Intramolecular C–H Activation by Alkylpalladium(II) Complexes: Insights into the Mechanism of the Palladium-Catalyzed Arylation Reaction

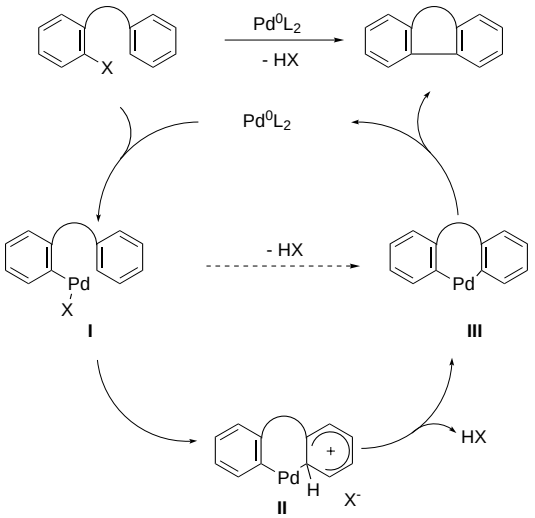
Belén Martín-Matute, Cristina Mateo, Diego J. Cárdenas, and Antonio M. Echavarren*[a]

Abstract: The cyclization of [ArOCH$_2$PdL$_2$Cl] complexes proceeds at room temperature in CH$_3$CN in the presence of base, such as KOPh or carbonate, to form palladacycles. The effect of substituents on the aryl moiety (*p*-MeO > H > *p*-NO$_2$) is as expected for an electrophilic aromatic substitution by electrophilic Pd^{II}. The absence of isotopic effect is also consistent with this proposal. Cyclopalladation proceeds with bidentate ligands (dppf, COD and phen); although the C–H activation reactions are slower in these cases. The starting [ArOCH$_2$Pd(PPh$_3$)$_2$Cl] and [ArOCH$_2$Pd(PPh$_3$)Cl]$_2$ complexes were prepared by transmetalation of organostannanes [(ArOCH$_2$)$_4$Sn] with [Pd(PPh$_3$)$_2$Cl$_2$] or [Pd(PPh$_3$)Cl$_2$]$_2$, respectively. Cleavage of palladacycles with HCl also gave [ArOCH$_2$PdL$_2$Cl] complexes.

Keywords: aromatic substitution · C–H activation · metallacycles · palladium

Introduction

Metalation reactions are key steps in many metal-catalyzed reactions.[1–3] In particular, the palladium-catalyzed arylation reaction has attracted much attention in organic synthesis since this reaction offers a straightforward solution for the construction of carbo- and heterocycles from the corresponding halides and triflates (X = Br, I, OTf) (Scheme 1).[4–7] The reaction is usually carried out with [Pd(OAc)$_2$] or [Pd(PPh$_3$)$_2$Cl$_2$] as the catalysts in polar solvents (DMF or DMAc) at relatively high temperatures (120–170 °C) in the presence of a base to trap HX. The addition of bulky, donor phosphanes, such as PCy$_3$, has been shown to accelerate the arylation.[6g] However, despite the synthetic interest of this reaction, little is known about its mechanism. A simplified mechanistic hypothesis for the arylation reaction is outlined in Scheme 1 (ligands L on Pd are removed for clarity). The arylpalladium(II) complex [PdAr(L)$_n$X] **I** (L = phosphane or solvent molecule, *n* = 1 or 2)[8] that is initially formed might react as an electrophile with the aryl ring to form **II**,[1a, 9, 10] which is then followed by a proton loss to form [PdArAr′(L)$_n$] **III**. Alternatively, complex **I** could directly give palladation intermediate **III**. Finally, reductive elimination of **III** would yield the biaryl product and the reactive Pd^0 species. Arenonium intermediates, such as **II**, have been proposed as intermediates for the cyclometalation of arenes as well as for the protonation of metal-aryl bonds, a reaction that is the reversal of the cyclometalation process.[11]



Scheme 1. Simplified mechanistic hypothesis for the arylation reaction.

In certain cases, (η^2-arene)alkyl palladium(II) complexes have been shown to evolve by C–H activation to afford palladacycles.[12, 13] Recently, alkylpalladium complex **IV** has been transformed into palladacycle **V** by the action of the strong base NaN(SiMe$_3$)$_2$ (Scheme 2).[14] Interestingly, selec-

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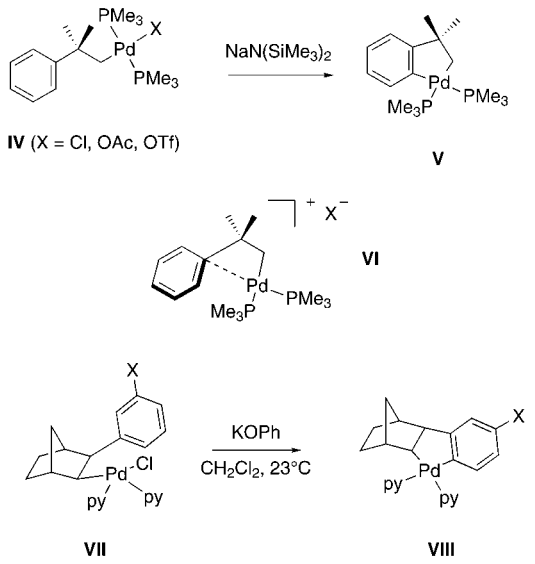
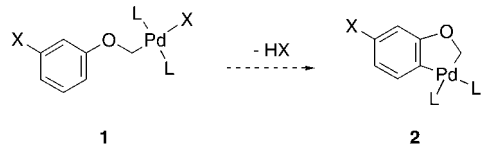


Scheme 2. Intermediate palladacycles.

tive cleavage of either the alkylpalladium or the arylpalladium bond of palladacycle **V** could be achieved by the use of different acids. In this work, (η^1-arene)alkyl palladium(II) complex **VI** was found to be an intermediate during cleavage of the arylpalladium bond by acid.[14]

The effect of aryl substituents on the rate of arylation has been studied with norbornyl-palladium(II) complex **VII** (Scheme 2).[15] In this case, the palladation was promoted by the milder base KOPh and palladacycle **VIII** was yielded. The reaction rate followed the order $X = MeO > H > NO_2$ as expected for an electrophilic aromatic substitution reaction. However, under catalytic conditions, the arylation reaction tolerates both electron-withdrawing and electron-releasing groups, which casts some doubts on this mechanistic proposal.[6d] Additionally, products derived from a 1,5-hydrogen abstraction have been observed in the reaction of some aryl triflates, which suggests that aryl radicals may be involved as intermediates.[6c]

As a model for the key step in the intramolecular palladium-catalyzed arylation reaction (Scheme 1), we decided to examine the conversion of alkylpalladium complex **1** into palladacycle **2** [Eq. (1)]. In particular, we wished to study

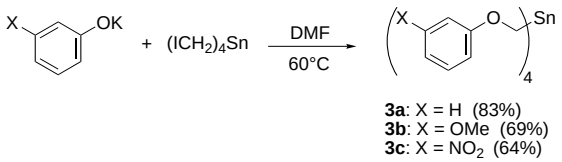


1 **2** (1)

the effect of the ligands, the aryl substituents and the added base on the palladation reaction. Complex **1**, required for the preparation of substituted palladacycles, was prepared by the intermolecular transmetalation of tetraorganostannanes with palladium(II) complexes. The intramolecular aryl C–H activation of alkylpalladium complex **1** gave palladacycle **2** [Eq. (1)]. This new route to palladacycle **2**, an important intermediate in palladium-catalyzed cascade reactions, is an alternative to those based on the intramolecular transmetalation of stannanes or silanes with aryl-Pd^{II}.[16]

Results

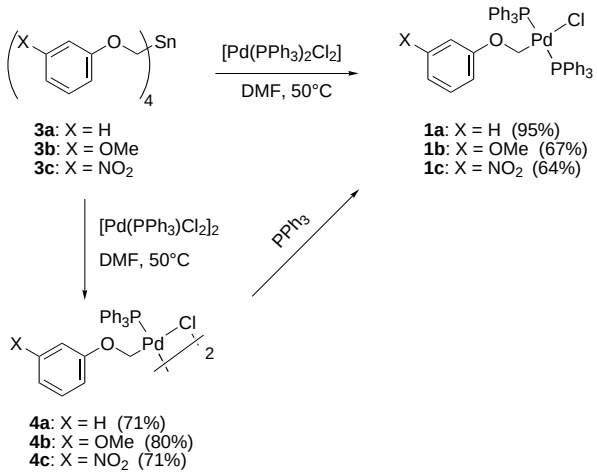
Synthesis of alkyl-palladium complexes: For the synthesis of alkylpalladium complexes of type **1** that bear substituents on the phenyl ring, we decided to try the transmetalation of tetraorganostannanes with palladium(II) complexes. The preparation of starting stannanes **3a–c** was readily carried out by treatment of $(ICH_2)_4Sn$[17] with a slight excess of potassium phenolate in DMF at 60 °C (64–83%) [Eq. (2)].



