pd(0), and Pt(0) complexes with haloarenes: a transition state with a negative charge on the ring caused by Pd–C bond formation,[8a,9b] which may be concerted,[11b] and a radical anion transition state resulting from an outer sphere 1-electron transfer[8b,10a] (Figure 7). Although the high ρ value is compatible with both transition states, several facts point out that the transition state is the one resulting from a 2-electron transfer. First, neither Pd(I) nor any product resulting from Ar• (biphenyl or benzene) was detected in the reaction mixture. While in several experiments of aryl halide oxidative addition to Ni(0) complexes of dippp[24] untractable ^{31}P NMR spectra were obtained as a result of distortion by Ni(I) paramagnetic impurities, this never happened with Pd(0) complexes. Second, the correlation to σ^- is used successfully for aromatic nucleophilic substitution reactions (S_NAr),[23a,c,d] which involves a transition state likely to be very similar to the one involved in the 2-electron transfer mechanisms. In the case of a reaction proceeding through a 1-electron transfer, described by Kochi[10a] for $Ni(PEt_3)_3$, a correlation to σ constants was used, although the linear fit was not good and using σ^- constants would make it even worse.



(a) (b)

Figure 7. Charged transition states for the reaction of Ni(0), Pd(0), or Pt(0) with haloarenes resulting from (a) a 2e donation and (b) a 1e transfer.

The two mechanisms, corresponding to the two ionic transition states, can be distinguished on the basis of the different activation entropies that they require.[25] Thus, a charged, S_NAr-like mechanism with its ordered transition state should involve large and negative activation entropy, while the outer sphere electron transfer mechanism should involve a relatively small entropy of activation. k°_{obs} values for formation of 2 from $Pd(dippp)_2$ and PhCl were evaluated by a series of $^{31}P\{^1H\}$ NMR monitored experiments in the 38–68 °C temperature range[26] (below 35 °C the reaction is too slow for effective NMR follow-up, and above 70 °C the peaks of complex 1 are broadened to an extent that prevents reliable integration). An Eyring plot (Figure 8) gives $\Delta H^\ddagger_{obs}$ = 28 ± 3 kcal/mol and $\Delta S^\ddagger_{obs}$ = −2 ± 8 eu.[27] The obtained parameters include, however, thermodynamic terms ΔH°_{dis} and ΔS°_{dis} for the preequilibrium in which the 14-electron intermediate 5 is formed in addition to the activation parameters $\Delta H^\ddagger_{OA}$ and $\Delta S^\ddagger_{OA}$ for the addition of PhCl to that intermediate (OA =

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[21] Although the reaction of $4\text{-}NO_2C_6H_4Cl$ is too fast to obtain accurate rate data based on ^{31}P NMR, the estimated rate correlated much better with σ^- than with σ.

[22] Gilliom, R. D. *Introduction to Physical Organic Chemistry*; Addison-Wesley; New York, 1970; pp 146–149.

[23] (a) Maskill, H. *The Physical Basis of Organic Chemistry*; Oxford University Press: New York, 1985; pp 451-453. (b) Reference 22, pp 150–152. (c) Jaffe, H. H. *Chem. Rev.* **1953**, *53*, 191. (d) Miller, J. *Aromatic Nucleophilic Substitution*, Elsevier: Amsterdam, 1968; p 66.

[24] Ben-David, Y.; Portnoy, M.; Milstein, D. Unpublished results.

[25] Reference 11a and references therein.

[26] k°_{obs} were measured for the start of the reaction; [PhCl] was estimated as 0.73 mol/L, and the ratio [1]/[dippp], as 2.

[27] The slope of the plot is equal to $\Delta H^\ddagger_{obs}/R$, and the intercept, to $\Delta S^\ddagger_{obs}/R + \ln(k_B/h)$ (see: Amdur, I.; Hammes, G. G. *Chemical Kinetics: Principles and Selected Topics*; McGraw-Hill, New York, 1966; p 56).

