Mechanism of the Stille Reaction. 2. Couplings of Aryl Triflates with Vinyltributyltin. Observation of Intermediates. A More Comprehensive Scheme

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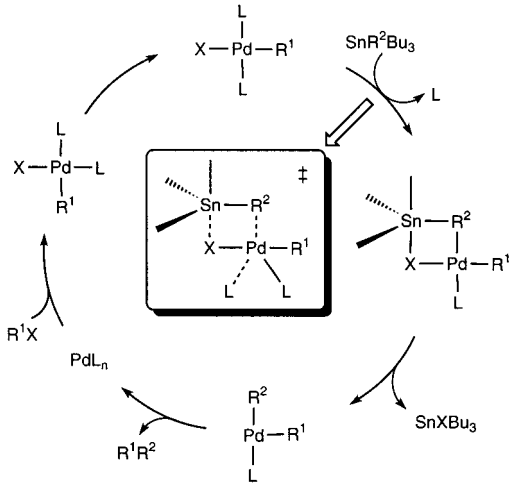
Abstract: The mechanism of the [PdL_4]-catalyzed couplings between R−OTf (R = pentahalophenyl; L = PPh_3, $AsPh_3$) and $Sn(CH{=}CH_2)Bu_3$ has been studied. The addition of LiCl favors the coupling for L = $AsPh_3$ in THF but retards it for L = PPh_3. Separate experiments show that for L = $AsPh_3$, LiCl accelerates the otherwise very slow and rate-determining oxidative addition of the aryl triflate to [PdL_4], leading to *trans*-[$PdRClL_2$]. Therefore, the overall process is accelerated. For L = PPh_3, the rate-determining step is the transmetalation. Complex *trans*-[$PdRXL_2$], with X = Cl, is formed in the presence of LiCl, whereas an equilibrium mixture mainly involving species with X = TfO, L, or S (S = solvent) is established in the absence of LiCl. Since the transmetalation is slower for X = Cl than for the other complexes, the overall process is retarded by addition of LiCl. The transmetalation in complexes *trans*-[$PdRXL_2$], with X = Cl, follows the S_E2(cyclic) mechanism proposed in Part 1 (Casado, A. L.; Espinet, P. *J. Am. Chem. Soc.* **1998**, *120*, 8978−8985), giving the coupling product R−CH=CH_2 directly. For X = TfO or L, rather stable intermediates *trans*-[$PdR(CH{=}CH_2)L_2$] are detected, supporting an S_E2(open) mechanism. The key intermediates undergoing transmetalation in the conditions and solvents most commonly used in the literature have been identified. The operation of S_E2(cyclic) and S_E2(open) pathways emphasizes common aspects of the Stille reaction with the Hiyama reaction where, using R^2SiF_3 that is chiral at the α-carbon of R^2, retention or inversion at the transmetalated chiral carbon can be induced. This helps us to understand the contradictory stereochemical outcomes in the literature for Stille couplings using R^2SnR_3 derivatives that are chiral at the α-carbon of R^2 and suggests that stereocontrol of the Stille reaction might be achieved.

Introduction

Recently, we have proposed a new mechanism for the Stille couplings of R^1I with R^2SnBu_3 (Scheme 1; X = I, R^1 = aryl, R^2 = vinyl or aryl).[1] The proposed transmetalation step consists of an associative L-for-R^2 substitution on the catalyst *trans*-[PdR^1IL_2]. The two most remarkable features in this new mechanism are (i) the role of X as a bridging group which assists the R^2 transfer between the two metal atoms via an "S_E2(cyclic)" mechanism (activated complex framed in the center of Scheme 1) and (ii) the immediate cis configuration and three coordination of the bis(organo)palladium(II) intermediate, which rapidly eliminates the coupling product $R^1{-}R^2$.[2]

The most commonly used electrophiles in Stille couplings are organic iodides, bromides, and triflates (trifluoromethyl sulfonates).[3] We restricted our proposal of an S_E2(cyclic) transmetalation to X = halide; i.e., the catalytic cycle in Scheme 1 would hold for organic iodides and bromides (for chlorides, although the transmetalation step works perfectly as an isolated reaction, the oxidative addition step is difficult, this often precluding the operation of the catalysis; see, however, recent advances in the activation of chlorides).[4] Moreover, we warned that other mechanisms could operate under different conditions, such as coordinating solvents or lack of halide in the system.

Scheme 1



In fact, couplings of triflates (X = OTf) show several distinct experimental features that cannot be understood within the frame of Scheme 1. One of the most striking aspects is the effect of the addition of LiCl. Stille et al. found the addition of stoichiometric LiCl necessary to achieve couplings of organic

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(1) Part 1: Casado, A. L.; Espinet, P. *J. Am. Chem. Soc.* **1998**, *120*, 8978−8985. A brief review on Stille couplings is given therein.

(2) For this nomenclature, see: Hatanaka, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1990**, *112*, 7794−7796.

(3) A comprehensive review of the synthetic applications of this reaction has appeared recently. See: Farina, V.; Krishnamurthy, V.; Scott, W. J. *The Stille Reaction*; Wiley: New York, 1998.

(4) (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 2411−2413. (b) Sturmer, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 3307−3308.

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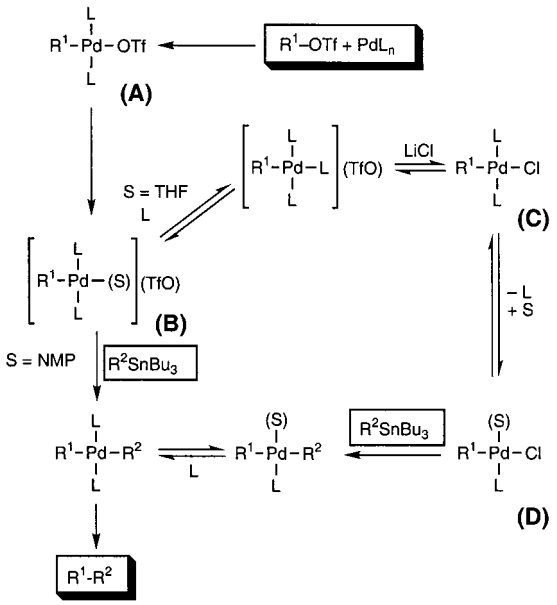
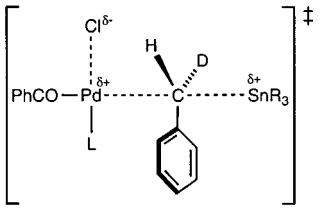
Scheme 2



triflates.[5] It was assumed that the role of the chloride ions was to replace the triflate in the coordination plane of an eventual triflatopalladium(II) species (formed upon oxidative addition of the organic triflate), leading to a chloropalladium(II) complex. The transmetalation should supposedly take place more readily on the latter than on the triflatopalladium(II) complex. Soon it became apparent that the requirement of LiCl is not general, and many exceptions have been reported. In fact, Piers et al. have reported cases where addition of LiCl retards the coupling.[6] Farina et al. have extensively studied this LiCl effect and have found it to be both accelerating and retarding, depending on the solvent (THF, or NMP = 1-methyl-2-pyrrolidinone), the organic triflate (R^1 = aryl or vinyl), and the neutral ancillary ligand (L = $AsPh_3$ or PPh_3).[7] From their own experiments and from other studies in the literature on related Pt systems,[8] they have proposed the existence of "at least two mechanistically distinct pathways for the transmetalation reaction",[9] summarized in Scheme 2, [7a,3] "a faster one proceeding via cationic species **B** and (with L = PPh_3) a slower one proceeding via ligand dissociation (through **D**)".[3] In THF solvent, LiCl would be necessary to induce coupling because the initial oxidative addition product **A** "is catalytically incompetent, whereas ligand substitution with chloride leads to the reactive species **C**".[3] It was suggested that "in the absence of Cl intermediates **A** and/or **B** may be too unstable to complete a catalytic cycle".[9] In highly polar solvents, like NMP, LiCl is often unnecessary and can be even an inhibitor of the coupling. Chen and He, who isolated the oxidative addition product $[Pd(C_6H_4Cl\text{-}p)(OSO_2R^F)(PPh_3)_2]$ (R^F = $HCF_2CF_2OCF_2CF_3$), also proposed a catalytic cycle through **C**.[10]

Chart 1



All these valuable studies showed clearly that the Stille reaction is a complex matter and its mechanism cannot be limited to just one pathway. Moreover, the importance of using neutral ligands of lower donicity toward Pd(II), which could decoordinate easily, was stressed and led to important synthetic improvements. However, the studies suffered from some limitations. The most important was that, since the different steps of the cycle were not studied separately, the kinetic measurements had to assume first-order kinetics overall for this multistep reaction; in other words, it was assumed that the transmetalation was rate-determining in all the experiments, regardless of the neutral ligand or the electrophile (triflate or halide) used.[7b] Another important drawback was that systems studied usually restricted the evidence on intermediates to ^{31}P NMR spectroscopy (if any evidence at all was available). Consequently, details on the true nature of the intermediates (e.g., stereochemistry at Pd) could not be conveniently assessed. This aspect, as we discuss later, is of some importance.

Thus, in the currently accepted mechanistic proposals (Scheme 2), it is assumed that all the transmetalation reactions involve Cl-for-R^2 or S-for-R^2 exchange (S = solvent or "empty site"). It is also assumed that the nucleophile should always attack a highly electrophilic reactive intermediate bearing an "empty" coordination site, such as *trans*-$[PdR^1(S)L_2]^+$ or *cis*-$[PdR^1(S)ClL]$, while neutral triflate complexes *trans*-$[PdR^1(OTf)L_2]$ or cationic complexes $[PdR^1L_3]^+$ are disregarded. The transmetalation mechanism (Scheme 2, transition states were not specified) leads to intermediates *trans*-$[PdR^1R^2L_2]$ in all cases, regardless of the configuration of the reactive intermediates. It can be remarked also that intermediates *trans*-$[PdR^1R^2L_2]$ have not previously been observed in any Stille coupling. The direct formation of the coupling product R^1-R^2 from the latter is not straightforward but requires the dissociation of L and subsequent isomerization to the cis form.[11] In spite of this, it has been taken for granted that the elimination process is a fast step in all cases.

A further point that needs to be discussed is the nature of the transmetalation transition states and the stereochemical implications on the transmetalated chiral carbons. This latter aspect of the Stille reaction has been rarely considered. In a seminal paper, Labadie and Stille found ≥65% inversion for the coupling of a chiral benzylic stannane and an acyl chloride.[12] They considered the dichotomy between cyclic and open transition states for the electrophilic cleavage of carbon−tin bonds and proposed the open transition state in Chart 1 (involving Cl-for-R substitution on a Pd complex which has previously dissociated an L ligand). They pointed out that the behavior they were observing (inversion via S_E2 open mechanism) might be due to the high polarity of the solvent used. Some years later, Falck et al. found ca. 98% retention of configuration in the coupling of chiral α-alkoxystannanes with acyl chlorides and remarked, "This is in stark contrast with

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(6) Piers, E.; Friesen, R. W.; Keay, B. A. *J. Chem. Soc., Chem. Commun.* **1985**, 809−810. (b) Piers, E.; Friesen, R. W. *J. Org. Chem.* **1986**, *51*, 3405−3406.

(7) (a) Farina, V.; Roth, G. P. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1995; Vol. 5, pp 1−53. (b) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585−9595.

(8) Stang, P. J.; Kowalski, M. H.; Schiavelli, M. D.; Longford, D. *J. Am. Chem. Soc.* **1989**, *111*, 3347−3356.

(9) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993**, *58*, 5434−5444.

(10) Chen, Q.-Y.; He, Y.-B. *Chin. J. Chem.* **1990**, 451−468.

(11) Tatsumi, K.; Hoffmann, R.; Yamamoto, A.; Stille, J. K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1857−1867.