(2)

3a: X = H (83%)
3b: X = OMe (69%)
3c: X = NO_2 (64%)

Reaction of **3a–c** with $[Pd(PPh_3)_2Cl_2]$ proceeded smoothly in DMF at 50 °C to give complexes **1a–c** (64–95%) (Scheme 3). Under these conditions, the double transmetalation reaction



Scheme 3. Reaction of organostannanes to yield Pd-complexes **1a–c**.

did not proceed to a significant extent. The methylene hydrogens of palladium complexes **1a–c** appeared in the ^{1}H NMR spectra ($CDCl_3$) as triplets at $\delta = 3.81–3.88$, coupled to the equivalent phosphorous atoms with $^3J(H,P) = 7.5–7.8$ Hz. The ^{31}P NMR spectrum showed singlets at $\delta = 28–30$, which confirms the *trans* configuration of the palladium complexes. On the other hand, treatment of stannanes **3a–c** with dimer $[Pd(PPh_3)Cl_2]_2$ led to complexes **4a–c** (71–80%) (Scheme 3). The methylene hydrogens of these complexes were observed at a lower field ($\delta = 4.40–4.54$) as doublets with $^3J(H,P) = 4.8–5.6$ Hz.

Complex **5**, with a 1,1′-bis(diphenylphosphino)ferrocene (dppf) ligand, was easily prepared from **1a** in 79% yield by a ligand exchange reaction with dppf in CH_2Cl_2 at 23 °C (Scheme 4). Cationic complex **6** was prepared in 83% yield by reaction of **1a** with $AgBF_4$ in CH_3CN.

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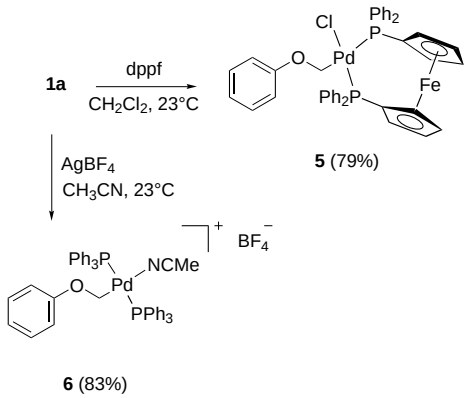
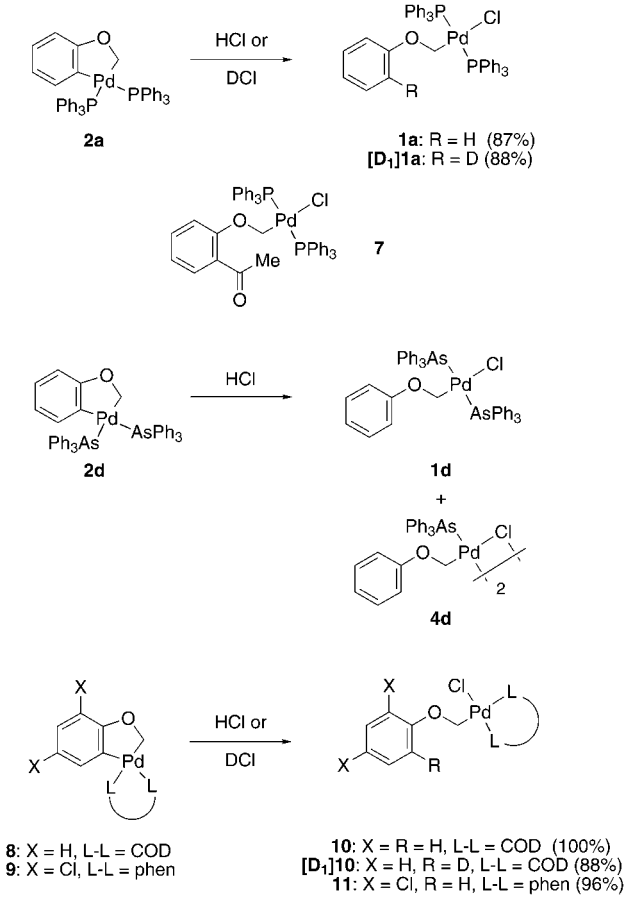


Scheme 4. Ligand exchange reaction from **1a**.

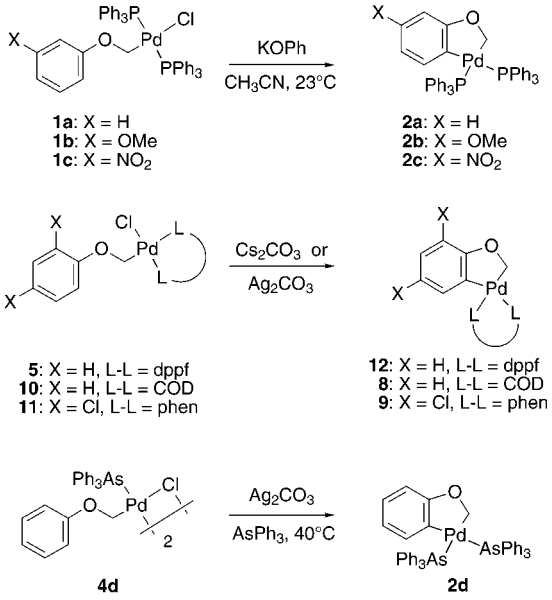
Alkyl-palladium complex **1a** was also prepared by regioselective cleavage of palladacycle **2a**[16] with HCl at 23 °C in 87 % yield (Scheme 5). Similarly, treatment with DCl yielded mono-deuterated **[D$_1$]1a**. In these experiments, HCl was generated by reaction of acetyl chloride with MeOH or by the addition of chlorotrimethylsilane to the wet solvent. When



Scheme 5. Deuteration experiments.

excess acetyl chloride was used, complex **7** was obtained as a by-product. This complex, which results from a Friedel–Crafts cleavage of the arylpalladium bond, could be obtained in almost quantitative yield by reaction of **2a** with acetyl chloride in CH_2Cl_2 at room temperature. Reaction of palladacycle **2d** with HCl led to mixtures of **1d** and dimer **4d**, which could be isolated as a pure substance. Reaction of palladacycles **8** and **9**[16] with HCl or DCl provided alkylpalladium complexes **10**, **[D$_1$]10**, and **11**.

Intramolecular aryl C–H activation: After much experimentation with a variety of bases (NaOH, py, 2,6-di-*tert*-butylpyridine, DBU, NaOAc, K_2CO_3, $NaHCO_3$, nBu_4NOH), the best results were obtained with KOPh in CH_3CN at 23 °C. Palladation could also be carried out at about the same rate with Cs_2CO_3, KO*t*Bu, or Ag_2CO_3 in CH_3CN. In the last case, however, poor reproducibility was observed in some instances, which is probably due to the very low solubility of this carbonate. In the case of **1a–c**, the reactions were best carried out with KOPh in CH_3CN at 23 °C to give palladacycles **2a–c** (Scheme 6).



Scheme 6. Synthesis of palladacycles.