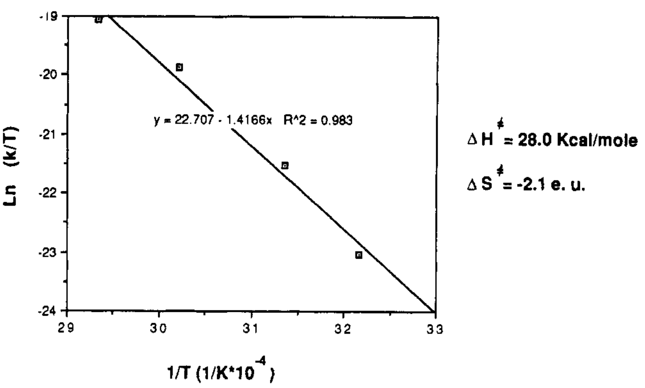


Figure 8. Eyring plot for the observed initial pseudo-first-order rate constant k°_{obs} for the reaction of 0.073 M 1 with a 10-fold excess of chlorobenzene in dioxane.

oxidative addition).

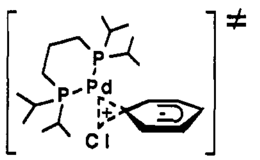
$$\Delta H^\ddagger_{obs} = \Delta H^\circ_{dis} + \Delta H^\ddagger_{OA} \qquad \Delta S^\ddagger_{obs} = \Delta S^\circ_{dis} + \Delta S^\ddagger_{OA}$$

Unfortunately, only $\Delta H^\ddagger_{OA}$ and $\Delta S^\ddagger_{OA}$, which cannot be calculated without knowing the equilibrium terms, are direct measures of the transition state involved in the oxidative addition step. Nevertheless, some general conclusions with regard to the observed activation parameters may be made. We expect that ΔH°_{dis} will be large and positive (since 5 is thermodynamically unfavorable, compared to 1). $\Delta H^\ddagger_{OA}$ is also expected to be positive, and therefore, the large combined value of 28 kcal/mol for $\Delta H^\ddagger_{obs}$ is not surprising (such a value is probably too high for each of the two enthalpy terms taken separately). ΔS°_{dis} undoubtedly should be large and positive. Therefore, the obtained value of $\Delta S^\ddagger_{obs}$ (−2 eu) means that $\Delta S^\ddagger_{OA}$ should be similar in magnitude to ΔS°_{dis} but negative in sign. Such a $\Delta S^\ddagger$ is likely to be a result of an ordered transition state with charge separation. A possibility of η^2-chloroarene precoordination as a part of the reaction pathway cannot be excluded, although we have not found evidence for this preequilibrium. Examples of arene precoordination preceding aromatic C–H and C–F oxidation were reported.[28]

The rates of the reaction of 1 and Pd(0) complexes in general, with haloarenes, follows the order $k_{ArI} > k_{ArBr} > k_{ArCl}$, opposite to the generally observed rate order in aromatic nucleophilic substitution. Fitton and Rick suggested (using the analogy to the S_NAr mechanism) that the transition state succeeding the Meisenheimer intermediate is rate-determining.[11c] This transition state is influenced mostly by the C–halogen bond strength, while the transition state preceding the intermediate is influenced mainly by the electrophilicity of the carbon atom being attacked. There are indeed some examples of aromatic nucleophilic substitution, especially with soft nucleophiles[29] where this is the situation and the order of reactivity of the aryl halides is reversed. Regardless of whether a Meisenheimer intermediate is involved, we can generally refer to a late transition state with a partially ruptured carbon–halogen bond.

Stabilization of the transition state through partial coordination of the halogen moiety to the metal center may also play a role. According to the Hammond postulate, the transition state in the S_NAr reaction is similar to the Meisenheimer intermediate. Assuming that the oxidative addition of a haloarene to the 14-electron Pd(0) fragment has a pathway similar to S_NAr reactions leads to a transition state that is ordered and charged (Figure 7a). The proximity of the electron-rich halogen, capable of σ donation, to the electron-deficient unsaturated metal center tempts us to suggest halogen coordination which can stabilize the transition state. The better electron donating iodoarenes are expected to provide higher stabilization than the chloroarenes,[30] resulting in the observed order of oxidative addition rate.

The following transition state is, thus, the most likely one.



Similar transition states were proposed for iodobenzene oxidative addition to $Pd(PPh_3)_4$,[11b,c] whereas Amatore suggested a concerted *neutral* transition state for this reaction,[11a] based on solvent polarity-independent activation parameters, although a value of $\rho = +2$ was obtained for this system.[11a,b] Though the case of aryl iodides may be debatable, we have unambiguously established a charged transition state for aryl chlorides.