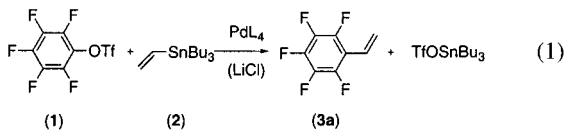
(12) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129−6137.

couplings between tetraalkylstannanes and benzoyl chloride where inversion of configuration has been demonstrated. The origins of this phenomenon and the potential involvement of the α-heteroatom warrant further investigation." [13] In a different context, the possible involvement of cyclic and open transition states in the Stille reaction was also considered in studies on the possible intramolecular nucleophilic assistance at some organotins bearing potentially coordinating arms.[14] By assuming as "plausible" either closed or open transition states in different solvents (depending on the solvent polarity), many overall rates observed for catalytic processes could be explained if the nucleophilic assistance was able to stabilize only "closed" transition states, but other rates did not fit this suggestion.[14c] These scarce precedents are intriguing and interesting and stress the need for a better evaluation of the likeliness of different plausible intermediates and transition states in different reaction conditions.

In this paper, we undertake the study of the Pd-catalyzed couplings between C_6F_5-OTf (**1**) and $Sn(CH=CH_2)Bu_3$ (**2**),[15] which has allowed us to achieve a number of interesting results: (a) The three steps (oxidative addition, transmetalation, and reductive elimination) of the same Stille cycle are studied separately. (b) The role of LiCl (whether accelerating, retarding, or neutral) in solvents of moderate polarity (THF, PhCl, CH_2Cl_2) is demonstrated by measuring its effect on the different steps involved in the cycle. (c) The organopalladium(II) intermediates formed upon oxidative addition of **1** to $Pd(PPh_3)_4$ are fully characterized, and their behavior toward transmetalation is kinetically studied. (d) A transmetalation intermediate, *trans*-$[PdRR'L_2]$, is detected and fully identified. (e) The key role of the coordination stereochemistry at Pd is revealed, a detailed view of the exchange at the transmetalation (which-for-which) is proposed, and an analysis of the consequences, including its stereochemical implications, is offered. These results, along with those in Part 1, afford a more complete picture of the Stille reaction using monodentate ligands.

Results

Coupling of C_6F_5-OTf with $Sn(CH=CH_2)Bu_3$ Catalyzed by $[PdL_4]$ (L = PPh_3, $AsPh_3$). The rate of reaction between C_6F_5-OTf (**1**) and $Sn(CH=CH_2)Bu_3$ (**2**) catalyzed by $[PdL_4]$ (eq 1) depends strongly on the neutral ligand L (PPh_3 or $AsPh_3$), the solvent, and whether LiCl is added. The conversion into



(1)

the coupling product $C_6F_5-CH=CH_2$ (**3a**) was studied by ^{19}F NMR under different conditions, and the results are summarized in Table 1.

These results show the following: (1) The addition of LiCl scarcely affects the coupling rates in PhCl (entries 1 vs 2, and 5 vs 6), probably because of its low solubility or low dissociation in this solvent. (2) $[Pd(PPh_3)_4]$ is a more efficient catalyst than $[Pd(AsPh_3)_4]$ in PhCl, and also in THF in the absence of LiCl (entries 1−3 vs 5−7). (3) The use of LiCl affects the rate of coupling in THF: the reaction catalyzed by $[Pd(PPh_3)_4]$ is strongly retarded (entry 3 vs 4), whereas that catalyzed by $[Pd(AsPh_3)_4]$ is accelerated (entry 7 vs 8). To understand the origin of these differences, the oxidative additions of **1** to $[PdL_4]$, and the transmetalations of the resulting organopalladium(II) intermediates with **2**, were studied separately.

Table 1. Coupling Reactions between C_6F_5-OTf (**1**) and $Sn(CH=CH_2)Bu_3$ (**2**) Catalyzed by $[PdL_4]$: Conversion to $C_6F_5-CH=CH_2$ (**3a**)[a]

				conversion (%)	
entry	L	solvent	additive[b]	10 h	24 h
1	PPh_3	PhCl	none	86	96
2	PPh_3	PhCl	LiCl	92	100
3	PPh_3	THF	none	65	100
4	PPh_3	THF	LiCl	0	6
5	$AsPh_3$	PhCl	none	6	7
6	$AsPh_3$	PhCl	LiCl	5	7
7	$AsPh_3$	THF	none	13	14
8	$AsPh_3$	THF	LiCl	79	87

[a] At 50 °C; [**1**] = [**2**] = 0.2 mol L^{-1}, $[PdL_4]$ = 0.01 mol L^{-1}. [b] [LiCl] = 0.2 mol L^{-1}.

Table 2. Organopalladium(II) Species Formed upon the Oxidative Addition of C_6F_5-OTf (**1**) to $[PdL_4]$[a]

entry	L	solvent	additive[b]	complex(es)[c]
1	PPh_3	PhCl	none	*trans*-$[PdR(OTf)L_2]$ $[PdRL_3]^+$
2	PPh_3	PhCl	LiCl	*trans*-$[PdR(OTf)L_2]$ $[PdRL_3]^+$ *trans*-$[PdRClL_2]$
3	PPh_3	THF	none	*trans*-$[PdR(THF)L_2]^+$ $[PdRL_3]^+$
4	PPh_3	THF	LiCl	*trans*-$[PdRClL_2]$
5	$AsPh_3$	PhCl	none	none
6	$AsPh_3$	PhCl	LiCl	none
7	$AsPh_3$	THF	none	none
8	$AsPh_3$	THF	LiCl	*trans*-$[PdRClL_2]$

[a] After 30 min at 20 °C; [**1**] = 0.2 mol L^{-1}, $[PdL_4]$ = 0.01 mol L^{-1}. [b] [LiCl] = 0.2 mol L^{-1}. [c] R = C_6F_5.

Oxidative Addition of C_6F_5-OTf to $[PdL_4]$. The reactions of C_6F_5-OTf (**1**) and $[PdL_4]$ (L = PPh_3, $AsPh_3$) in a 20:1 mol ratio (similar to that used in the catalytic reactions) were carried out with and without LiCl, and the resulting organopalladium(II) species (Table 2) were identified by ^{19}F and $^{31}P\{^1H\}$ NMR.

The oxidative addition of C_6F_5-OTf (**1**) to $[Pd(PPh_3)_4]$ was very fast either in PhCl or in THF (Scheme 3). In PhCl, it led to *trans*-$[Pd(C_6F_5)(OTf)(PPh_3)_2]$ (**4a**) as the major organopalladium(II) product, but $[Pd(C_6F_5)(PPh_3)_3]^+$ (**5a**$^+$) was also formed in a smaller amount. In THF, *trans*-$[Pd(C_6F_5)(THF)(PPh_3)_2]^+$ (**7a**$^+$), **4a**, and **5a**$^+$ were formed (**4a, 5a·**(TfO), and **7a·**(TfO) are involved in dynamic equilibria, analyzed later for the corresponding $C_6Cl_2F_3$ complexes). When the reaction was carried out in the presence of LiCl, the final products depended on the solvent. In THF, *trans*-$[Pd(C_6F_5)Cl(PPh_3)_2]$ (**6a**) was the only product detected. These results are in agreement with those found by Jutand and Mosleh for other aryl triflates in DMF (dimethylformamide), except that in that case $[PdAr(PPh_3)_3]^+$ species were not detected.[16] In PhCl, the main products were **4a** and **5a**$^+$, and only a small amount of **6a** was formed. In separate experiments, complex **6a** was quantitatively formed by treatment of **4a** with LiCl in THF at ambient temperature, whereas no reaction was observed in PhCl. All the compounds were identified by comparison with original samples prepared separately.

In contrast, the oxidative addition of **1** to $[Pd(AsPh_3)_4]$ was very slow. No reaction was observed in THF or PhCl after 30

(13) Ye, J.; Bath, R. K.; Falck, J. R. *J. Am. Chem. Soc.* **1994**, *116*, 1−5.
(14) (a) Vedejs, E.; Haight, A. R.; Moss, W. O. *J. Am. Chem. Soc.* **1992**, *114*, 6556−6558. (b) Brown, J. M.; Pearson, M.; Jastrzebsky, J. T. B. H.; van Koten, G. *J. Chem. Soc., Chem. Commun.* **1992**, 1440−1441. (c) Farina, V. *Pure Appl. Chem.* **1996**, *68*, 73−78.
(15) **1** was used because of the advantages provided by fluorophenyl derivatives in mechanistic studies involving Pd(II) derivatives. Some previous examples are given by Casado and Espinet (Casado, A. L.; Espinet, P. *Organometallics* **1998**, *17*, 3677−3683), as well as in refs 1, 17, 22, and 32.

Scheme 3

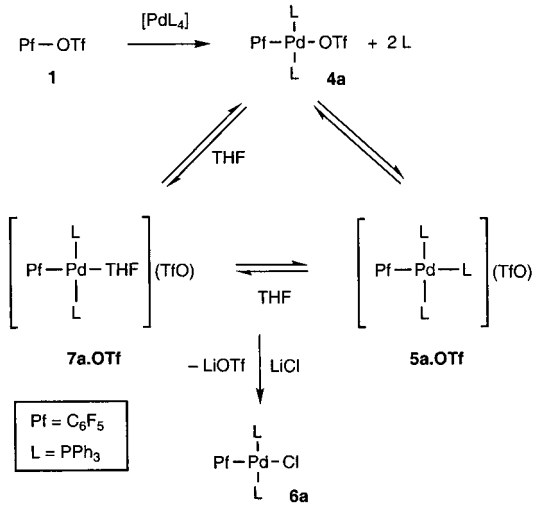


Table 3. Transmetalation Reactions between *trans*-[Pd(C_6F_5)XL_2] and Sn(CH=CH_2)Bu_3 (**2**): Conversion to C_6F_5—CH=CH_2 (**3a**)[a]

					conversion (%)	
entry	X	L	solvent	additive[b]	2 h	10 h
1	Cl	PPh_3	PhCl	none	0	0
2	Cl	PPh_3	PhCl	PPh_3	0	0
3	TfO	PPh_3	PhCl	none	20	94
4	TfO	PPh_3	PhCl	PPh_3	0	2
5	Cl	PPh_3	THF	none	8	65
6	Cl	PPh_3	THF	PPh_3	0	0
7	TfO	PPh_3	THF	none	81	100
8	TfO	PPh_3	THF	PPh_3	1	9
9	Cl	$AsPh_3$	PhCl	none	15	39
10	Cl	$AsPh_3$	PhCl	$AsPh_3$	4	12
11	TfO	$AsPh_3$	PhCl	none	28	51
12	TfO	$AsPh_3$	PhCl	$AsPh_3$	23	46
13	Cl	$AsPh_3$	THF	none	92	100
14	Cl	$AsPh_3$	THF	$AsPh_3$	36	100
15	TfO	$AsPh_3$	THF	none	100	100
16	TfO	$AsPh_3$	THF	$AsPh_3$	100	100

[a] At 23 °C; [**2**] = 0.2 mol L^{-1}, [Pd] = 0.01 mol L^{-1}. [b] [Additive] = 0.02 mol L^{-1}.

min at ambient temperature. The addition of LiCl did not produce any perceptible effect in PhCl, but it accelerated very efficiently the reaction in THF, yielding *trans*-[Pd(C_6F_5)Cl-($AsPh_3$)$_2$] (**6b**).

The results presented in Table 3 and discussed later show that, in THF, the transmetalation step is always faster for triflates than for halides. Hence, it can be concluded that the low yields found in couplings between **1** and **2** catalyzed by [Pd($AsPh_3$)$_4$] in the absence of solubilized LiCl are due to the slowness of the oxidative addition step (note the correspondence between Tables 1 and 2, entries 5−7). In other words, although the Stille coupling rate is often controlled by the transmetalation step, *in the case of aryl triflates in THF, the oxidative addition is very slow and becomes rate-determining*.