A detailed kinetic study was not possible since an accurate determination of the palladacycle and base concentrations could not be carried out, due to partial precipitation of the palladacycles and low solubility of the base. Nevertheless, the qualitative effect of the substituents on the reactivity could be determined for a family of complexes by monitoring the disappearance of starting materials by ^{1}H NMR spectroscopy in CD_3CN, while allowing the reactions to proceed to completion under the same temperature and concentration (Table 1). Thus, the parent alkylpalladium complex **1a** was converted into **2a** at 23 °C with KOPh (1.5 h, 97 %, entry 1) or Ag_2CO_3 (4 h, quantitative, entry 2). The reaction of *p*-methoxy analogue **1b** was completed in 15 minutes with KOPh to give **2b** in 95 % yield (entry 3). Substrate **1c**, with an electron-withdrawing substituent, reacted more slowly. **2c** was obtained in 94 % yield after 15 hours (entry 4). Interestingly, the reaction of **1a** with KOPh in CH_3CN was almost

Table 1. Aryl C–H activation of alkylpalladium complexes promoted by bases.[a]

Entry	Alkylpalladium (*c*, mM)	Base (equiv)[b]	Reaction time [h]	Palladacycle	Yield [%]
1	**1a** (20)	KOPh (1)	1.5	**2a**	97
2	**1a** (5)	Ag_2CO_3 (4)	4	**2a**	100
3	**1b** (20)	KOPh (1)	0.25	**2b**	95
4	**1c** (20)	KOPh (1)	15	**2c**	94
5	**5** (20)	Cs_2CO_3 (5)	50	**12**	96
6	**10** (50)	Ag_2CO_3 (4)	24	**8**	75
7	**11** (40)	Ag_2CO_3 (4)	18[c]	**9**	100
8	**4d** (6)	Ag_2CO_3 (10)	4[d]	**2d**	76

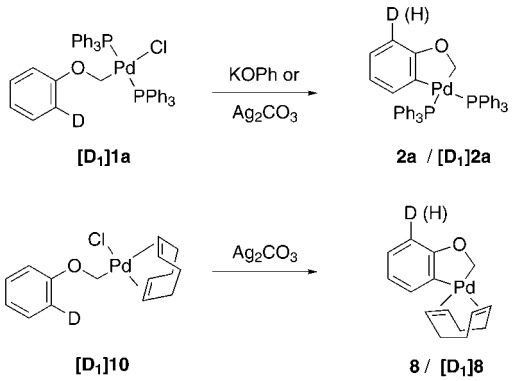
[a] Unless otherwise stated, the reactions were carried out at 23 °C in CH_3CN. [b] Equivalents refers to mol of base per mol of alkylpalladium. [c] Reaction carried out at 50 °C. [d] Reaction carried out in the presence of $AsPh_3$ (2 equiv) at 40 °C.

completely inhibited by the addition of 1 equivalent of PPh_3, which led only to traces of **2a** after 20 hours at 23 °C.

To determine the effect of chelating ligands, the activation of substrates **5**, **10**, and **11** with the appropriate bases was also studied (Scheme 6). Thus, the reaction of **5**, with the chelating diphosphane ligand (dppf), in the presence of Cs_2CO_3 was more sluggish than those of **1a–c** (50 h, 23 °C), although palladacycle **12** was still obtained in excellent yield (96%) (Table 1, entry 5). The activation of **10** with 1,5-cyclooctadiene (COD) as the chelating ligand was carried out with the base Ag_2CO_3 at 23 °C to give **8** in 75% yield; the reaction was slower than that of **1a** with this base (compare entries 2 and 6). The reaction of **11**, which bears 1,10-phenanthroline (phen) as the ligand, with Ag_2CO_3 had to be carried out at 50 °C to yield palladacycle **9** (entry 7).

Treatment of dimer **4a** or cationic complex **6** with KOPh in CH_3CN at 23 °C failed to give any palladacycle and led only to decomposition. However, reaction of dimer **4d** with Ag_2CO_3 in the presence of two equivalents of $AsPh_3$ gave palladacycle **2d** in 76% yield (entry 8).

The activation of monodeuterated substrates **[D$_1$]1a** and **[D$_1$]10** with KOPh or Ag_2CO_3 in CH_3CN at 23 °C led to palladacycles **2a** and **8**, respectively, which were partially deuterated at C-3 (Scheme 7). The degree of deuteration was determined by ^{1}H NMR spectroscopy as 48 ± 3% (average of more than three experiments), which corresponds to the absence of an isotopic effect for the intramolecular C–H activation by the alkylpalladium complex.



Scheme 7. H/D subsitution reaction.

Discussion

The reactivity order obtained in the cyclopalladation of substrates **1a–c** (Table 1) is in accord with those previously obtained in the transformation of palladium complex **VII** into **VIII** (Scheme 2),[15] and strongly suggests that the palladation reaction in these cases proceeds by an electrophilic aromatic substitution pathway. The lack of isotopic effect seen in reactions with **[D$_1$]1a** and **[D$_1$]10** demonstrates that the C–H bond breaking event does not take place during the rate-determining step, which has also been observed for most electrophilic aromatic substitutions.[18] Furthermore, the selective cleavage of the aryl–Pd bond of the palladacycles by protic acids and acetyl chloride (Scheme 5) is also consistent with an electrophilic pathway that proceeds at the aryl carbon that is *ipso* to the Pd atom.[19]

The inhibition observed in the palladation of the aryl group of **1a** by addition of PPh_3 indicates that dissociation of PPh_3 is a requirement for C–H activation. The fact that the alkylpalladium complexes **5**, **10**, and **11** with different bidentate ligands undergo cyclopalladation appears to be contradictory with this conclusion. However, as summarized in Table 1, the reactions of these substrates were slower in all cases than those of **1a–c**. The cyclopalladation of substrates **5**, **10**, and **11** could be explained by partial ligand dissociation of the chelating ligands to give tricoordinated complexes as reactive intermediates or by a slower associative partial cleavage of the chelate in the C–H activation step.

With regard to the bases, the best results were obtained with the use of relatively mild carbonates or phenolates, although the reactions could also be performed with a stronger base, such as KO*t*Bu. Since formation of the arylpalladium bond can be reversed by a protic acid, the base might be simply shifting the equilibrium between the alkylpalladium complexes **1a–c**, **5**, **10**, and **11** and the corresponding palladacycles (Scheme 6). This is consistent with the fact that milder pyridine bases are not effective for C–H activation, since their conjugate acids are acidic enough to cleave the aryl–Pd bond. Alternatively, nucleophilic bases may be playing a more active role by substituting the chloride ligand before the activation step. Indeed, reaction of alkyl- and arylpalladium(II) complexes with alkoxydes is known to give rise to stable alkylpalladium(II) alkoxo[20] and hydroxo complexes.[21, 22] Furthermore, the reaction of dichloro(diphosphane)platinum(II) complexes with Ag_2CO_3 leads to (diphosphane)carbonatoplatinum(II) complexes.[23] However, the fact that cationic complex **6**, with a labile acetonitrile ligand, failed to activate the aryl C–H bond suggests that chloride dissociation does not take place before C–H activation and that formation of alkylpalladium(II) complexes with a carbonato or OX (X = Ph or *t*Bu) ligand is not a productive pathway.

Dimeric complex **4a** was expected to react with the solvent or the base under these reaction conditions to form [$PhOCH_2Pd(PPh_3)L$] (L = CH_3CN or base) complexes. However, **4a** did not afford a palladacycle analogous to **2a** with a PPh_3 and CH_3CN ligand. This complex, and that with two CH_3CN ligands, was obtained in $CDCl_3$ solution by reaction of **2a** with [$Pd(CH_3CN)_2Cl_2$], although they were not isolated. The observed decomposition of **4a** suggests that complex

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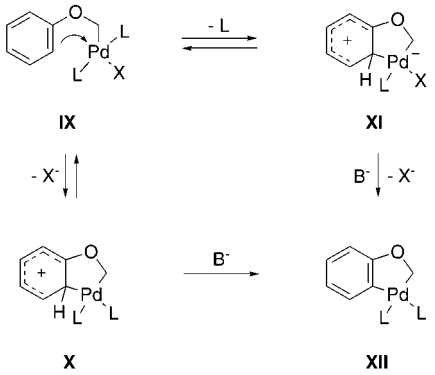
$[PhOCH_2Pd(PPh_3)L]$ is not productive and supports a reaction pathway that involves the attack of the arene on the Pd atom without previous dissociation of a phosphane ligand. The successful activation reaction of dimer **4d** in the presence of $AsPh_3$ most likely proceeds by prior formation of monomer **1d**.