Conclusions

Oxidative addition of aryl chlorides to Pd(0) or, for that matter, reaction of any aryl halide with a chelated Pd(0) complex, was studied here for the first time. Oxidative addition of aryl chlorides to the trigonal complex, $Pd(dippp)_2$ (**1**), involves facile generation of two 14-electron complexes, Pd(dippp) (**5**), major, and $Pd(\eta^1\text{-dippp})_2$ (**6**), minor. These species undergo rate-determining oxidative addition of the aryl chloride. The transition state for this reaction with **5** involves charge separation, and it is probably stabilized by chloride coordination to Pd. In other words, the reaction is essentially a nucleophilic aromatic substitution, taking place even with aryl chlorides substituted with electron-donating groups. Thus, the chelated complex, Pd(dippp) (**5**), whose existence was demonstrated by spin inversion transfer, behaves as a strong nucleophile, in accordance not only with its highly unsaturated nature and high electron density but also with the expected increased nucleophilicity as a result of the "bent" P–Pd–P geometry.

A problem frequently encountered in the design of catalytic cycles is that what is good for one step is detrimental for another, e.g. the conflicting requirements of oxidative addition and insertion or the reductive elimination reaction. The ability of the dippp ligand to function in both chelating and monodentate modes enables its Pd(0) complex to adopt the desired structure for the particular transformation and makes it superior to other potentially reactive Pd(0) complexes of chelating, basic phosphines.

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[28] (a) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 4240; *J. Am. Chem. Soc.* **1984**, *106*, 1650; *Acc. Chem. Res.* **1989**, *22*, 91. (b) Belt, S. T.; Duckett, S. B.; Hilliwell, M.; Perutz, R. N. *J. Chem. Soc., Chem. Commun.* **1989**, 928. Jones, W. D.; Partridge, M. G.; Perutz, R. N. *J. Chem. Soc., Chem. Commun.* **1991**, 264.

[29] Reference 23d, pp 18–22 and references therein.

[30] Gomes-Canneiro, T. M.; Jackson, R. D.; Downing, J. H.; Orpen, A. G.; Pringle, P. G. *J. Chem. Soc., Chem. Commun.* **1991**, 317. Kulawiec, R. J.; Faller, J. W.; Crabtree, R. H. *Organometallics* **1990**, *9*, 745.

Experimental Section

1. **General Information.** All procedures with air- and moisture-sensitive compounds were performed in a nitrogen-filled glovebox (Vacuum Atmospheres, equipped with an MO-40 purification system) or on a high-vacuum line. All solvents were reagent grade or better. Dioxane and pentane (Frutarom) were distilled over sodium/benzophenone ketyl. Dioxane was predried over KOH pellets before the distillation. Dimethylformamide (Merck) was dried over KOH pellets and distilled over barium oxide. All solvents were degassed and stored under high-purity nitrogen after the distillation. Chlorobenzene and other chloroarenes were purchased from Merck, Sigma, or Fluka at the highest available purity and were used as received, except for *p*-chlorobenzaldehyde, which was purified by vacuum distillation and stored under nitrogen. The dippp ligand was prepared according to a procedure reported by Tani.[31] Preparation and characterization of $\mathrm{Pd(dippp)_2}$, Pd(dippp)(Ar)Cl, and Pd(dippp)($\mathrm{P^iPr_2{}^nBu}$), as well as the $\mathrm{P^iPr_2{}^nBu}$ ligand, are described in the preceding paper.[7]

^{31}P NMR measurements were recorded at 109 MHz on a Bruker WH270 spectrometer. The inversion transfer experiments were performed at 202 MHz on a Bruker AM500. ^{31}P chemical shifts are reported in ppm downfield from phosphoric acid and were referenced to external 85% $\mathrm{H_3PO_4}$. The probe temperature was carefully calibrated with a thermocouple.

2. **Kinetic Measurements of Aryl Chloride Oxidative Addition to $\mathbf{Pd(dippp)_2}$.** The oxidative addition process was monitored by $^{31}\mathrm{P}\{^1\mathrm{H}\}$ NMR. In a typical procedure, 120 mg of the $\mathrm{Pd(dippp)_2}$ complex (1) was dissolved in 2 mL of dioxane. The yellow solution was added to an appropriate amount of the dippp ligand (only in the series of experiments for ligand dependence evaluation). The solution was then added to an appropriate amount of chloroarene. The volume of the solution was complemented to 2.5 mL with dioxane. The solution was then placed in a sealed 10-mm NMR tube, which was inserted into the NMR spectrometer probe, preset at the desired temperature. The monitoring program was started after 2 min of temperature equilibration and included periodical FID acquisition at constant intervals. The delay was varied in different experiments from 10 to 40 min, depending on experimental conditions.