Equilibria between *trans*-[PdR(OTf)L_2] or *trans*-[PdRIL_2] and Cationic Complexes in Solution. As shown in Table 2, equilibrium mixtures of *trans*-[PdR(OTf)L_2], [PdRL_3]$^+$, and

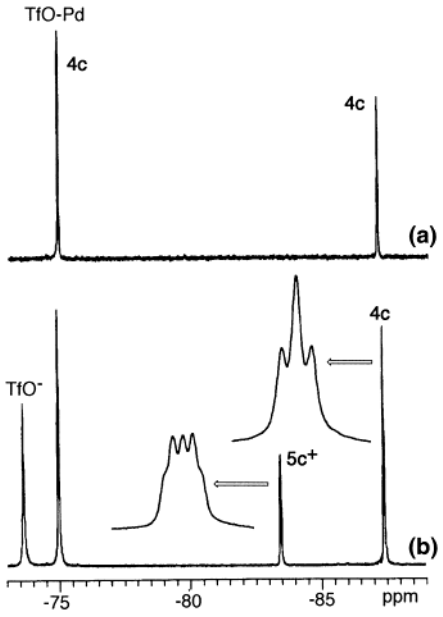
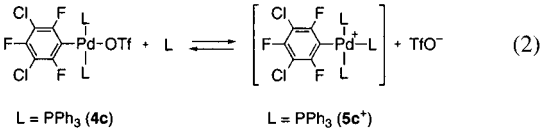


Figure 1. (a) ^{19}F NMR spectrum (282 MHz, PhCl, room temperature, triflate and F_{ortho} signals) of *trans*-[Pd($C_6Cl_2F_3$)(OTf)(PPh_3)$_2$] (**4c**). (b) Spectrum after addition of free PPh_3 (Pd:PPh_3 = 1:8).

[PdR(THF)(PPh_3)$_2$]$^+$ (in THF) are formed upon oxidative addition of R−OTf to [PdL_4] (L = PPh_3). To facilitate the study of these equilibria by ^{19}F and ^{31}P NMR techniques, we prepared the corresponding complexes with R = 3,5-$C_6Cl_2F_3$, which behave similarly to those with R = C_6F_5 but show simpler and more informative NMR spectra.[17]

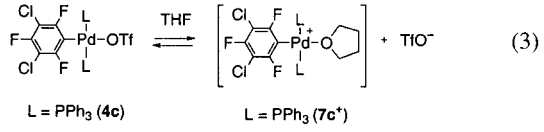
The complex *trans*-[Pd($C_6Cl_2F_3$)(OTf)(PPh_3)$_2$] (**4c**) is stable in noncoordinating solvents ($CDCl_3$, CH_2Cl_2, or PhCl), and the coordinated triflate gives sharp ^{19}F NMR resonances (singlet, Figure 1a). The addition of PPh_3 gave rise to new signals corresponding to [Pd($C_6Cl_2F_3$)(PPh_3)$_3$](TfO) (**5c**$^+$(TfO)) in equilibrium with **4c** (eq 2 and Figure 1b). The F_{para} (not shown in



(2)

Figure 1) and triflate signals are singlets, but the multiplicity of the F_{ortho} signals changes from a triplet in **4c** ($^4J_{F(ortho)-P(cis)}$ = 7.7 Hz) to a doublet of triplets in **5c**$^+$ ($^4J_{F(ortho)-P(trans)}$ = 10.5 Hz; $^4J_{F(ortho)-P(cis)}$ = 4.5 Hz).

In THF (a solvent similar in polarity to PhCl, but more coordinating), the spectra of *trans*-[Pd($C_6Cl_2F_3$)(OTf)(PPh_3)$_2$] (**4c**) show a strong temperature dependence, since **4c** is involved in a slow equilibrium with *trans*-[Pd($C_6Cl_2F_3$)(THF)(PPh_3)$_2$]-(TfO) (**7c**$^+$(TfO), eq 3). At low temperatures **4c** is very



(3)

predominant, but above room temperature it has almost disappeared (Figure 2), so it can be considered that at 50 °C the

(16) Jutand, A.; Mosleh, A. *Organometallics* **1995**, *14*, 1810−1817. We disagree, however, in the formulation of the neutral compound as an ionic pair [PdAr(PPh_3)$_2$]$^+$·TfO$^-$ involving a 14-e cation. In our case, the IR spectra in Nujol clearly show coordinated triflate for **4a**−**d**. Our formulation is in agreement with the result reported in ref 10. We believe that the observation of anionic triflate, reported by Jutand and Mosleh to support the ionic formulation, might be due to the following reaction in the preparation of the KBr pellet (the IR spectra are reported in KBr): [PdAr(OTf)(PPh_3)$_2$] + KBr → [PdArBr(PPh_3)$_2$] + K(TfO).

(17) Espinet, P.; Martínez-Ilarduya, J. M.; Pérez-Briso, C.; Casado, A. L.; Alonso, M. A. *J. Organomet. Chem.* **1998**, *551*, 9−20. In fact, the only reason 3,5-$C_6Cl_2F_3$ was not used for the whole study was the commercial availability of C_6F_5OH, which facilitated the preparation of the corresponding triflate **1**.

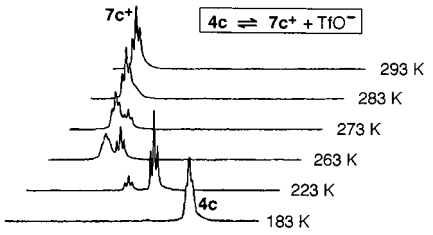
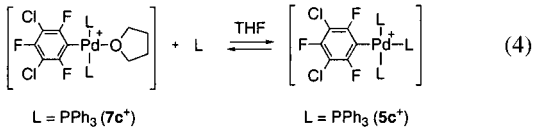


Figure 2. Temperature dependence of equilibrium (3) in THF. Only the F_{ortho} signals of the $C_6Cl_2F_3$ group are shown. Simultaneous conversion between signals for covalent and ionic triflate is observed.

equilibrium is fully displaced to the right, toward **7c**$^+$. In the presence of PPh_3, an equilibrium of **7c**·(TfO) with [Pd($C_6Cl_2F_3$)-(PPh_3)$_3$](TfO) (**5c**·(TfO)) is established (eq 4).



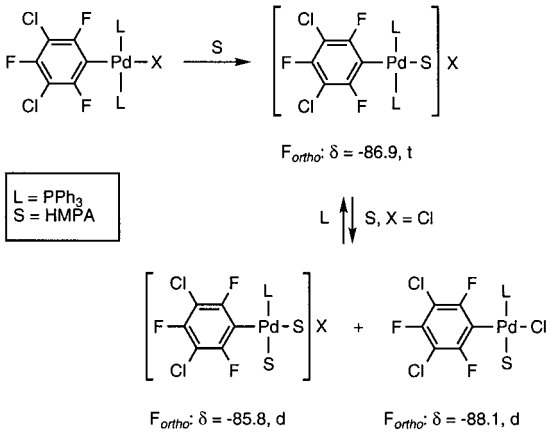
(4)

Some equilibrium constants at 50 °C were obtained by NMR analysis (see Experimental Section),[18] from which it is possible to calculate the extent of these equilibria in the catalytic mixtures (where the Pd:free L ratio is 1:2). For eq 2 in PhCl, $K = 3.4 \times 10^{-3}$ affords **4c**/**5c**$^+$ = 92/8 under catalytic conditions. In CH_2Cl_2, a more polar noncoordinating solvent, the equilibrium constant is much bigger than that in PhCl ($K = 1.0$; **4c**/**5c**$^+$ = 34/66 under catalytic conditions), suggesting that the ionic complex **5c**·(TfO) is noticeably stabilized by solvation. In fact, the equilibrium in PhCl can be shifted to the right by increasing the ionic strength of the solvent medium upon addition of [NBu_4]-[ClO_4]. In THF at 50 °C, **4c** is fully transformed into **7c**$^+$; for eq 4, $K = 2.13$ L mol^{-1} affords **7c**$^+$/**5c**$^+$= 96/4 for a solution 10^{-2} M in Pd.

The cationic complexes **5c**$^+$ and **7c**$^+$ were synthesized separately and fully characterized as their BF_4^- salts. Their behavior in $CDCl_3$ or PhCl was studied by NMR techniques (see Experimental Section). No coordination of tetrafluoroborate was observed, showing that, differently from triflate, BF_4^- does not compete with L or THF for the coordination site. The PPh_3 ligand trans to the aryl group is rather weakly coordinated, and equilibrium (4) is established in THF solution (eq 4), as observed for **4c** at 50 °C.[19]

Furthermore, we checked the behavior of *trans*-[Pd($C_6Cl_2F_3$)X(PPh_3)$_2$] (X = Cl, I, or OTf) and [Pd($C_6Cl_2F_3$)(PPh_3)$_3$]-BF_4 in some solvents commonly used in Stille couplings at 50 °C. In HMPA (hexamethylphosphoramide), a solvent used by Stille in ref 12, the F_{ortho} signals of a 1:1 mixture of [Pd($C_6Cl_2F_3$)(PPh_3)$_3$]BF_4 and PPh_3 showed only a triplet. This same triplet was also the only signal observed in 1:2 mixtures (usual catalytic proportions) of *trans*-[Pd($C_6Cl_2F_3$)X(PPh_3)$_2$] (X = Cl, I, or OTf) with PPh_3 and must be assigned to *trans*-[Pd($C_6Cl_2F_3$)(HMPA)(PPh_3)$_2$]X formed quantitatively in situ. In the absence of free PPh_3, *trans*-[Pd($C_6Cl_2F_3$)Cl(PPh_3)$_2$] gave only 62.5% of *trans*-[Pd($C_6Cl_2F_3$)(HMPA)(PPh_3)$_2$]Cl, and the corresponding triplet was flanked by two doublet signals (20% for the one at lower field of the triplet, 17.5% for that at higher field). In a 1:2:20 mixture *trans*-[Pd($C_6Cl_2F_3$)Cl(PPh_3)$_2$]:PPh_3:LiCl, only the triplet (53%) and the low-field doublet (47%) were observed. These observations suggest that the complex giving rise to the low-field doublet contains one phosphine and one chloride, while that producing the high-field doublet contains one phosphine but no chloride; accordingly, the assignments shown in Scheme 4 are proposed. In NMP, the results were somewhat different: the triplet observed for *trans*-[Pd($C_6Cl_2F_3$)I(PPh_3)$_2$] (**8**) moved 1.7 ppm downfield upon addition of $AgBF_4$ to force the formation of [Pd($C_6Cl_2F_3$)(NMP)-(PPh_3)$_2$]BF_4; this suggests that **8** stays as the neutral complex in NMP solution. However, [Pd($C_6Cl_2F_3$)(OTf)(PPh_3)$_2$] was fully converted to [Pd($C_6Cl_2F_3$)(NMP)(PPh_3)$_2$](TfO) upon being dissolved in NMP, and their signals were unaffected by addition of free PPh_3 (to make Pd:PPh_3 = 1:4). Thus, NMP as solvent (probably coordinating as a ketone) is less coordinating than HMPA and is able to displace triflate and PPh_3 trans to R, but cannot displace halides trans to R, or phosphine cis to R.[20]

Scheme 4



The existence of similar dissociation equilibria for [PdPhX-(PPh_3)$_2$] (X = Cl, Br, I, OAc) in DMF (dimethylformamide) has been demonstrated recently, and the corresponding dissociation constants have been determined by chronoamperometry. They follow the order Cl < Br < I < OAc.[21]

Substitution of PPh_3 for I$^-$ in [PdR(PPh_3)$_3$]$^+$ and in *trans*-[PdR(THF)(PPh_3)$_2$]$^+$. The last step in the Stille cycle is the reductive coupling producing R^1R^2, which requires a cis arrangement of R^1 and R^2 in the Pd complex undergoing reductive elimination.[11] The cyclic mechanism in Scheme 1 necessarily leads to a cis arrangement of R^1 and R^2 followed by fast coupling. However, in cases when a cyclic mechanism cannot operate due to the inability of the Pd complex to make an extra Pd−X−Sn bridge (for instance, with [PdR^1(PPh_3)$_3$]$^+$), the transmetalation becomes (as viewed from the metal) a simple associative substitution reaction with the α carbon of R^2 acting

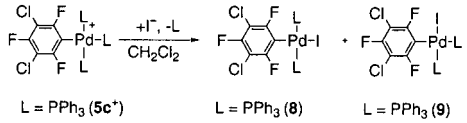
(18) Note that, for simplicity, these adimensional constants are defined as K = [cation][TfO$^-$]/[**4c**][L] regardless of the solvent, although in some solvents ionic pairs are formed. This means that the constants are valid only in the conditions specified in the text.