A mechanism for the C–H activation event that is consistent with all of the above results is shown in Scheme 8. The electrophilic substitution reaction of complex **IX** could



Scheme 8. Mechanism for the C–H activation.

give either **X** or **XI** by substitution of the anionic or neutral ligand, respectively. Most likely, the ligand substitution reaction proceeds by an associative mechanism, since reactions of Pd^{II} complexes that involve an initial dissociation of L are a rarity.[24] The strong retarding effect of added PPh_3 and the fact that bidentate ligands lead to slower palladations suggest that the reaction proceeds through intermediates of type **XI**. Finally, the external attack of the base could shift the unfavorable equilibrium between **IX** and **XI** to give palladacycle **XII**.

Conclusion

We have studied the effect of ligands and substituents on the aryl moiety on the intramolecular palladation reaction of complexes of type **1** to form palladacycles **2** as a model for the palladium-catalyzed intramolecular arylation reaction. This reaction proceeds at room temperature in CH_3CN in the presence of relatively mild bases, such as KOPh or carbonates. The reaction is inhibited by excess PPh_3, which indicates that ligand dissociation is involved in the process. Although the palladation also proceeds with bidentate ligands (dppf, COD and phen), the C–H activation reactions were slower in these cases. The effect of substituents on the aryl moiety and the absence of isotopic effect are consistent with an electrophilic aromatic substitution mechanism for the palladation reaction.

We have also developed a simple method for the synthesis of alkylpalladium complex **1** that is based on the transmetalation of symmetrical tetraorganostananes with Pd^{II} complexes. This procedure allows for the synthesis of substituted palladacycles, which is more flexible than that previously based on a truncated Stille coupling reaction.

Experimental Section

General: NMR spectra were recorded at 23 °C. ^{13}C and ^{31}P NMR spectra were proton-decoupled. Elemental analyses were performed at the Universidad Autónoma de Madrid (SIdI). Solvents were purified and dried with standard procedures. Chromatography purifications were carried out on flash grade silica gel with distilled solvents. Trituration means stirring with the stated solvent, filtering and washing with the same solvent. The saturated aqueous NH_4Cl solution was buffered by the addition of NH_4OH (final pH 8). All reactions were carried out under an argon atmosphere.

Palladacycles **2a**, **2d**, **9**, and **12** had been obtained previously by intramolecular transmetalation of the arylpalladium(II) derivative of (2-iodophenoxymethyl)tributylstannane or by ligand exchange reaction from **2a**.[16]

$[Pd(PPh_3)_2Cl_2]$ and $[Pd(PPh_3)Cl_2]_2$ were prepared in 90–100% yield as follows: A solution of Li_2PdCl_4 was first obtained by treating a suspension of $PdCl_2$ (1.03 g, 5.8 mmol) and LiCl (495 mg, 11.6 mmol) in MeOH (10 mL) under refluxing conditions for 1 h. After cooling, the red solution was treated with PPh_3 (2 or 1 equiv, respectively) for 30 min at 23 °C. The solid was filtered off and washed with MeOH and Et_2O to give the complexes as powdered solids.[25]

The HCl and DCl solutions in CH_2Cl_2 were prepared by reaction of acetyl chloride (3 mmol) in CH_2Cl_2 (3 mL) at 0 °C with methanol (3 mmol) or $[D_4]$-methanol at 0 °C for 30 min.

Tetra(iodomethyl)stannane: This stannane was prepared according to the procedure in ref. [18] and obtained as a white solid: m.p. 74–76 °C, (ref. [17] 76 °C); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.29$ [s, $^2J(H,Sn) = 10.1$ Hz, 8H]; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.11$; EI-MS (70 eV): m/z(%): 681.75 (5) $[M]^+$, 542.8 (100), 260.9 (27), 246.9 (50), 140.9 (21); elemental analysis calcd (%) for $C_4H_8I_4Sn$ (681.6): C 7.04, H 1.18; found: C 7.22, H 1.18.

Tetraphenoxymethylstannane (3a): A suspension of tetra(iodomethyl)-stannane (1.210 g, 1.77 mmol) and potassium phenolate (1.400 g, 10.64 mmol) was heated in DMF (20 mL) at 50 °C for 16 h. After being cooled to 23 °C, a saturated aqueous solution of NH_4Cl (pH 8, 25 mL) was added, and the mixture was extracted with Et_2O. The Et_2O extract was dried with Na_2SO_4 and evaporated. The residue was purified by chromatography (CH_2Cl_2) to give **3a** as a colorless oil (796 mg, 83%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.31–7.26$ (m, 8H), 6.98–6.91 (m, 12H), 4.36 (s, $^2J(H,Sn) = 20.0$ Hz, 8H]; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.36$, 129.52, 120.93, 113.98, 58.79; EI-MS (70 eV): m/z (%): 441.0 (40) $[M - C_7H_7O]^+$, 226.9 (23), 121.0 (9) 107.1 (64), 91.1 (96), 77.0 (100).

Tetra(3-methoxyphenoxy)methylstannane (3b): A suspension of tetra(iodomethyl)stannane (1.275 mg, 1.88 mmol) and potassium 3-methoxyphenolate (1.820 g, 11.22 mmol) was heated in DMF (12 mL) at 50 °C for 16 h. After being cooled to 23 °C, a saturated aqueous solution of NH_4Cl (pH 8, 10 mL) was added, and the mixture was extracted with Et_2O. The Et_2O extract was dried with Na_2SO_4 and evaporated. The residue was purified by chromatography (CH_2Cl_2) to give **3b** as a colorless oil (855 mg, 69%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.21$ (t, $J = 8.1$ Hz, 4H), 6.58–6.52 (m, 12H), 4.39 (s, $^2J(H,Sn) = 5.0$ Hz, 8H), 3.79 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 161.67$, 160.53, 106.03, 129.85, 106.03, 100.45, 58.93, 55.11; elemental analysis calcd (%) for $C_{32}H_{36}O_8Sn$ (666.1): C 57.59, H 5.44; found: C 57.38, H 5.53.

Tetra(3-nitrophenoxymethyl)stannane (3c): A suspension of tetra(iodomethyl)stannane (534 mg, 0.78 mmol) and potassium 3-nitrophenolate (833 mg, 4.70 mmol) was heated in DMF (4 mL) at 50 °C for 16 h. After being cooled to 23 °C, a saturated aqueous solution of NH_4Cl (pH 8, 10 mL) was added, and the mixture was extracted with Et_2O. The Et_2O extract was dried with Na_2SO_4 and evaporated. The residue was purified by chromatography (CH_2Cl_2) to give **3c** as a yellow solid (365 mg, 64%): m.p. 88–90 °C; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.79$ (ddd, $J = 8.2$, 2.1, 0.8 Hz, 4H), 7.73 (t, $J = 2.2$ Hz, 4H), 7.40 (t, $J = 8.2$ Hz, 4H), 7.21 (m, 4H), 4.59 (s, $^2J(H,Sn) = 7.5$ Hz, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.86$, 149.2, 130.09, 121.34, 116.35, 107.87, 58.87; elemental analysis calcd (%) for $C_{32}H_{24}N_4O_{12}Sn$ (726.0): C 46.25, H 3.33, N 7.70; found: C 46.30, H 3.38, N 7.44.

***trans*-Chloro(phenoxymethyl)bis(triphenylphosphane)palladium (1a)**

Method a: A solution of **3a** (180 mg, 0.31 mmol) in DMF (3 mL) was added to a suspension of $[Pd(PPh_3)_2Cl_2]$ (230 mg, 0.33 mmol) in DMF (7 mL). The mixture was heated at 50 °C for 13 h. After being cooled to 23 °C, the solvent was evaporated and the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated and the residue was triturated with Et_2O to give **1a** as a pale yellow solid (234 mg, 95 %).

Method b: A solution of HCl in CH_2Cl_2 (1M, 2.7 mL, 2.7 mmol) was added to a solution of **2a** (500 mg, 0.68 mmol) in CH_2Cl_2 (15 mL). The mixture was stirred at 23 °C for 1 h. The solvent was evaporated and the residue was triturated with Et_2O to give **2a** as a pale yellow solid (450 mg, 87 %): ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.73-7.71$ (m, 12H), 7.41 – 7.30 (m, 18H), 6.94 (brt, $J = 7.6$ Hz, 2H), 6.72 (brt, $J = 7.2$ Hz, 1H), 6.24 (d, $J = 7.8$ Hz, 2H), 3.88 (brt, ^3J(H,P) = 7.8 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 159.82, 134.70 (brs, PPh_3), 131.10 (brt, ^1J(C,P) = 22.1 Hz, PPh_3), 130.03 (brs, PPh_3), 128.45, 128.11 (brs, PPh_3), 119.60, 114.46, 65.84; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 28.12$.