Fourier-transformed spectra were plotted, including integrations of the peaks, using an AI (absolute intensity) parameter equal to 1. The relative part of a complex phosphine integration in the whole integration defined the relative part of the complex in the reaction mixture. Raw data from the spectra were processed using the Exel and Cricket Graph programs on a Macintosh personal computer.

3. **Demonstration of Chemical Equilibrium between the Cis and Trans Products of Oxidative Addition.** *cis*-(dippp)Pd(Ph)Cl (2) (30 mg) and dippp (21 mg, 1.25 equiv) were dissolved in dioxane (3 mL). The solution was heated overnight at 70 °C in a pressure bottle. The presence of the trans product in the reaction mixture was confirmed by $^{31}\mathrm{P}\{^1\mathrm{H}\}$ NMR [$\delta = 24.5$ (s)]. In another experiment, a dioxane solution of *cis*-(dippp)Pd(*p*-MeC(O)Ph)Cl, *trans*-(η^1-dippp)$_2$Pd(*p*-MeC(O)Ph)Cl, and dippp, obtained after completion of the reaction between $\mathrm{Pd(dippp)_2}$ and 4-MeC(O)$\mathrm{C_6H_4Cl}$ in a sealed 10-mm NMR tube, was kept in the same tube in the spectrometer at 60 °C for 8 h. Several spectra, recorded during this period, exhibited that the ratio between the two complexes remained unchanged.

4. **Inversion Transfer Experiment.** The complex (dippp)Pd($\mathrm{P^iPr_2{}^nBu}$) (100 mg) and the ligand $\mathrm{P^iPr_2{}^nBu}$ (31 mg, 1 equiv) were dissolved in dioxane (2.5 mL), and the solution was placed in a sealed NMR tube (10 mm). The tube was kept in the spectrometer at the desired temperature for at least 30 min. Then, the program containing the following pulse sequence was applied: RD–π_{sel}–τ_{mix}–$\pi/4$–acquistion. The selective π pulse was applied to the central peak of the triplet assigned to the coordinated $\mathrm{P^iPr_2{}^nBu}$ ligand. Rapid switching of the transmitter from a very low power for the selective pulse to a high power for the acquisition pulse was achieved by use of a BFX5 fast switching decoupler. The mixing (evolution) time was changed during the program according to a variable delay list file. Sixteen scans were accumulated for each value of the τ_{mix} from the list.

The collected FIDs were Fourier-transformed and recorded. Stack plots of the relevant signals (the triplet of the coordinated $\mathrm{P^iPr_2{}^nBu}$ ligand and the singlet of the free ligand) were drawn, using an AI parameter equal to 1. The intensities of the central peak of the triplet and of the singlet vs τ_{mix} formed two sets of data points. Parameter fitting of these sets to the functions described by Led and Gesmar[32a] and Campbell[32b] was performed using the RS1 program on an IBM-PC computer. From the obtained parameters and using the free ligand phosphorus T_1 relaxation time (determined independently by a standard inversion recovery technique[33]), the kinetic first-order rates were calculated.[34]

Acknowledgment. We thank Dr. R. Poupko of the Department of Chemical Services for his assistance in NMR measurements. We are grateful to the Hoechst, AG, Co., Frankfurt, Germany, for their generous gift of chemicals. This work was supported by the Basic Research Foundation administered by the Israel Academy of Sciences and Humanities.

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[31] Tani, K.; Tanigawa, E.; Tatsubo, Y.; Otsuka, S. *J. Organomet. Chem.* **1985**, *279*, 87.

[32] (a) Led, J. J.; Gesmar, H. *J. Magn. Reson.* **1982**, *44*, 444. (b) Campbell, I. D.; Dobson, C. M.; Ratcliffe, R. G.; Williams, R. J. P. *J. Magn. Reson.* **1978**, *29*, 397.

[33] Sanders, J. K. M.; Hunter, B. K. *Modern NMR Spectroscopy. A Guide for Chemists*; Oxford University Press: Oxford, U. K., 1987; pp 61–65.

[34] In these calculations, the line widths and the multiplicities of the exchanging signals should be taken into account in order to get the correct correlation between the measured peak heights and the spin populations that appear in the relevant equations.