(19) The ^{19}F NMR spectra of **5c**$^+$ in wet $CDCl_3$ showed additional signals due to *trans*-[Pd($C_6Cl_2F_3$)(OH_2)(PPh_3)$_2$]$^+$. The "unexpected" competence for the trans coordination site of the weak but hard THF (or OH_2) versus the strong but soft PPh_3 is associated with the trans influence of the ligands involved (Hartley, F. R. *Chem. Soc. Rev.* **1973**, *2*, 163−179). The well-known destabilizing effect of two mutually trans soft ligands attached to a soft metal center has been named the "antisymbiotic effect" (Pearson, R. G. *Inorg. Chem.* **1973**, *12*, 712−713), and more recently "transphobia" (Vicente, J.; Arcas, A.; Bautista, D.; Jones, P. G. *Organometallics* **1997**, *16*, 2127−2138. Vicente, J.; Abad, J. A.; Frankland, A. D.; Ramírez de Arellano, M. C. *Chem. Eur. J.* **1999**, *5*, 3067−3076).

(20) Many complexes with O-donor HMPA or with DMF are known. See: Goggin, P. L. Sulfoxides, Amides, Amine Oxides and Related Ligands. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds; Pergamon Press: Oxford, 1987; Vol. 2, pp 487−503.

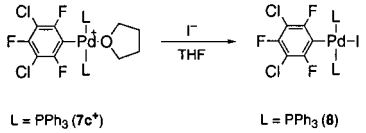
(21) Amatore, C.; Carré, E.; Jutand, A. *Acta Chem. Scand.* **1998**, *52*, 100−106.

as the entering ligand. R^2 can then go trans or cis to R^1, or competitively to both sites, depending on the trans effects of R^1 and the other ligands. A cis to R^1 substitution leads to cis R^1-R^2 arrangement and fast coupling (at least with monodentate ligands), whereas a trans substitution leads to trans R^1-R^2 arrangement and slower coupling (topomerization is needed, which can be slow). This means that we are more likely to observe a *trans*-R^1R^2Pd intermediate (if formed) than a *cis*-R^1R^2Pd. In other words, we should not expect necessarily to see both intermediates, even if substitution at both sites was taking place: we could detect only a trans intermediate, and still a cis substitution could be taking place in addition to the trans substitution. For this reason, to check the cis or trans stereoselectivity of a simple associative substitution of PPh_3 on $[Pd(C_6Cl_2F_3)(PPh_3)_3]^+$ (**5c**$^+$), I^- was chosen as a model nucleophile. Complex **5c**·(BF_4) was reacted with $(NBu_4)I$ in CH_2Cl_2. After 5 min at room temperature, *trans*-$[Pd(C_6Cl_2F_3)I(PPh_3)_2]$ (**8**) and *cis*-$[Pd(C_6Cl_2F_3)I(PPh_3)_2]$ (**9**) had formed in a ca. 1:5 ratio (eq 5). Since the rate of isomerization of **9** to **8** is



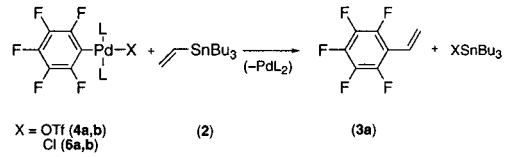
negligible under these conditions,[22] the observed ratio corresponds to the kinetic outcome of the substitution reaction. Although the PPh_3 trans to the aryl group is substituted faster, the substitution of the PPh_3 in the cis position occurs also at a noticeable rate (1/5), suggesting that the trans effects for $C_6Cl_2F_3$ and PPh_3 differ by less than 1 order of magnitude.[23] This suggests that, in an open transmetalation using stannane, cis and trans ligand substitutions by the entering R^2 group will be probably competitive, both occurring with detectable rates. As discussed later, this is, in fact, the case.

On the other hand, when the same model substitution reaction with I^- was carried out on either *trans*-$[Pd(C_6Cl_2F_3)(OTf)(PPh_3)_2]$ (**4c**) or *trans*-$[Pd(C_6Cl_2F_3)(THF)(PPh_3)_2]BF_4$ (**7c**·(BF_4)) in THF (both complexes give the cation *trans*-$[Pd(C_6Cl_2F_3)(THF)(PPh_3)_2]^+$ (**7c**$^+$) in THF), the only product observed was *trans*-$[Pd(C_6Cl_2F_3)I(PPh_3)_2]$ (**8**), showing that the substitution of the THF ligand was very favorable kinetically in this case (eq 6).



(6)

Transmetalation on Organopalladium(II) Complexes Formed after the Oxidative Addition. The transmetalation reactions between either *trans*-$[Pd(C_6F_5)(OTf)L_2]$ (L = PPh_3 (**4a**), $AsPh_3$ (**4b**)) or *trans*-$[Pd(C_6F_5)ClL_2]$ (L = PPh_3 (**6a**), $AsPh_3$ (**6b**)) and $Sn(CH{=}CH_2)Bu_3$ (**2**) to give the coupling product $C_6F_5-CH{=}CH_2$ (**3a**) were studied in PhCl and THF by ^{19}F NMR (eq 7). The Pd:Sn stoichiometry was 1:20, similar



(7)

(22) Casado, A. L.; Espinet, P. *Organometallics* **1998**, *17*, 954−959.

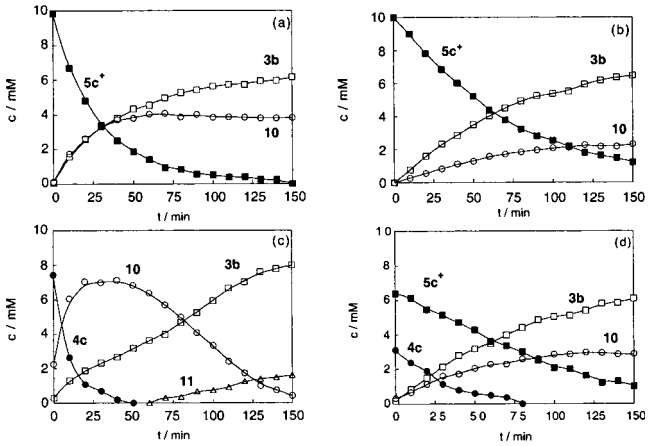


Figure 3. Reaction profiles of the transmetalation reactions between $Sn(CH{=}CH_2)Bu_3$ (**2**) and the following complexes: (a) $[Pd(C_6Cl_2F_3)(PPh_3)_3]BF_4$ (**5c**·(BF_4)); (b) **5c**·(BF_4) + $2PPh_3$; (c) *trans*-$[Pd(C_6Cl_2F_3)(OTf)(PPh_3)_2]$ (**4c**); (d) **4c** + $2PPh_3$. [Pd] = 0.01 mol L^{-1}, [Sn] = 0.2 mol L^{-1} in CH_2Cl_2 at 50 °C. Byproduct: $C_6Cl_2F_3-SnBu_3$ (**11**).

to that used in the catalytic reactions. The results are summarized in Table 3. An exact interpretation of each result is difficult because of the many factors involved, as will be discussed later, but it is clear that in all cases the triflato complexes reacted faster than their corresponding chloro complexes. In the couplings catalyzed by $[Pd(PPh_3)_4]$ in THF (Table 1, entry 4), where the oxidative addition is fast, the transmetalation is rate-determining.[24] *Since the presence of Cl*$^-$ *converts the triflato complex in the corresponding chloro complex, the net effect upon addition of LiCl is retardation.*

We have seen that, under catalytic conditions, the species *trans*-$[PdR(OTf)L_2]$ can be in equilibrium with $[PdRL_3]^+$, $[PdR(THF)L_2]^+$, or both. To gain some knowledge of the transmetalation step, the reactions of *trans*-$[Pd(C_6Cl_2F_3)(OTf)(PPh_3)_2]$ (**4c**) and $[Pd(C_6Cl_2F_3)(PPh_3)_3]BF_4$ (**5c**·BF_4) with **2** were monitored by ^{19}F NMR in CH_2Cl_2.[25] Some profiles are shown in Figure 3.

The most remarkable finding was the formation of *trans*-$[Pd(C_6Cl_2F_3)(CH{=}CH_2)(PPh_3)_2]$ (**10**) as an observable intermediate, which slowly decomposes to the coupling product $C_6Cl_2F_3-CH{=}CH_2$ (**3b**). Because of this decomposition, complex **10** could not be isolated as a pure compound, but it was unambiguously characterized by NMR studies on crude samples containing about 70% of **10** (see Experimental Section).[26] Its ^1H NMR spectrum shows three resonances for the vinyl protons, coupled to each other (^1H COSY) and also coupled to the two equivalent ^{31}P nuclei of the PPh_3 ligands ($^1H-^{31}P$ HMQC).[27] This latter coupling was evidenced by it suppression in a ^1H-

(23) This seems to be in agreement with the trans effect data for comparable groups reported in the following: Tobe, M. L. Substitution Reactions. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, 1987; Vol. 2, pp 281−329.

(24) It could be argued that the formation of the coupling product involves transmetalation plus coupling, and the latter could also be the rate-determining step. However, as we report later in this section, transmetalated intermediates (such as **10**) are not observed in either PhCl or THF, supporting that the coupling in these solvents is much faster than the transmetalation. Under these circumstances, the rates observed can be taken as transmetalation rates.

(25) Dichloromethane is noncoordinating and avoids solvolysis processes in the complexes occurring during the experiments. This comparative study was not be performed in PhCl because of the low solubility of $[Pd(C_6Cl_2F_3)(PPh_3)_3]BF_4$ (**5c**$^+$·BF_4^-).

(26) An alternative attempt to synthesize **10**, the treatment of **4c** with vinylmagnesium chloride in cold toluene, led to a mixture of **10**, *trans*-$[Pd(C_6Cl_2F_3)Cl(PPh_3)_2]$ (**6c**), and unreacted **4c**.

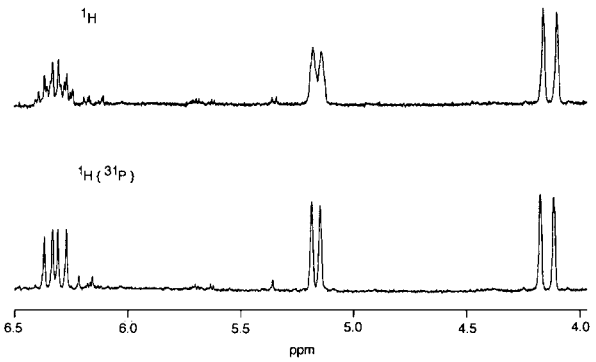
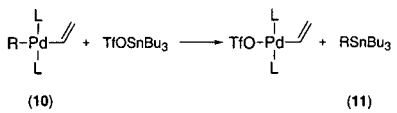


Figure 4. ^{1}H (upper) and ^{1}H{^{31}P} (lower) NMR (300 MHz, $CDCl_3$, room temperature) spectra of the vinyl resonances in a sample of *trans*-[$Pd(C_6Cl_2F_3)(CH{=}CH_2)(PPh_3)_2$] (**10**).

{^{31}P} NMR spectrum (Figure 4). The trans arrangement of the molecule was confirmed in its ^{31}P{^{1}H} NMR spectrum, which shows only one signal (triplet of doublets because of ^{19}F−^{31}P couplings). The ^{19}F NMR spectrum showed a triplet for the F_{ortho} and a triplet for the F_{para} atoms. This multiplicity arises from ^{19}F−^{31}P couplings, which were clearly observable in a ^{19}F−^{31}P HMQC experiment. To the best of our knowledge, this is the first time that an intermediate between the transmetalation and the coupling steps in a Stille cycle is observed and unambiguously characterized.