***trans*-Chloro(2-deuterophenoxymethyl)bis(triphenylphosphane)palladium ([D$_1$]1a)**: A solution of DCl in CH_2Cl_2 (0.96M, 1.2 mL, 1.14 mmol) was added to a solution of **2a** (210 mg, 0.29 mmol) in CH_2Cl_2 (6 mL). The mixture was stirred at 23 °C for 3.5 h. The solvent was evaporated and the residue was triturated with Et_2O to give **[D$_1$]2a** as a pale yellow solid (194 mg, 88 %). The degree of deuteration was determined by integration of the signal at $\delta = 6.24$ in the ^{1}H NMR spectrum ($CDCl_3$).

***trans*-Chloro(4-methoxyphenoxymethyl)bis(triphenylphosphane)-palladium (1b)**

Method a: A solution of **3b** (200 mg, 0.30 mmol) in DMF (3 mL) was added to a suspension of $[Pd(PPh_3)_2Cl_2]$ (189 mg, 0.27 mmol) in DMF (5 mL). The mixture was heated at 50 °C for 13 h. After being cooled to 23 °C, the solvent was evaporated and the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated and the residue was triturated with Et_2O to give **1b** as a pale yellow solid (143 mg, 67 %).

Method b: A solution of **4b** (100 mg, 0.93 mmol) and triphenylphosphane (62 mg. 0.23 mmol) in CH_2Cl_2 (4 mL) was stirred at 23 °C for 30 min. The solvent was evaporated and the residue was triturated with Et_2O to give **1b** as a pale yellow solid (123 mg, 96 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 7.80 – 7.65 (m, 12H), 7.40 – 7.27 (m, 18H), 6.83 (t, $J = 8.1$ Hz, 1H), 6.29 (d, $J = 8.1$ Hz, 1H), 5.87 (d, $J = 8.3$ Hz, 1H), 5.72 (brs, 1H), 3.86 (brt, ^3J(H,P) = 7.5 Hz, 2H), 3.59 (brs, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 161.64, 160.54, 135.31 (t, ^2J(C,P) = 6.0 Hz; CH, PPh_3), 131.58 (t, ^1J(C,P) = 21.6 Hz; C, PPh_3), 130.50, 129.27, 128.55 (brs; PPh_3), 107.39, 105.84, 101.26, 66.31, 55.49; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 28.11$; FAB-MS: *m*/*z* (%): 766.9 (16) $[M - Cl]^+$, 505.1 (22), 154.1 (100); elemental analysis calcd (%) for $C_{44}H_{39}ClO_2P_2Pd$ (802.1): C 65.76, H 4.89; found: C 65.40, H 4.91.

***trans*-Chloro(4-nitrophenoxymethyl)bis(triphenylphosphane)palladium (1c)**

Method a: A solution of **3c** (62 mg, 0.09 mmol) in DMF (1 mL) was added to a suspension of $[Pd(PPh_3)_2Cl_2]$ (57 mg, 0.08 mmol) in DMF (1.5 mL). The mixture was heated at 50 °C for 13 h. After being cooled to 23 °C, the solvent was evaporated and the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated and the residue was triturated with Et_2O to give **1c** as a pale yellow solid (60 mg, 91 %).

Method b: A solution of **4b** (50 mg, 0.05 mmol) and triphenylphosphane (30 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) was stirred at 23 °C for 30 min. The solvent was evaporated and the residue was triturated with Et_2O to give **1c** as a pale yellow solid (66 mg, 90 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.8-$ 7.7 (m, 12H), 7.52 (d, $J = 8.1$ Hz, 1H), 7.4 – 7.3 (m, 18H), 7.01 (t, $J = 8.1$ Hz, 1H), 6.82 (brs, 1H), 6.43 (brd, $J = 8.1$ Hz, 1H), 3.81 (brt, ^3J(H,P) = 7.5 Hz, 2H); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 28.25$; FAB-MS: *m*/*z* (%): 782.2 (6) $[M - Cl]^+$, 520.1 (3), 368.1 (6).

***trans*-Chloro(phenoxymethyl)(triphenylphosphane)palladium dimer (4a)**: A solution of **3a** (420 mg, 0.77 mmol) in DMF (6 mL) was added to a suspension of $[Pd(PPh_3)Cl_2]_2$ (605 mg, 0.69 mmol) in DMF (6 mL). The mixture was stirred at 50 °C for 13 h. After being cooled to 23 °C, the solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, the residue was triturated with Et_2O to give **4a** as a pale yellow solid (550 mg, 71 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.75-7.62$ (m, 12H), 7.44 – 7.27 (m, 18H), 7.14 (brt, $J = 7.5$ Hz, 4H), 6.92 (brd, $J = 7.7$ Hz, 6H), 4.54 (d, ^3J(H,P) = 4.8 Hz, 4H); FAB-MS: *m*/*z* (%): 987.1 (4) $[M - Cl]^+$, 773.1 (6), 475.1 (16), 339.2 (100), 263.1 (15); elemental analysis calcd (%) for $C_{50}H_{44}Cl_2O_2P_2Pd_2$ (1022.6): C 58.73, H 4.34; found: C 58.06, H 4.50.

***trans*-Chloro(3-methoxyphenoxymethyl)(triphenylphosphane)palladium dimer (4b)**: A solution of **3b** (500 mg, 0.75 mmol) in DMF (1 mL) was added to a suspension of $[Pd(PPh_3)Cl_2]_2$ (320 mg, 0.37 mmol) in DMF (3 mL). The mixture was stirred at 50 °C for 13 h. After being cooled to 23 °C, the solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, and the residue was triturated with Et_2O to give **4b** as a pale yellow solid (622 mg, 80 %): ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.65$ (dd, $J = 11.3$ Hz, 6.9 Hz, 12H), 7.41 – 7.24(m, 18H), 7.03 (t, $J = 8.1$ Hz, 2H), 6.52 – 6.46 (m, 6H), 4.53 (d, ^3J(H,P) = 5.4 Hz, 4H), 3.72 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 160.89, 160.67, 135.05 (d, ^2J(C,P) = 12.3 Hz, PPh_3), 131.60 (d, ^1J(C,P) = 11.0 Hz, PPh_3), 130.83, 129.66, 128.57 (d, ^3J(C,P) = 11.0 Hz, PPh_3), 108.44, 107.21, 101.70, 67.29 (d, ^2J(C,P) = 7.3 Hz), 55.82; ^{31}P NMR (202.5 MHz, $CDCl_3$): $\delta = 37.21$; elemental analysis calcd (%) for $C_{52}H_{48}Cl_2O_4P_2Pd_2$ (1080.1): C 57.69, H 4.47; found: C 57.50, H 4.58.

***trans*-Chloro(3-nitrophenoxymethyl)(triphenylphosphane)palladium dimer (4c)**: To a suspension of $[Pd(PPh_3)Cl_2]_2$ (101 mg, 0.11 mmol) in DMF (1 mL) was added a solution of **3b** (170 mg, 0.23 mmol) in DMF (2 mL). The mixture was stirred at 50 °C for 15 h. After being cooled to 23 °C, the solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, the residue was triturated with Et_2O to give **4c** as a pale yellow solid (90 mg, 71 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.74-7.24$ (m, 38H), 4.40 (d, ^3J(H,P) = 5.6 Hz, 4H]; FAB-MS: *m*/*z* (%): 1076.9 (3) $[M - Cl]^+$, 520.0 (10), 339.1 (100), 263.1 (91), 154.0 (71).