The analysis of the profiles in Figure 3 reveals some interesting kinetic features: (i) Although complex **10** is an intermediate between **5c**$^+$ and **3b** (upper part of Scheme 5), the profile for the formation of **3b** (Figure 3a,b) shows that it is being formed at a considerable rate at early stages of the reaction, when the concentration of intermediate **10** is still very low. Thus, a more direct transformation from **5c**$^+$ to **3b** must be occurring simultaneously (lower part of Scheme 5). This contribution is also clear in the transmetalation on **4c** (Figure 3c). The direct transformation of **4c** into **3b**, contributing from the beginning, is responsible for the additional curvature of the profile of **3b** until **4c** disappears (initial 50 min). Once all the starting material has been consumed, the formation of **3b** via **10** becomes dominant. Indeed, crude samples of **10** decomposed in solution, giving **3b** quantitatively. (ii) In all cases, the addition of free PPh_3 retards the formation of both **10** and the final product **3b** (this was also observed in the decomposition of crude samples of **10**). This L-retardation effect is not as pronounced in CH_2Cl_2 as in other solvents (see Table 3). (iii) In the case of **4c**, the addition of free PPh_3 caused fast formation of **5c**$^+$ (Figure 3d), in agreement with eq 3. (iv) A byproduct, $C_6Cl_2F_3{-}SnBu_3$ (**11**), was formed from **10** when the concentration of the latter was very high (Figure 3c). The addition of PPh_3 inhibited the formation of **11** (Figure 3d). Compound **11** is apparently formed from **10** by anionic-ligand exchange (eq 8), which is strongly retarded by free L.[28] Note that the formation of these byproducts



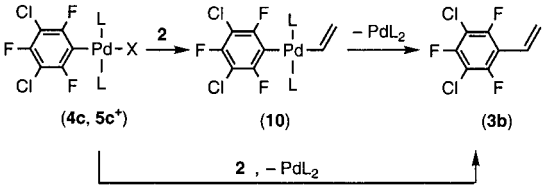
(8)

could eventually give rise to homocoupling products in ligand-free or ligand-poor catalytic process, while this complication should be inhibited in ligand-rich catalysis.

(27) Braun, S.; Kalinowski, H.-O.; Berger, S. *100 and More Basic NMR Experiments*; VCH: New York, 1996.

(28) A similar exchange process takes place between [$Pd(C_6Cl_2F_3)_2(AsPh_3)_2$] and $SnXBu_3$ (X = Cl, Br, I) and is retarded by free $AsPh_3$. Casado, A. L. Doctoral Thesis, Universidad de Valladolid, March 1998.

Scheme 5

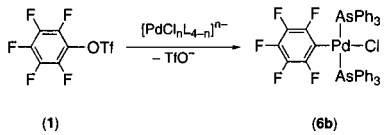


The compound *trans*-[$Pd(C_6Cl_2F_3)(THF)(PPh_3)_2$]($BF_4$) (**7c**·($BF_4$)) also led to **10** upon treatment with **2** in CH_2Cl_2, at a rate similar to that found for **4c**. Again, a small amount of byproduct **11** was detected. The possible formation of **10** in other solvents used in the catalytic couplings was also checked. Complex [$Pd(C_6Cl_2F_3)(OTf)(PPh_3)_2$] (**4c**) did not produce **10** in PhCl or THF. Compound **5c**·(BF_4) yielded **10** in both solvents, THF and PhCl. Compound **7c**·(BF_4) yielded some **10** in PhCl, but not in THF. Finally, *trans*-[$Pd(C_6Cl_2F_3)Cl(PPh_3)_2$] (**6c**) did not produce **10** in any of the three solvents.

Discussion

The origin of the complex behavior of the Stille coupling resides in the variety of factors controlling the overall outcome of the reaction. First, these determine which step is the slowest in the catalytic cycle, which can be either the oxidative addition, the transmetalation, or even the reductive elimination,[29] depending on the systems involved and the conditions used. Furthermore, the transmetalation step can be occurring at different rates on one or more different organopalladium(II) intermediates, which in turn are conditioned by the organic electrophile used, the solvent, the addition or not of LiCl, and the ancillary ligands.

Which Step Is Rate Determining in the Catalytic Cycle? Role of LiCl in the Stille Coupling Using Aryl Triflates. The low rates found in the [PdL_4]-catalyzed couplings of $C_6F_5{-}$OTf (**1**) and $Sn(CH{=}CH_2)Bu_3$ (**2**) in THF or PhCl (Table 2) for L = $AsPh_3$ are clearly due to the slowness of the oxidative addition of **1** to a [$Pd(AsPh_3)_n$] species, so that this step becomes rate-determining. Amatore et al.,[30] and Jutand and Mosleh,[16] have shown recently that, in the presence of chloride ions, species of the type [PdL_2Cl]$^-$ are formed and undergo oxidative addition of aryl triflates to give *trans*-[PdR^1ClL_2]. According to this, it seems clear that the addition of LiCl in THF accelerates the oxidative addition step (rate-determining for L = $AsPh_3$) because it induces the formation of more nucleophilic species [$PdCl_n(AsPh_3)_{4-n}$]$^{n-}$ (eq 9). A similar proposal has been made



(9)

by Reetz et al. in order to explain the beneficial role of a phosphonium chloride in the oxidative addition of aryl chlorides to palladium(0) complexes.[31]

(29) For examples of Stille couplings frustrated at the reductive elimination step, see: (a) Cárdenas, D. J.; Mateo, C.; Echavarren, A. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2445−2447. (b) Mateo, C.; Cárdenas, D. J.; Fernández-Rivas, C.; Echavarren, A. M. *Chem. Eur. J.* **1996**, *2*, 1596−1606. See also: (c) Mateo, C.; Fernández-Rivas, C.; Echavarren, A. M.; Cárdenas, D. J. *Organometallics* **1997**, *16*, 1997−1999. (d) Mateo, C.; Fernández-Rivas, C.; Cárdenas, D. J.; Echavarren, A. M. *Organometallics* **1998**, *17*, 3661−3669.

(30) Amatore, C.; Jutand, A.; Suárez, A. *J. Am. Chem. Soc.* **1993**, *115*, 9531−9541 and references therein.

(31) Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 481−483.

In contrast, the couplings catalyzed by $[Pd(PPh_3)_4]$ in THF are retarded by LiCl. In this case, the oxidative addition of the aryl triflate **1** to $[Pd(PPh_3)_4]$ is fast, regardless of whether LiCl is added. In the absence of LiCl, the oxidative addition gives complexes *trans*-$[Pd(C_6F_5)X(PPh_3)_2]$ (X = TfO (**4a**), PPh_3 (**5a**$^+$), or THF (**7a**$^+$)), but in the presence of LiCl, the product is *trans*-$[Pd(C_6F_5)Cl(PPh_3)_2]$ (**6a**). The transmetalation on any of them is slower than the oxidative addition and is rate-determining. Since the transmetalation is slower on **6a** than on either **4a**, **5a**$^+$, or **7a**$^+$ (Table 3), the presence of LiCl produces a net retarding effect on the catalytic coupling.

In summary, the addition of LiCl produces overall acceleration only when the oxidative addition is slow and rate-determining, which can happen when $[PdL_4]$ is not very nucleophilic (poor donor L). Otherwise, a retardation is produced, at least in solvents of moderate polarity. In this respect, it is interesting to note that the oxidative addition to not very nucleophilic $[PdL_4]$ species can become fast in very polar solvents, as shown by some results of Farina et al. on $[Pd(AsPh_3)_4]$.[9] This is probably due to stabilization of a polar transition state in the oxidative addition. In such a case, no beneficial effect should be expected upon LiCl addition.

Mechanism of the Transmetalation Step in the Stille Coupling with Triflates. In the presence of LiCl, and in solvents of moderate polarity and that are not highly coordinating, the transmetalation step occurs on intermediates *trans*-$[PdR^1ClL_2]$, following the associative "S_E2(cyclic)" mechanism outlined in Scheme 1, which was discussed in detail in Part 1 of this work.[1] It is characterized by an R^2-for-L exchange leading directly to a cis arrangement of R^1 and R^2 around the Pd center. The formation of the cross-coupling product after the transmetalation is immediate, and this avoids the detection by NMR at room temperature of any transmetalation product prior to the coupling product. An important retarding effect upon addition of free neutral ligand L is found experimentally.

In the absence of LiCl and using PhCl, THF, or CH_2Cl_2 as solvent, the transmetalation can occur on *trans*-$[PdR^1(OTf)L_2]$, $[PdR^1L_3]^+$, or *trans*-$[PdR^1(THF)L_2]^+$. Our experiments show that, under certain conditions, important amounts of the intermediate *trans*-$[PdR^1(CH{=}CH_2)L_2]$ (**10**) are produced. This observable intermediate has a noticeable stability, as is to be expected since it should isomerize to a cis arrangement prior to reductive elimination of **3b**. This behavior is in contrast with the nondetection of intermediates in the "S_E2(cyclic)" mechanism, where a cis arrangement for R^1 and R^2 is necessarily produced.

The experiments using $[NBu_4]I$ as the nucleophile (eq 5 and related experiments) show that, in an open mechanism, the entering nucleophile can either display high preference for the trans position or produce competing substitution of the ligands cis and trans to R^1, depending on the complex on which the substitution occurs. Similarly, in an open transmetalation using vinyl stannane as the nucleophile, the possible pathways for the formation and the fate of the transmetalation products are those summarized in Scheme 6 (L^1 = L or S). The formation of the coupling product from **12** requires only dissociation, whereas that from **10** requires also topomerization;[11] the later can be slow, making **10** observable.[32]

Initial approach of the vinyl stannane acting as a π-ligand seems very plausible,[33] as it would be for alkynyl stannanes also. For the most general case of stannanes with R^2 groups

Scheme 6

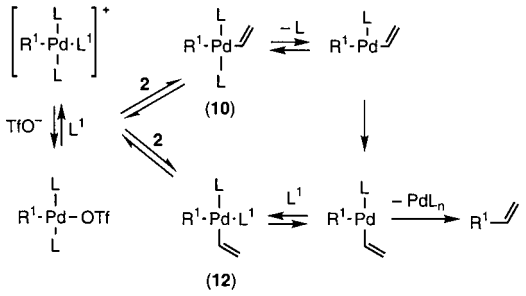
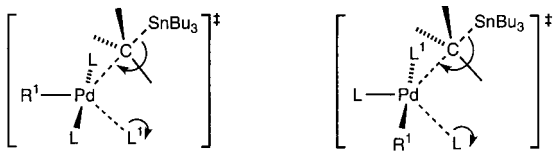


Chart 2



unable or less able to coordinate (such as benzyl or phenyl), a direct coordination of the α carbon should be proposed for the associative substitution of L, S, or TfO^-. Regardless of the initial stages of interaction, eventually the transition state has to involve coordination of the α carbon, as shown in Chart 2 (**2.I** for substitution trans to R^1; **2.II** for substitution cis to R^1). A slower transmetalation is to be expected for less nucleophilic stannanes, as observed, and this supports the contention that the substitution follows an associative mechanism. This mechanism is exactly an S_E2 electrophilic cleavage, with the Pd complex acting as the electrophile. Solvent molecules or TfO^- could assist the elimination of the leaving group SnR_3^+.

In the reactions monitored in CH_2Cl_2, the coupling product is being formed at a rate higher than could be expected from the decomposition of **10** only. This proves that, besides the trans-to-R^1 substitution, there is also a cis-to-R^1 substitution. Since this competing cis and trans substitution is observed in cases where the ligands lack bridging ability (as in $[Pd(C_6Cl_2F_3)(PPh_3)_3]^+$ (**5a**$^+$)), this means that two "S_E2(open)" mechanisms are operating (as observed for I^- as nucleophile in eq 5), which bring the entering group either cis or trans to R^1. We label them "S_E2(open-cis)" and "S_E2(open-trans)", respectively.

Cyclic and open pathways might operate in the transmetalation on *trans*-$[Pd(C_6Cl_2F_3)(OTf)(PPh_3)_2]$ (**4c**), due to the potential bridging ability of triflate. In the polar CH_2Cl_2, the reaction profile in Figure 3c reveals two parallel pathways producing **3b**: the fast formation of **10** indicates the dominance of an S_E2(open-trans) pathway (ca. 80%), probably due to the easy displacement of the poorly coordinating anionic triflate group. The other smaller contribution, following a cis substitution, can be assigned to either an S_E2(cyclic) or an S_E2(open-cis) transfer. In the less polar (and also noncoordinating) PhCl, **4c** did not produce **10**, showing that the reaction occurs almost exclusively by substitution of the cis PPh_3 ligand. Moreover, a sharp retarding effect upon addition of PPh_3 was noticed here (Table 3). This suggests that, in that case, the cis transmetalation follows an S_E2(cyclic) rather than an S_E2(open-cis) pathway. Interestingly, when the reaction was carried out using a solution of NBu_4ClO_4 in PhCl, the formation of **10** was again detected, showing that the increase produced in the polarity of the solvent accelerates the S_E2(open-trans) pathway. These results stress

(32) We have shown in a closely related $[PdR_2L_2]$ system that the main barrier to cis−trans isomerization was not the dissociation of L, but the cis−trans topomerization in the three-coordinate species: Casado, A. L.; Casares, J. A.; Espinet, P. *Inorg. Chem.* **1998**, *37*, 4154−4156.

(33) Cationic palladium complexes with coordinated styrene derivatives have been characterized unambiguously: Rix, F. C.; Brookhart, M.; White, P. S. *J. Am. Chem. Soc.* **1996**, *118*, 2436−2448.

the importance of the nature of the ligand being replaced and the solvent: the ease of displacement of anionic ligands (TfO^-) from neutral complexes should be accelerated in polar solvents, where the polar transition state (Chart 2, **2.I**, L^1 = OTf, X) should be stabilized, decreasing the activation energy toward its substitution. Much less an effect should be expected for the replacement of neutral ligands, whether from neutral or from cationic species. In THF, *trans*-$[Pd(C_6Cl_2F_3)(THF)(PPh_3)_2]^+$ is formed almost quantitatively in solution, and the transmetalation in this case led selectively to cis substitution, suggesting that THF is inducing an "S_E2(cyclic)" transmetalation. This is supported by the fact that *trans*-$[Pd(C_6Cl_2F_3)(THF)(PPh_3)_2][BF_4]$ does not produce **10** in THF. In PhCl the displacement of coordinated THF is easier and a noticeable amount of **10** is formed.

A Generalization of the Mechanism of the Transmetalation Step and Stereochemical Implications in the Stille Coupling. In a general case, the transmetalation has to occur on *trans*-$[PdR^1XL_2]$ (X = halide), *trans*-$[PdR^1L_3]^+$, *trans*-$[PdR^1(S)L_2]^+$ (S = solvent), *trans*-$[PdR^1(OTf)L_2]$, $[PdR^1(S)_2L]^+$, or *trans*-$[PdR^1X(S)L]$, which are the species observed in this work. They are exchanging in solution, and their ratios depend on factors such as the concentration of free L, the nature of L, the solvent polarity, the solvent coordinating ability, the nature of R^1, and the temperature. Thus, the situation is complex and can change dramatically depending on the factors mentioned. Each case needs to be studied separately since the actual mechanism will depend on the species existing and undergoing fast transmetalation in those reaction conditions. It is interesting that, in contrast to previous assumptions (Scheme 2), the transmetalation does not necessarily occur on a poorly coordinated complex, nor involve S substitution, nor afford a trans complex.

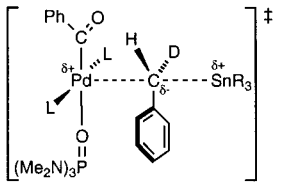
The studies in this paper led us to propose intermediates which are different from those proposed in the literature so far. The most common reaction conditions used in catalysis are $T \geq 50$ °C, Pd:L = 1:2, L = PPh_3, absence of LiCl for RX (X = halide), addition of LiCl for R−OTf. According to our observations, under these conditions the last three species listed in the previous paragraph are never observed. Thus, intermediates proposed in the literature such as **D** (see Scheme 2) look very unlikely in any solvent.

When highly coordinating polar solvents, such as HMPA, are used, they are able to displace any halide, triflate, or L trans to R^1, to give *trans*-$[PdR^1(HMPA)L_2]^+$ on which the transmetalation occurs. Hence, in HMPA, intermediates such as **C** and **D** in Scheme 2 are also highly improbable. Moreover, the intermediate actually observed in solution in our work, *trans*-$[PdR^1(HMPA)L_2]^+$, would not lead to the transition state proposed in the literature (Chart 1), and for this reason that transition state is very improbable (note that, although some **D** seems to be formed in the presence of very large amounts of LiCl in HMPA, LiCl was not added in the study by Labadie and Stille, which will be discussed later).[12]

NMP displaces OTf or PPh_3 but cannot displace halides; hence, the transmetalation should occur on *trans*-$[PdR^1(NMP)L_2]^+$ in the absence of LiCl but on $[PdR^1ClL_2]$ when LiCl has been added to help the oxidative addition. In other words, in the presence of LiCl, the intermediates **B** and **D** proposed in the literature (Scheme 2) are both unlikely.

In THF at 50 °C, the triflate is displaced, and in the presence of PPh_3, *trans*-$[PdR^1L_3]^+$ and *trans*-$[PdR^1(THF)L_2]^+$ (**7c**$^+$/**5c**$^+$ = 96/4 for a solution 10^{-2} M in Pd) are the intermediates available for transmetalation, but this mixture can be modified as a function of temperature, concentration, and proportion of PPh_3. In the presence of LiCl, however, the only intermediate observed is *trans*-$[PdR^1XL_2]$.

Chart 3



The existence of two transmetalation pathways in the Stille reaction, S_E2(cyclic) and S_E2(open), has important stereochemical consequences.[34] The steps following transmetalation in the cycle (isomerization and reductive elimination) are known to occur with retention of configuration at sp^3 carbons. Hence, the transmetalation step determines the stereochemical outcome of the overall coupling reaction with chiral organotins. This step has to bring about retention of configuration for an S_E2(cyclic) pathway. For an S_E2(open) mechanism, the studies on bromination of stannanes show that the bromination occurs predominantly with retention of configuration, but it switches to inversion under the influence of steric requirements, such as in *sec*-butyltrineopentyltin.[34]

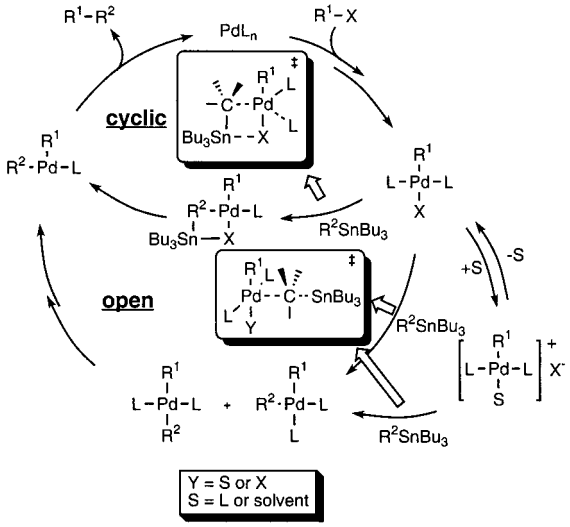
In fact, the contradictory stereochemical outcomes reported in the literature can be nicely reconciled on this basis and add further support to our mechanistic analysis of the transmetalation step.[12,13] Thus, the 98% retention of configuration reported by Falck et al. in the coupling of chiral α-alkoxystannanes with acyl chlorides in toluene (these conditions should favor strongly the S_E2(cyclic) pathway because they favor $[Pd(acyl)ClL_2]$ over other species) suggests that this pathway can be very steroselective and leads to retention. On the other hand, Labadie and Stille found inversion (≥65%) in the coupling of a chiral benzylic stannane to an acyl chloride in HMPA. Here, our results suggest that the transmetalation must be occurring on $[Pd(COPh)(HMPA)(PPh_3)_2]Cl$ (Chart 3), rather than on $[Pd(COPh)Cl(PPh_3)_2]$ (Chart 1), as assumed in the original paper. Since the bridging ability of HMPA is very poor, we should expect an S_E2(open) mechanism. The stereoselectivity reported by Stille is perfectly compatible with an open mechanism leading to inversion, which might be favored by the steric requirement of the metal complex.

A More Comprehensive Catalytic Cycle for the Stille Reaction. The studies presented in this paper suggest that the Pd-catalyzed coupling of organotin reagents and organic electrophiles can follow any of two paths which differ in the transmetalation step (which could be competing depending on the conditions). These are represented together in Scheme 7, which shows also the structures proposed for the corresponding activated complexes.

One of the paths (upper part of Scheme 7) involves an S_E(cyclic) transmetalation step. It requires an X ligand able to act as bridging group, implies an L-for-R^2 replacement at the Pd center, and leads directly to a cis arrangement followed by immediate coupling. This pathway is strongly retarded by free L. This mechanism should be very favored in nonpolar solvents and in the presence of good bridging groups (halides).

(34) These two limiting mechanisms have been proposed for the electrophilic cleavage of Sn−R bonds with X_2 (X = Br, I) in the following: Rahm, A.; Pereyre, M. *J. Am. Chem. Soc.* **1977**, *99*, 1672−1673. Although the Pd−Sn transmetalation can be formally regarded as a similar reaction, the behavior of the organopalladium(II) intermediates cannot be immediately deduced from that of X_2 electrophiles, since the structure of the Pd(II) complexes intermediates (ligands and geometry) determines the transmetalation pathway.

Scheme 7



The second pathway (lower part of Scheme 7) follows an S_E(open) transmetalation mechanism. It is the only possible path in the absence of bridging ligands but can also operate in their presence, under appropriate conditions, when they are displaced from the coordination sphere. It implies X-for-R^2 or L-for-R^2 replacement at the Pd center, leads competitively to cis and trans arrangements, and seems to be less retarded by added L. This mechanism should be favored by the use of (1) polar, coordinating solvents that lack bridging ability and (2) easily leaving, poorly coordinating anionic ligands that lack bridging ability. Note that if the solvent is able to act as a bridging ligand, $[PdR^1(S)L_2]^+$ could induce a cyclic mechanism (upper part of Scheme 7, with S playing the role of X).

The geometry of the transmetalation product, *cis*- or *trans*-$[PdR^1R^2L_2]$, although mechanistically very relevant, can be less important from a synthetic viewpoint, since the isomerization step is fast under the usual catalytic conditions. However, it could become important if very efficient catalyzed cross couplings running at lower temperatures are developed. Moreover, the stability of *trans*-$[PdR^1R^2L_2]$ can eventually give rise to some homocoupling side products.

Finally, it is worth noting that the double pathway found for the Stille reaction emphasizes its common aspects with the Hiyama reaction where, using R^2SiF_3 that is chiral at the α-carbon of R^2, retention or inversion at the transmetalated chiral carbon can be induced.[2] It seems reasonable that controlling the reaction conditions of the Stille coupling in order to favor either the cyclic or the open pathway, stereocontrol of the Stille reaction might also be achieved. A more detailed investigation of these aspects is in progress.

Experimental Section

All reactions were carried out under N_2. Solvents were distilled from sodium/benzophenone (THF, diethyl ether) or CaH_2 (PhCl, CH_2Cl_2, $CHCl_3$, HMPA, NMP) and stored under N_2. Infrared spectra (in cm^{-1}) were recorded on a Perkin-Elmer FT-IR 1720 X spectrometer. Combustion analyses were done on a Perkin-Elmer 2400 CHN microanalyzer. Mass spectra were taken on a Hewlett-Packard 5980 spectrometer (70 eV, EI). High-resolution spectra were taken on a HRMS VG Autospec M spectrometer (70 eV, EI). ^{1}H, ^{1}H{^{31}P}, ^{1}H COSY, ^{1}H−^{31}P HMQC, ^{13}C{^{1}H}, ^{19}F, ^{19}F−^{31}P HMQC, ^{31}P{^{1}H}, and ^{119}Sn{^{1}H} NMR experiments were run on a Bruker ARX-300 spectrometer equipped with a VT-100 variable-temperature probe. Chemical shifts are reported in ppm from $SiMe_4$ (^{1}H, ^{13}C), CCl_3F (^{19}F) in $CDCl_3$, 85% H_3PO_4 (^{31}P), or net $SnMe_4$ (^{119}Sn) at room temperature. When recorded in more than one solvent, the solvents and the chemical shifts are indicated separated by bars. In nondeuterated solvents, a capillary of acetone-d_6 was used for the lock; the chemical shifts given result from setting the following absolute (SF) frequencies for zero: 282.407650 MHz for ^{19}F and 121.496145 for ^{31}P. The fine structure descriptions given (including coupling constants *J*, in Hz) correspond to $CDCl_3$.