***trans*-Chloro(phenoxymethyl)[1,1′-bis(diphenylphosphane)ferrocene]palladium (5)**: A solution of **1a** (200 mg, 0.26 mmol) and 1,1′-bis(diphenylphosphane)ferrocene (144 mg, 0.26 mmol) in CH_2Cl_2 (8 mL) was stirred at 23 °C for 30 min. The solvent was evaporated and the residue was triturated with Et_2O to give **6** as an orange solid (163 mg, 79 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.93-7.87$ (m, 4H), 7.59 (dd, $J = 11.5$, 7.4 Hz, 4H), 7.44 – 7.36 (m, 8H), 7.26 – 7.18 (m, 8H), 6.89 (t, $J = 6.8$ Hz, 1H), 4.87 (brd, ^3J(H,P) = 5.3 Hz, 2H), 4.50 (brs, 2H), 4.40 (brs, 2H), 4.04 (brs, 2H), 3.31 (brs, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 159.66$, 134.84 (d, ^2J(C,P) = 12.6 Hz; PPh_3), 134.80 (d, ^2J(C,P) = 12.6 Hz; PPh_3), 133.43 (d, ^1J(C,P) = 52.6 Hz; PPh_3), 133.12 (d, ^1J(C,P) = 29.4 Hz; PPh_3), 130.66 (brs; PPh_3), 129.99 (brs; PPh_3), 128.65, 128.47 (d, ^3J(C,P) = 10.5 Hz; PPh_3), 127.82 (d, ^3J(C,P) = 10.5 Hz; PPh_3), 119.64, 115.93, 74.44 (d, $J = 6.3$ Hz), 73.21 (d, $J = 8.4$ Hz), 71.62 (three signals were missing due to overlapping); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 35.75$ (d, ^2J(P,P) = 49.1Hz, 1P), 8.77 (d, ^2J(P,P) = 49.1 Hz, 1P); elemental analysis calcd (%) for $C_{52}H_{48}Cl_2O_4P_2Pd_2$ (802.4): C 61.30, H 4.39; found: C 61.10, H 4.63.

***trans*-(Phenoxymethyl)(acetonitrile)bis(triphenylphosphane)palladium tetrafluoroborate (6)**: A suspension of **1a** (150 mg, 0.20 mmol) and $AgBF_4$ (41 mg, 0.21 mmol) in CH_3CN (10 mL) was stirred at 23 °C for 1 h. The solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, the residue was triturated with Et_2O to give **6** as a yellow solid (142 mg, 83 %): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.65-7.27$ (m, 30H), 6.91 (m, 2H), 6.73 (t, $J =$ 7.3 Hz, 1H), 6.02 (brd, $J = 7.7$ Hz, 2H), 4.07 (t, ^3J(H,P) = 8.1 Hz, 2H), 1.46 (brs, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 159.19$, 134.07 (brt, ^2J(C,P) = 6.5 Hz, PPh_3), 132.35 (brs, PPh_3), 131.40 (brs, PPh_3), 129.08 (brt, ^3J(C,P) = 4.9 Hz, PPh_3), 128.75, 128.71, 128.40, 120.58, 114.06, 63.05, 1.57 (1C signal was not observed); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 27.97$; FAB-MS: *m*/*z* (%): 737.1 (37) $[C_{43}H_{36}OP_2Pd]$, 630.1 (16), 475.0 (29), 399.1 (100), 263.0 (25), 183.0 (29). The structure was confirmed by a ^{1}H – ^{13}C (HMQC) correlation.

***trans*-Chloro(2-acetylphenoxymethyl)bis(triphenylphosphane)palladium (7)**: Acetyl chloride (107 mg, 1.350 mmol) was added to a suspension of palladacycle **2a** (100 mg, 0.135 mmol) in THF (2 mL). The mixture was stirred at 23 °C for 15 min. The solvent was evaporated and the residue was triturated with Et_2O to give **7** as a white solid (108 mg, 99 %): ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.76-7.66$ (m, 12H), 7.48 (dd, $J = 7.5$, 1.6 Hz, 1H), 7.43 – 7.26 (m, 18H), 7.04 – 6.97 (m, 1H), 6.73 (t, $J = 7.5$ Hz, 1H), 6.31 (d, $J =$ 8.1 Hz, 1H), 3.78 (t, $^3J = 8.7$ Hz, 2H), 2.18 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 200.14$, 160.50, 135.18 (t, ^2J(C,P) = 6.3 Hz; PPh_3), 133.45, 131.12 (t, ^1J(C,P) = 22.2 Hz; PPh_3), 130.74 (brs, PPh_3), 129,78, 128.70 (t, ^3J(C,P) = 4.9 Hz; PPh_3), 127.68, 119.68, 113.30, 65.49, 32.33; ^{31}P NMR

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(202.5 MHz, $CDCl_3$): $\delta = 29.00$; FAB-MS: m/z (%): 779.1 (6) $[M]^+$, 516.7 (30), 263.1 (18), 154.1 (100), 77.0 (18).

***trans*-Chloro(phenoxymethyl)(triphenylphosphine)palladium dimer (4d)** and ***trans*-chloro(phenoxymethyl)-bis(triphenylarsine)palladium (1d)**: A solution of palladacycle **2d** (56 mg, 0.068 mmol) in CH_2Cl_2 (4 mL) was treated with a 1.0 M solution of anhydrous HCl in CH_2Cl_2 (0.34 mL, 0.34 mmol). The resulting mixture was stirred at 23 °C for 15 min. The residue obtained by evaporation of the solvent was triturated with Et_2O to give a yellow solid (42 mg) which consists of a 2:1 mixture of dimer (**4d**) and monomer (**1d**). The pure dimeric derivative can be obtained by repeating the trituration process. On the other hand, monomer **1d** is the only product formed that is detectable by ^1H NMR spectroscopy when treating **4d** (or the mixture of complexes resulting from the reaction) with a slight excess of $AsPh_3$ in $CDCl_3$. When trying to isolate **1d** by precipitation or trituration with Et_2O, either dimer **4d** or a mixture of complexes was obtained due to the ready dissociation of $AsPh_3$ from the dimer and the relatively low solubility of the monomer. **1d**: ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.75-7.55$ (br m, 12H), 7.50–7.35 (br m, 18H), 6.95 (m, 2H), 6.76 (m, 1H), 6.34 (br d, $J = 8.0$ Hz, 2H), 4.16 (s, 2H); **4d**: ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.69$ (m, 12H), 7.45–7.30 (m, 18H), 7.13 (m, 4H), 6.97 (br d, $J = 7.4$ Hz, 4H), 6.91 (m, 2H), 4.68 (s, 4H); FAB-MS: m/z: 1074.8 $[M-Cl]^+$, 967.8 $[M-PhOCH_2]^+$, 860.8; elemental analysis calcd (%) for $C_{50}H_{44}As_2Cl_2O_2Pd_2$ (1110.46): C 54.08, H 3.99; found: C 54.33, H 4.13.

(η^4-1,5-Cyclooctadiene)(methylenoxy-1,2-phenylen)palladium (8)

Method a: A suspension of **2a** (500 mg, 0.68 mmol) and $[Pd(COD)Cl_2]$ (194 mg, 0.68 mmol) in CH_2Cl_2 (3.5 mL) was stirred at 23 °C for 1 h. The precipitate was filtered off to give $[Pd(PPh_3)_2Cl_2]$ (475 mg, quantitative). The filtrate was evaporated and the resulting solid was triturated with Et_2O to give **8** as a pale yellow solid (156 mg, 72%).

Method b: A suspension of **10** (85 mg, 0.24 mmol) and Ag_2CO_3 (264 mg, 0.96 mmol) in CH_3CN (5 mL) was stirred at 23 °C for 24 h. The solvent was evaporated and the residue was triturated with Et_2O to give **8** (58 mg, 75%): ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.11$ (dd, $J = 7.4$, 1.6 Hz, 1H), 7.02 (td, $J = 7.3$, 1.6 Hz, 1H), 6.81 (dd, $J = 8.0$, 1.3 Hz, 1H), 6.68 (td, $J = 7.3$, 1.3 Hz, 1H), 6.09–6.08 (m, 2H), 5.77 (s, 2H), 5.52–5.50 (m, 2H), 2.67–2.47 (m, 8H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 173.76$, 146.33, 134.88, 127.27, 117.56, 114.29, 110.34, 109.16, 88.79, 29.05, 28.54.