C_6F_5OH, Tf_2O, and C_6F_5−CH=CH_2 (**3a**, ^{19}F NMR (PhCl/THF) δ −139.95/−141.08 (m, *o*-C*F*), −152.92/−154.40 (t, $^3J_{FF}$ = 20.8 Hz, *p*-C*F*), −159.63/−161.20 (m, *m*-C*F*)) were used as purchased (Aldrich). LiCl was flame vacuum-dried and stored under N_2 prior to use. Sn(CH=CH_2)Bu_3 (**2**),[1] $[Pd(PPh_3)_4]$,[35] $[Pd(AsPh_3)_4]$,[36] $C_6Cl_2F_3$−CH=CH_2 (**3b**),[1] $[Pd_2(C_6F_5)_2(\mu\text{-}Cl)_2(tht)_2]$,[37] *trans*-$[Pd(C_6Cl_2F_3)Cl(PPh_3)_2]$ (**6c**),[17] *trans*-$[Pd(C_6Cl_2F_3)Cl(AsPh_3)_2]$ (**6d**),[1] *cis*-$[Pd(C_6Cl_2F_3)I(PPh_3)_2]$ (**9**),[17] and *trans*-$[Pd(C_6Cl_2F_3)I(PPh_3)_2]$ (**8**)[17] were prepared as reported.

C_6F_5−OTf (1). To solution of C_6F_5OH (2.00 g, 10.9 mmol) in CH_2Cl_2 (15 mL) at −78 °C was added NEt_3 (4.0 mL, 28.0 mmol). Tf_2O (2.0 mL, 11.9 mmol) was then added dropwise via syringe. The mixture was stirred for 10 min into the cold bath and then for 30 min at ambient temperature. The resulting red solution was quenched with aqueous $NaHCO_3$ and sequentially washed with 10% hydrochloric acid (30 mL), brine (30 mL), and water (30 mL). The organic layer was separated, dried over $MgSO_4$, and evaporated. The residual yellow oil was vacuum-distilled (40 °C/0.5 mmHg), giving **1** as a colorless liquid (2.25 g, 73%): *d* = 1.60. IR (liquid on NaCl): 1520 (s), 1146 (s), 1231 (s), 1134 (s), 1000 (s), 799 (m), 758 (m), 612 (m). ^{13}C{^{1}H} ($CDCl_3$): δ 143.0 (m, *C*F), 139.7 (m, *C*F), 139.4 (m, *C*), 136.3 (m, *C*F), 118.4 (q, $^1J_{CF}$ = 321 Hz, *C*F_3). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −73.27/−69.45/−69.98 (t, $^6J_{FF}$ = 6.8 Hz, C*F*$_3$), −150.98/−147.35/−149.03 (m, *o*-C*F*), −153.11/−148.82/−151.00 (t, $^3J_{FF}$ = 22.3, *p*-C*F*), −160.22/−156.02/−158.08 (m, *m*-C*F*). MS *m*/*z* (relative intensity): 316 (0.3) [M^+], 183 (3), 155 (8), 69 (100) [CF_3^+]. HRMS: calcd for $C_7F_8SO_3$, *m*/*z* 315.9440; found, *m*/*z* 315.9441.

***trans*-[PdR(OTf)L_2] (R = C_6F_5, L = PPh_3, 4a; L = $AsPh_3$, 4b; R = $C_6Cl_2F_3$, L = PPh_3, 4c; L = $AsPh_3$, 4d).** The corresponding complex **6a**−**d** (0.105 mmol) was added to a stirred solution of AgOTf (26.9 mg, 0.105 mmol) in acetone/CH_2Cl_2 (3/3 mL) shielded from the light. The mixture was stirred for 30 min. The AgCl formed was carefully filtered out, and the solution was evaporated to dryness, affording white solids **4a**−**d** which were washed with *n*-pentane (2 × 1 mL) and vacuum-dried.

4a (88%). IR (KBr): 1505 (vs), 1468 (vs), 1436 (vs), 1313 (s), 1232 (vs), 1212 (vs), 1180 (s), 1097 (s), 1022 (vs), 958 (vs), 743 (s), 694 (vs), 633 (s), 523 (vs), 510 (vs), 497 (m). ^{1}H NMR ($CDCl_3$): δ 7.7−7.5 (m, 2 C*H*), 7.5−7.3 (m, 3 C*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −79.21/−74.88/−75.5 (s, C*F*$_3$), −117.76/−113.15/−113.76 (m, *o*-C*F*), −161.30/−157.25/−158.9 (t, $^3J_{FF}$ = 18.9 Hz, *p*-C*F*), −162.07/−157.51/−158.96 (m, *m*-C*F*). ^{31}P{^{1}H} NMR ($CDCl_3$/PhCl/THF): δ 23.50/27.83/27.95 (td, $^4J_{FP}$ = 7.9 Hz, $^6J_{FP}$ = 2.9 Hz). Anal. Calcd for $C_{43}H_{30}F_8O_3P_2PdS$: C, 54.53; H, 3.19. Found: C, 54.33; H, 3.21.

4b (90%). IR (KBr): 1505 (vs), 1465 (vs), 1438 (vs), 1324 (s), 1233 (vs), 1216 (vs), 1027 (vs), 956 (vs), 742 (vs), 692 (vs), 631 (s), 467 (m). ^{1}H NMR ($CDCl_3$): δ 7.5−7.3 (m, 3 C*H*), 7.2−7.0 (m, 2 C*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −78.46/−74.16/−74.83 (s, C*F*$_3$), −117.12/−112.64/−113.22 (m, *o*-C*F*), −160.23/−156.18/−157.82 (t, $^3J_{FF}$ = 20.1 Hz, *p*-C*F*), −161.75/−157.26/−158.76 (m, *m*-C*F*). Anal. Calcd for $C_{43}H_{30}As_2F_8O_3PdS$: C, 49.90; H, 2.92. Found: C, 49.55; H, 2.82.

4c (60%). IR (KBr): 1483 (s), 1436 (vs), 1409 (vs), 1326 (vs), 1234 (vs), 1208 (vs), 1099 (s), 1023 (s), 779 (m), 774 (m), 693 (vs), 632 (m), 523 (vs), 511 (s). IR (THF): 1299 (vs), 1284 (vs), 1270 (s). ^{1}H ($CDCl_3$): δ 7.65−7.59 (m, 2 C*H*), 7.5−7.3 (m, 3 C*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −79.23/−74.88/−75.54 (s, C*F*$_3$), −91.55/−87.07/−87.29 (t, $^4J_{FP}$ = 7.7 Hz, *o*-C*F*), −119.59/−115.21/−116.21 (s, *p*-C*F*). ^{31}P{^{1}H} NMR ($CDCl_3$/PhCl/THF): δ 23.37/27.64/27.8 (td, $^4J_{FP}$ = 7.7 Hz, $^6J_{FP}$ = 2.9 Hz). Anal. Calcd for $C_{43}H_{30}Cl_2F_6O_3P_2PdS$: C, 52.70; H, 3.09. Found: C, 52.57; H, 3.08.

(35) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121−123.
(36) $[Pd(AsPh_3)_4]$ was prepared as described in ref 35 for $[Pd(PPh_3)_4]$.
(37) Usón, R.; Forniés, J.; Martínez, F.; Tomás, M. *J. Chem. Soc., Dalton Trans.* **1980**, 888−893.

4d (76%). IR (KBr): 1437 (vs), 1412 (vs), 1316 (vs), 1232 (vs), 1211 (vs), 1186 (vs), 1022 (vs), 781 (s), 738 (vs), 693 (vs), 634 (s), 466 (s). ^{1}H ($CDCl_3$): δ 7.6−7.5 (m, 2 C*H*), 7.5−7.4 (m, 3 C*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −78.46/−74.11/−74.78 (s, CF_3), −90.97/−86.58/−86.75 (s, *o*-C*F*), −118.64/−114.26/−115.44 (s, *p*-C*F*). Anal. Calcd for $C_{43}H_{30}As_2Cl_2F_6O_3PdS$: C, 48.36; H, 2.83. Found: C, 48.17; H, 2.80.

[PdR(PPh$_3$)$_3$](BF$_4$) (R = C$_6$F$_5$, 5a·(BF$_4$); R = C$_6$Cl$_2$F$_3$, 5c·(BF$_4$)). The corresponding complex **6a,c** (0.157 mmol) was added to a stirred solution of $AgBF_4$ (30.5 mg, 0.157 mmol) in acetone/CH_2Cl_2 (3/3 mL) shielded from the light. The mixture was stirred for 30 min. The AgCl formed was carefully filtered off, and PPh_3 (41.1 mg, 0.157 mmol) was added to the solution. The mixture was stirred for 30 min and evaporated to dryness, affording **5a,c·**[BF_4] as white solids which were washed with diethyl ether (2 × 1 mL) and vacuum-dried.

5a·[BF$_4$] (91%). IR (KBr): 1481 (m), 1435 (vs), 1403 (s), 1097 (vs), 1051 (vs), 777 (m), 746 (s), 700 (vs), 523 (vs), 511 (s), 493 (m). ^{1}H ($CDCl_3$): δ 7.5−7.0 (m, C*H*). ^{19}F NMR ($CDCl_3$/PhCl): δ −113.16/−108.28 (m, *o*-C*F*), −154.29/−146.20 (s, ^{9}BF_4^-), −154.34/−146.25 (s, ^{10}BF_4^-), −158.50/−154.70 (t, $^3J_{FF}$ = 20.1 Hz, *p*-C*F*), −158.96/−154.77 (m, *m*-C*F*). ^{31}P{^{1}H} NMR ($CDCl_3$/PhCl): δ 23.18/26.99 (d, $^2J_{PP}$ = 26.5 Hz, 2 *P*), 18.67/22.53 (m, *P*). Anal. Calcd for $C_{60}H_{45}BF_9P_3Pd$: C, 62.82; H, 3.95. Found: C, 62.71; H, 4.06.

5c·[BF$_4$] (82%). IR (KBr): 1435 (vs), 1403 (vs), 1097 (vs), 1051 (vs), 777 (m), 746 (s), 700 (vs), 523 (vs), 511 (vs), 493 (m). ^{1}H ($CDCl_3$): δ 7.4−7.2 (m, 3 C*H*), 7.1−7.0 (m, 2 C*H*). ^{19}F NMR ($CDCl_3$/THF/PhCl): δ −87.73/−82.66/−82.98 (dt, $^{4,trans}J_{FP}$ = 10.5 Hz, $^{4,cis}J_{FP}$ = 4.5 Hz, *o*-C*F*), −154.58/−148.34/−146.43 (s, ^{10}BF_4^-), −154.64/−148.39/−146.49 (s, ^{11}BF_4^-), −116.75/−114.11/−112.83 (s, *p*-C*F*). ^{31}P-{^{1}H} NMR ($CDCl_3$/THF/PhCl): δ 22.93/26.6/26.83 (dtd, $^2J_{PP}$ = 26.9 Hz, $^{4,cis}J_{FP}$ = 4.5 Hz, $^{6,cis}J_{FP}$ = 29 Hz, 2 *P*), 18.31/22.55/22.03 (tt, $^2J_{PP}$ = 26.9 Hz, $^{4,trans}J_{FP}$ = 10.5 Hz, *P*). Anal. Calcd for $C_{60}H_{45}P_3BCl_2F_7Pd$: C, 61.07; H, 3.84. Found: C, 61.18; H, 4.22.

***trans*-[Pd(C$_6$F$_5$)ClL$_2$] (L = PPh$_3$, 6a; AsPh$_3$, 6b).** L (3.88 mmol) was added to a stirred suspension of $[Pd_2(C_6F_5)_2(\mu\text{-}Cl)_2(tht)_2]$ (700 mg, 0.882 mmol), yielding a white precipitate. The mixture was stirred for 1 h and evaporated to dryness. The solid was washed with diethyl ether and recrystallized at −28 °C from CH_2Cl_2.

6a (98%). IR (KBr): 1502 (s), 1458 (vs), 1433 (vs), 1098 (s), 952 (vs), 744 (s), 693 (vs), 523 (vs), 513 (s), 498 (m). ^{1}H ($CDCl_3$): δ 7.7−7.6 (m, 2 C*H*), 7.45−7.3 (m, 3 C*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −117.40/−112.59/−113.34 (m, *o*-C*F*), −162.82/−158.53/−160.12 (t, $^3J_{FF}$ = 20.1 Hz, *p*-C*F*), −163.16/−158.61/−160.43 (m, *m*-C*F*). ^{31}P-{^{1}H} NMR ($CDCl_3$/PhCl/THF): δ 24.93/29.36/29.31 (td, $^4J_{FP}$ = 7.3 Hz, $^6J_{FP}$ = 2.4 Hz). Anal. Calcd for $C_{42}H_{30}ClF_5P_2Pd$: C, 60.52; H, 3.63. Found: C, 60.76; H, 3.77.

6b (95%). IR (KBr): 1057 (vs), 1045 (vs), 780 (vs), 702 (vs). ^{1}H ($CDCl_3$): δ 7.62 (m, 2 C*H*), 7.45−7.30 (m, 3 C*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −116.46/−111.82/−112.51 (m, *o*-C*F*), −161.77/−157.59/−159.33 (t, $^3J_{FF}$ = 20.3 Hz, *p*-C*F*), −163.00/−158.44/−160.02 (m, *m*-C*F*). Anal. Calcd for $C_{42}H_{30}As_2ClF_5Pd$: C, 54.75; H, 3.28. Found: C, 54.53; H, 3.44.

***trans*-[Pd(C$_6$Cl$_2$F$_3$)(THF)(PPh$_3$)$_2$](BF$_4$) (7c·(BF$_4$)).** Complex **6c** (0.136 g, 0.157 mmol) was added to a stirred solution of $AgBF_4$ (30.5 mg, 0.157 mmol) in THF (6 mL) shielded from the light. The mixture was stirred for 30 min. The AgCl formed was carefully filtered off, and the solution was evaporated to dryness. The white residue was dissolved in CH_2CH_2 (2 mL) and THF (one drop), layered with *n*-hexane (3 mL), and kept at −28 °C. Separated microcrystalline **7c·**[BF_4] was collected and dried with N_2 (55%). IR (KBr): 1634 (m), 1482 (m), 1435 (vs), 1410 (vs), 1098 (vs), 1084 (s), 1053 (s), 998 (m), 779 (m), 744 (m), 707 (m), 693 (vs), 523 (vs), 511 (s), 495 (m). ^{1}H NMR ($CDCl_3$): δ 7.6−7.4 (m, 30 H, C*H*), 3.72 (m, 4 H, OCH_2), 1.84 (m, 4 H, CCH_2). ^{19}F NMR ($CDCl_3$/PhCl/THF): δ −91.87/−87.36/−87.40 (t, $^4J_{FP}$ = 7.6 Hz, *o*-C*F*), −118.58/−114.52/−116.18 (t, $^6J_{FP}$ = 2.9 Hz, *p*-C*F*), −154.71/−145.04/−154.21 (s, BF_4^-). ^{31}P{^{1}H} NMR ($CDCl_3$/PhCl/THF): δ 23.44/27.46/27.50 (td, $^4J_{FP}$ = 7.5 Hz, $^6J_{FP}$ = 3.0 Hz). Anal. Calcd for $C_{46}H_{38}BCl_2F_7OP_2Pd$: C, 55.82; H, 3.87. Found: C, 55.77; H, 3.68.

Sn(C$_6$Cl$_2$F$_3$)Bu$_3$ (11). $SnClBu_3$ (3.48 mL, 12.8 mmol) was slowly added to a solution of [Li($C_6Cl_2F_3$)] (14.02 mmol) in diethyl ether (60 mL) at −78 °C. The mixture was stirred for 16 h, allowing the bath to reach room temperature. The resulting white suspension was quenched with aqueous $NaHCO_3$. The organic phase was separated, washed with water (2 × 50 mL), and then dried over $MgSO_4$. The solvent was evaporated, and the residue was flash-chromatographed (silicagel/*n*-hexane), giving **11** as a colorless liquid (5.56 g, 89%). d = 1.23 g/mL. IR (liq on NaCl): 2959 (vs), 2922 (vs), 1407 (vs), 1059 (vs), 1046 (s), 781 (s), 667 (m). ^{1}H NMR δ ($CDCl_3$): 1.53 (m, CH_2), 1.34 (m, CH_2), 1.21 (m, CH_2), 0.93 (m, CH_3). ^{13}C{^{1}H} NMR δ ($CDCl_3$): 160.23 (ddd, $^1J_{CF}$ = 238.3 Hz, $^3J_{CF}$ = 22.5 Hz, $^3J_{CF}$ = 5.1 Hz, *o*-C*F*), 155.4 (dt, $^1J_{CF}$ = 250.4 Hz, $^3J_{CF}$ = 5.5 Hz, *p*-C*F*), 110.5 (dt, $^2J_{CF}$ = 54.1 Hz, $^4J_{CF}$ = 3.5 Hz, *C*Sn), 106.2 (ddd, $^2J_{CF}$ = 29.8 Hz, $^2J_{CF}$ = 20.6 Hz, $^4J_{CF}$ = 5.8 Hz, *C*Cl), 28.7 (s, sat $^3J_{CSn}$ = 20.8 Hz, *C*H_2Me), 27.1 (s, sat $^2J_{C^{119}Sn}$ = 64.1 Hz, sat $^2J_{C^{117}Sn}$ = 62.9 Hz, *C*H_2), 13.5 (s, sat $^4J_{HSn}$ = 2.8 Hz, *C*H_3), 11.4 (t, $^4J_{CF}$ = 2.0 Hz, sat $^1J_{C^{119}Sn}$ = 358.8 Hz, sat $^1J_{C^{117}Sn}$ = 343.0, Sn*C*H_2). ^{19}F NMR ($CDCl_3$/THF): δ −95.05/−91.21 (d, $^4J_{FF}$ = 2.4 Hz, sat $^3J_{FSn}$ = 5.9 Hz, *o*-C*F*), −110.99/−107.94 (t, $^4J_{FF}$ = 2.4 Hz, sat $^5J_{FSn}$ = 3.4 Hz, *p*-C*F*). ^{119}Sn{^{1}H} NMR ($CDCl_3$) δ −21.47 (td, $^3J_{FSn}$ = 5.9 Hz, $^5J_{FSn}$ = 3.4 Hz). EM *m*/*z* (relative intensity): 433 (7) [M^+ − C_4H_9], 377 (18) [M^+ − 2C_4H_9], 321 (26) [M^+ − 3C_4H_9], 139 (42), 41 (100). Anal. Calcd for $C_{18}H_{27}Cl_2F_3Sn$: C, 44.22; H, 5.55. Found: C, 44.43; H, 5.27.

Signals Observed for Complexes Dissolved in Solvents Commonly Used in Stille Couplings in Different Conditions. [Pd(C$_6$Cl$_2$F$_3$)Cl(PPh$_3$)$_2$]. ^{19}F NMR (HMPA): δ −85.78 (d, $^4J_{FP}$ = 10.84 Hz, *o*-C*F*), −86.87 (t, $^4J_{FP}$ = 6.7 Hz, *o*-C*F*), −88.05 (d, $^4J_{FP}$ = 9.6 Hz, *o*-C*F*), −117.35 (s, *p*-C*F*), −117.59 (s, *p*-C*F*), −121.01 (s, *p*-C*F*).

[Pd(C$_6$Cl$_2$F$_3$)Cl(PPh$_3$)$_2$]:PPh$_3$:LiCl (1:2:20). ^{19}F NMR (HMPA): δ −86.87 (t, $^4J_{FP}$ = 6.7 Hz, *o*-C*F*), −88.05 (d, $^4J_{FP}$ = 9.6 Hz, *o*-C*F*), −117.59 (s, *p*-C*F*), −121.01 (s, *p*-C*F*).

[Pd(C$_6$Cl$_2$F$_3$)X(PPh$_3$)$_2$] (X = Cl, I):PPh$_3$ (1:2). ^{19}F NMR (HMPA): δ −86.87 (t, $^4J_{FP}$ = 6.5 Hz, *o*-C*F*), −117.59 (s, *p*-C*F*).

[Pd(C$_6$Cl$_2$F$_3$)(OTf)(PPh$_3$)$_2$]:PPh$_3$ (1:2). ^{19}F NMR (HMPA): δ −74.12 (s, CF_3), −86.86 (t, $^4J_{FP}$ = 6.5 Hz, *o*-C*F*), −117.58 (s, *p*-C*F*).

[Pd(C$_6$Cl$_2$F$_3$)(PPh$_3$)$_3$](BF$_4$):PPh$_3$ (1:1). ^{19}F NMR (HMPA): δ −86.85 (t, $^4J_{FP}$ = 6.5 Hz, *o*-C*F*), −117.58 (s, *p*-C*F*), −147.59 (s, ^{10}BF_4^-), −147.64 (s, ^{11}BF_4^-).

[Pd(C$_6$Cl$_2$F$_3$)I(PPh$_3$)$_2$]. ^{19}F NMR (NMP): δ −88.07 (t, $^4J_{FP}$ = 6.5 Hz, *o*-C*F*), −117.65 (s, *p*-C*F*). After addition of 1 equiv of $AgBF_4$: −86.35 (t, $^4J_{FP}$ = 7.1 Hz, *o*-C*F*), −115.62 (s, *p*-C*F*).

[Pd(C$_6$Cl$_2$F$_3$)(OTf)(PPh$_3$)$_2$]. ^{19}F NMR (NMP): δ −74.56 (s, CF_3), −86.37 (t, $^4J_{FP}$ = 7.6 Hz, *o*-C*F*), −115.64 (s, *p*-C*F*).

Catalytic and Stoichiometric Experiments. These were carried out in NMR tubes (5 mm) similarly as reported before.[1]

Determination of Equilibria in Equations 2 and 3. NMR tubes (5 mm) were charged with **4c** (5.9 ± 0.1 mg) and an excess of PPh_3. The samples were dissolved under N_2 in THF, PhCl, or CH_2Cl_2 and taken to a volume of 600 ± 5 μL, giving a concentration of (10.0 ± 0.2) × 10^{-2} mol L^{-1} in Pd. An acetone-d_6 capillary was introduced (for NMR lock), and the tubes were placed into a thermostated probe at 323.2 ± 0.2 K (the temperature was checked by an ethylene glycol standard method). After several minutes, ^{19}F and ^{31}P{^{1}H} spectra were carefully acquired using relaxation times long enough for meaningful integration of signals of the complexes **4c**, **5c**$^+$, or **7c**$^+$, and free PPh_3. Numerical analysis leads to the *K* values reported for eqs 2 and 3.

NMR Characterization of *trans*-[Pd(C$_6$Cl$_2$F$_3$)(CH=CH$_2$)(PPh$_3$)$_2$] (10). A crude sample of **10** was obtained as follows. Complex **4c** (300 mg, 0.306 mmol) was dissolved in CH_2Cl_2 (30 mL) and heated at 50 °C in a septum-capped tube. Organotin **2** (1.80 mL, 6.12 mmol) was then added via syringe, whereupon the solution suddenly turned deep brown. After 30 min, the mixture was cooled in an ice bath and evaporated to dryness. The residue was washed with cold *n*-hexane (2 × 10 mL) to remove the excess of **2** and then extracted in diethyl ether (3 × 10 mL). Evaporation of the ethereal solution at 0 °C afforded a greenish powder which contained about 70% of **10**. This degree of purity sufficed for unambiguous NMR characterization. ^{1}H NMR ($CDCl_3$): δ 7.5−7.3 (m, arom-C*H*), 6.32 (ddt, $^{trans}J_{HH}$ = 18.3 Hz, $^{cis}J_{HH}$ = 11.3 Hz, $^3J_{HP}$ = 9.0 Hz, C*H*Pd), 5.16 (broad d, $^{cis}J_{HH}$ = 11.3 Hz, $^4J_{HP}$ < 3 Hz, CC*H*), 4.14 (broad d, $^{trans}J_{HH}$ = 18.3 Hz, $^4J_{HP}$ < 3 Hz, CC*H*). ^{19}F NMR ($CDCl_3$/PhCl/THF/CH_2Cl_2): δ −90.85/−85.79/−86.10/−86.67 (t, $^4J_{FP}$ = 3.1 Hz, *o*-C*F*), −123.13/−118.22/−119.46/−

119.51 (t, $^6J_{FP}$ = 2.0 Hz, *p*-C*F*). $^{31}P\{^1H\}$ NMR ($CDCl_3$/PhCl/THF/CH_2Cl_2): δ 28.38/32.72/32.7/32.0 (td, $^4J_{FP}$ = 3.1 Hz, $^6J_{FP}$ = 2.0 Hz).

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