[Methylenoxy-1,2-(3,5-dichloro)phenylen)](1,10-phenanthroline-N^1,N^{10})-palladium (9): A solution of **11** (100 mg, 0.2 mmol) and Ag_2CO_3 (221 mg, 0.80 mmol) in CH_3CN (5 mL) was stirred at 50 °C for 18 h. The solvent was evaporated and the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated and the residue was triturated with Et_2O to give **9** as a yellow solid (90 mg, quantitative). The ^1H NMR spectrum was identical to that of **9** prepared by ligand exchange from **2a**.[16b]

***trans*-Chloro-phenoxymethyl)(η^4-1,5-cyclooctadiene)palladium (10)**: A solution of HCl in CH_2Cl_2 (1 M, 0.96 mL, 0.96 mmol) was added to a solution of **8** (77 mg, 0.24 mmol) in CH_2Cl_2 and the mixture was stirred at 23 °C for 2 h. The solvent was evaporated and the residue was triturated with Et_2O to give **10** as a white solid (85 mg, quantitative): ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.31$ (br t, $J = 8.3$ Hz, 2H), 7.15 (br d, $J = 8.0$ Hz, 2H), 7.00 (br t, $J = 7.2$ Hz, 1H), 5.91 (br s, 2H), 5.23 (s, 2H), 5.13 (br s, 2H), 2.70–2.30 (m, 8H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 158.40$, 129.69, 123.88, 121.68, 114.86, 105.66, 72.99, 30.40, 27.58.

***trans*-Chloro-(2,4-dichlorophenoxymethyl)(1,10-phenanthroline-N^1,N^{10})-palladium (11)**: Me_3SiCl (0.3 mL, 2.28 mmol)was added to a solution of **9** (105 mg, 0.23 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred at 23 °C for 1 h. The solvent was evaporated and the residue was triturated with Et_2O to give **11** as a yellow solid (108 mg, 96%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 9.65$ (dd, $J = 5.3$, 1.4 Hz, 1H), 9.44 (dd, $J = 4.8$, 1.6 Hz, 1H), 8.48 (dd, $J = 8.2$, 1.4 Hz, 1H), 8.42 (dd, $J = 8.2$, 1.6 Hz, 1H), 8.18 (d, $J = 8.9$ Hz, 1H), 7.90 (s, 2H), 7.89 (dd, $J = 8.2$, 5.3 Hz, 1H), 7.83 (dd, $J = 8.2$, 4.8 Hz, 1H), 7.25 (dd, $J = 8.9$, 2.5 Hz, 1H), 7.19 (d, $J = 2.5$ Hz, 1H), 5.35 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 153.58$, 151.46, 149.62, 146.94, 137.88, 137.49, 129.88, 129.20, 128.76, 128.12, 127.08, 126.81, 125.33, 125.08, 124.75, 122.48, 116.49, 58.09 (one signal was not observed due to overlapping).

(Methylenoxy-1,2-phenylen)bis(triphenylphosphane)palladium (2a)

Method a: A suspension of **1a** (50 mg, 0.06 mmol) and KOPh (9 mg, 0.06 mmol) in CH_3CN (3 mL) was stirred at 23 °C for 90 min. The solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, the residue was triturated with Et_2O to give **2a** as a white solid (46 mg, 97%).

Method b: A suspension of **1a** (18 mg, 0.023 mmol) and Ag_2CO_3 (32 mg, 0.12 mmol) in CH_3CN (5 mL) was stirred at 23 °C for 4 h. The solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, the residue was triturated with Et_2O to give **2a** as a white solid (17 mg, quantitative). The NMR spectra were identical to that of **2a** prepared from (2-iodophenoxymethyl)tributylstannane.[16a,b]

[Methylenoxy-1,2-(4-methoxyphenylen)]bis(triphenylphosphane)palladium (2b): A suspension of **1b** (50 mg, 0.06 mmol) and KOPh (9 mg, 0.06 mmol) in CH_3CN (3 mL) was stirred at 23 °C for 15 h. The solvent was evaporated, the residue was partially dissolved in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated, the residue was triturated with Et_2O to give **2b** as a white solid (45 mg, 95%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.44-7.02$ (m, 30H), 6.44 (t, $J = 7.8$ Hz, 1H), 6.33 (t, $J = 2.4$ Hz, 1H), 5.69 (br d, $J = 7.5$ Hz, 1H), 5.12 (dd, $^3J(H,P) = 5.4$, 3.2 Hz, 2H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.06$, 158.15, 141.66 (d, $J(C,P) = 6.32$ Hz), 135.24 (d, $J(C,P) = 14.0$ Hz, PPh_3), 134.20 (d, $J(C,P) = 13.0$ Hz, PPh_3), 133.92, 135.24 (br s, PPh_3), 131.97 (br s, PPh_3), 129.82 (br s, PPh_3), 127.46 (br s, PPh_3), 127.98 (d, $J(C,P) = 8.4$ Hz, PPh_3), 127.85(d, $J(C,P) = 8.4$ Hz, PPh_3), 103.21 (d, $J(C,P) = 8.4$ Hz), 93.76, 92.66 (d, $J(C,P) = 6.3$ Hz), 54.83; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 28.52$ (d, $^2J(P,P) = 25.9$ Hz, 1P), 25.74 (d, $^2J(P,P) = 25.9$ Hz, 1P).

[Methylenoxy-1,2-(4-nitrophenylen)]bis(triphenylphosphane)palladium (2c): A suspension of **1c** (50 mg, 0.06 mmol) and KOPh (8 mg, 0.06 mmol) in CH_3CN (3 mL) was stirred at 23 °C for 16 h. Addition of methanol led to a precipitate, which was filtered and washed with Et_2O to give **2c** as a yellow solid (45 mg, 94%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.63-6.63$ (m, 31H), 6.90 (br d, $J = 6.9$ Hz, 1H), 6.66 (br t, $J = 6.9$ Hz, 1H), 5.18 (dd, $^3J(H,P) = 5.4$, 3.2 Hz, 2H); ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 28.64$ (d, $^2J(P,P) = 27.6$ Hz, 1P), 24.81 (d, $^2J(P,P) = 27.6$ Hz, 1P].

(Methylenoxy-1,2-phenylen)bis(triphenylarsine)palladium (2d): A mixture of **4d** (7 mg, 0.0064 mmol), $AsPh_3$ (4 mg, 0.013 mmol) and Ag_2CO_3 (18 mg, 0.065 mmol) in CH_3CN (2 mL) was stirred at 40 °C for 4 h. After evaporation of the solvent, the residue was suspended in CH_2Cl_2 and filtered through Celite. The filtrate was evaporated to dryness and the resulting solid was triturated with Et_2O, filtered and washed with Et_2O to give **2d** as a pale yellow solid (8 mg, 76%), identical to that obtained before.[16]

(Methylenoxy-1,2-phenylen)[1,1′-bis(diphenylphosphino)ferrocene]palladium (12): A mixture of **5** (40 mg, 0.05 mmol) and Cs_2CO_3 (81 mg, 0.25 mmol) in CH_3CN (2.5 mL) was stirred at 23 °C for 50 h. The solvent was evaporated and the residue was triturated with Et_2O to give **12** as an orange solid (36 mg, 96%). The NMR spectra were identical to that of **12** prepared from (2-iodophenoxymethyl)tributylstannane or by ligand exchange reaction from **2a**.[16]

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[1] Reviews: a) G. Dyker, *Angew. Chem.* **1999**, *111*, 1808; *Angew. Chem. Int. Ed.* **1999**, *38*, 1698; b) A. D. Ryabov, *Chem. Rev.* **1990**, *90*, 403.

[2] Reviews on metalation by late transition metals: a) J. Spencer, M. Pfeffer, *Adv. Met. Org. Chem.* **1998**, *6*, 103; b) A. E. Shilov, G. B. Shul'pin, *Chem. Rev.* **1985**, *85*, 245; c) A. Sen, *Acc. Chem. Res.* **1985**, *28*, 154; d) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kakitani, M. Sonoda, N. Chatani, *Pure Appl. Chem.* **1994**, *66*, 1527.

[3] Lead references on the mechanism of the metalation of arenes: a) A. Vigalok, O. Uzan, L. J. W. Shimon, Y. Ben-David, J. M. L. Martin, D. Milstein, *J. Am. Chem. Soc.* **1998**, *120*, 12539; b) T. Matsubara, N. Koga, D. Musaev, K. Morokuma, *J. Am. Chem. Soc.* **1998**, *120*, 12692; c) B. Biswas, M. Sugimoto, S. Sakaki, *Organometallics* **2000**, *19*, 3895.

[4] Synthesis of biaryls: a) W. Stadlbauer, R. Laschober, T. Kappe, *Liebigs Ann. Chem.* **1990**, 531; b) P. P. Deshpande, O. R. Martin, *Tetrahedron Lett.* **1990**, *31*, 6313; c) T. Hosoya, E. Takashiro, T. Matsumoto, K. Suzuki, *J. Am. Chem. Soc.* **1994**, *116*, 1004; d) G. Bringmann, T. Pabst, P. Henschel, J. Kraus, K. Peters, E.-M. Peters, D. S. Rycroft, J. D. Connolly, *J. Am. Chem. Soc.* **2000**, *122*, 9127, and references therein.

[5] Synthesis of heterocycles: a) D. E. Ames, D. Bull, *Tetrahedron* **1982**, *38*, 383; b) D. E. Ames, A. Opalko, *Synthesis* **1983**, 234; c) D. E. Ames, A. Opalko, *Tetrahedron* **1984**, *40*, 1919; d) T. Kuroda, F. Suzuki, *Tetrahedron Lett.* **1991**, *32*, 6915; e) A. P. Kozikowski, D. Ma, *Tetrahedron Lett.* **1991**, *32*, 3317.

[6] Synthesis of polyarenes: a) J. E. Rice, Z.-W. Cai, Z.-M. He, E. J. LaVoie, *J. Org. Chem.* **1995**, *60*, 8101; b) J. E. Rice, Z.-W. Cai, *J. Org. Chem.* **1993**, *58*, 1415; c) J. E. Rice, Z.-W. Cai, *Tetrahedron Lett.* **1992**, *33*, 1675; d) J. J. González, N. García, B. Gómez-Lor, A. M. Echavarren, *J. Org. Chem.* **1997**, *62*, 1286; e) Ó. de Frutos, B. Gómez-Lor, T. Granier, M. A. Monge, E. Gutiérez-Puebla, A. M. Echavarren, *Angew. Chem.* **1999**, *111*, 186; *Angew. Chem. Int. Ed.* **1999**, *38*, 204; f) B.; Gómez-Lor, Ó. de Frutos, A. M. Echavarren, *Chem. Commun.* **1999**, 2431; g) L. Wang, P. B. Shevlin, *Tetrahedron Lett.* **2000**, *41*, 285; h) H. A. Reisch, M. S. Bratcher, L. T. Scott, *Org. Lett.* **2000**, *2*, 1427.

[7] For the intermolecular palladium-catalyzed arylation, see: a) Y. Akita, A. Inoue, K. Yamamoto, A. Ohta, T. Kurihara, M. Shimizu, *Heterocycles* **1985**, *23*, 2327; b) Y. Aoyagi, A. Inoue, I. Koizumi, R. Hashimoto, K. Tokunaga, K. Gohma, J. Komatsu, K. Sekine, A. Miyafuji, J. Kunoh, R. Honma, Y. Akita, A. Ohta, *Heterocycles* **1992**, *33*, 257; c) G. Dyker, *Angew. Chem.* **1992**, *104*, 1079; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1023; d) G. Dyker, *J. Org. Chem.* **1993**, *58*, 6426; e) G. Dyker, *Chem. Ber.* **1994**, *127*, 739; f) G. Dyker, J. Körning, F. Nerenz, P. Siemsen, S. Sostmann, A. Wiegand, P. G. Jones, P. Bubensitschek, *Pure Appl. Chem.* **1996**, *68*, 323; g) G. Dyker, P. Siemsen, S. Sostmann, A. Wiegand, I. Dox, P. G. Jones, *Chem. Ber.* **1997**, *130*, 261; h) T. Satoh, Y. Kawamura, M. Miura, M. Nomura, *Angew. Chem.* **1997**, *109*, 1820; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1740.

[8] Pd^0 may coordinate with the added halide to form reactive anionic species: C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000**, *33*, 314, and references therein.

[9] V. Farina, *Comprehensive Organometallic Chemistry II*, *Vol. 12* (Eds.: E W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, Chapter 3.4, pp. 228–229.

[10] An electrophilic pathway has been shown to operate in other palladation reactions: A. J. Canty, *Comprehensive Organometallic Chemistry II*, *Vol. 9* (Eds.: E W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon, Oxford, **1995**, Chapter 5, and references therein.

[11] a) A. J. Canty, G. van Koten, *Acc. Chem. Res.* **1995**, *28*, 406; b) D. M. Grove, G. van Koten, J. N. Louwen, J. G. Noltes, A. L. Spek, H. J. C. Ubbels, *J. Am. Chem. Soc.* **1982**, *104*, 6609; c) J. Terhijden, G. van Koten, I. C. Vinke, A. L. Spek, *J. Am. Chem. Soc.* **1985**, *107*, 2891.

[12] a) C.-S. Li, D.-C. Jou, C.-H. Cheng, *Organometallics* **1993**, *12*, 3945; b) C.-H. Li, F.-L. Liao, S.-L.Wang, *J. Chem. Soc. Chem. Commun.* **1991**, 710; c) H. Ossor, M. Pfeffer, J. T. B. H. Jastrzebski, C. H. Stam, *Inorg. Chem.* **1987**, *26*, 1169.

[13] For lead examples of other metals, see: iridium: a) P. O. Stoutland, R. G. Bergman, *J. Am. Chem. Soc.* **1988**, *110*, 5732; rhodium: b) W. D. Jones, F. J. Feher, *J. Am. Chem. Soc.* **1986**, *108*, 4814.

[14] E. Carmona, J. Cámpora, J. A. López, P. Valerga, E. Spillner, *Angew. Chem.* **1999**, *111*, 199; Angew. *Chem. Int. Ed.* **1999**, *38*, 147.

[15] M. Catellani, G. P. Chiusoli, *J. Organomet. Chem.* **1992**, *425*, 151.

[16] a) D. J. Cárdenas, C. Mateo, A. M. Echavarren, *Angew. Chem.* **1994**, *106*, 2529; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2445; b) C. Mateo, D. J. Cárdenas, C. Fernández-Rivas, A. M. Echavarren, *Chem. Eur. J.* **1996**, *2*, 1596; c) C. Mateo, C. Fernández-Rivas, A. M. Echavarren, D. J. Cárdenas, *Organometallics* **1997**, *16*, 1997; d) C. Mateo, C. Fernández-Rivas, D. J. Cárdenas, A. M. Echavarren, *Organometallics* **1998**, *17*, 3661.

[17] a) D. Seyferth, S. B. Andrews, *J. Organomet. Chem.* **1971**, *30*, 151; b) D. Seyferth, S. B. Andrews, R. L. Lamber, *J. Organomet. Chem.* **1971**, *37*, 69.

[18] M. Zollinger, *Adv. Phys. Org. Chem.* **1964**, *2*, 163.

[19] Cleavage of palladacycles by protic acid is a key step in a recent synthesis of 9-alkylidene-9*H*-fluorenes catalyzed by palladium: Q. Tian, R. C. Larock, *Org. Lett.* **2000**, *2*, 3329.

[20] a) G. M. Kapreijn, A. Dervisi, D. M. Grove, H. Kooijman, M. T. Lakin, A. L. Spek, G. van Koten, *J. Am. Chem. Soc.* **1995**, *117*, 10939; b) G. M. Kapreijn, D. M. Grove, H. Kooijman, W. J. J. Smeets, A. L. Spek, G. van Koten, *Inorg. Chem.* **1996**, *35*, 526.

[21] a) V. V. Grushin, C. Bensimon, H. Alper, *Organometallics* **1995**, *14*, 3259; b) V. V. Grushin, H. Alper, *Organometallics* **1996**, *15*, 5242.

[22] J. Ruiz, N. Cutillas, J. Torregrosa, G. García, G. López, P. A. Chaloner, P. B. Hitchcock, R. M. Harrison, *J. Chem. Soc. Dalton Trans.* **1994**, 2353, and references therein.

[23] a) M. A. Andrews, G. L. Gould, E. J. Voss, *Inorg. Chem.* **1996**, *35*, 5740; b) M. A. Andrews; G. L. Gould, W. T. Klooster, K. S. Koenig, E. J. Voss, *Inorg. Chem.* **1996**, *35*, 5478; c) U. Abram, D. B. Dell'Amico, F. Calderazzo, L. Marchetti, J. Strahle, *J. Chem. Soc. Dalton Trans.* **1999**, 4093.

[24] R. J. Cross, *Adv. Inorg. Chem.* **1989**, *34*, 219.

[25] R. F. Heck, *Palladium Reagents in Organic Syntheses*, Academic, London, **1985**, p. 18.

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