Mechanism of the Stille Reaction. 1. The Transmetalation Step. Coupling of R^1I and R^2SnBu_3 Catalyzed by *trans*-$[PdR^1IL_2]$ (R^1 = $C_6Cl_2F_3$; R^2 = Vinyl, 4-Methoxyphenyl; L = $AsPh_3$)

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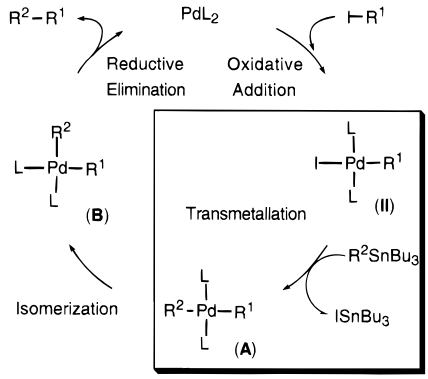
Abstract: The so far accepted mechanism of the Stille reaction (palladium-catalyzed cross-coupling of organotin reagents with organic electrophiles) is criticized. Based on kinetic studies on catalytic reactions, and on reactions with isolated intermediates, a corrected mechanism is proposed. The couplings between R^1I (**1**) (R^1 = $C_6Cl_2F_3$ = 3,5-dichlorotrifluorophenyl) and R^2SnBu_3 (R^2 = CH=CH_2, **2a**; C_6H_4-4-OCH_3, **2b**), catalyzed by *trans*-$[PdR^1I(AsPh_3)_2]$ (**3a**), give R^1-R^2 and obey a first-order law, $r_{obs} = a[\mathbf{3a}][\mathbf{2a}]/(b + [AsPh_3])$, with a = $(2.31 \pm 0.09) \times 10^{-5}$ s^{-1} and b = $(6.9 \pm 0.3) \times 10^{-4}$ mol L^{-1}, for [**1**] = [**2a**] = 0−0.2 mol L^{-1}, [**3a**] = 0−0.02 mol L^{-1}, and $[AsPh_3]$ = 0−0.07 mol L^{-1}, at 322.6 K in THF. The only organopalladium(II) intermediate detected under catalytic conditions is **3a**. The apparent activation parameters found for the coupling of **1** with **2a** support an associative transmetalation step ($\Delta H^{\ddagger}_{obs}$ = 50 ± 2 kJ mol^{-1}, $\Delta S^{\ddagger}_{obs}$ = −155 ± 7 J K^{-1} mol^{-1} in THF; and $\Delta H^{\ddagger}_{obs}$ = 70.0 ± 1.7 kJ mol^{-1}, $\Delta S^{\ddagger}_{obs}$ = −104 ± 6 J K^{-1} mol^{-1} in chlorobenzene, with $[\mathbf{1}]_0$ = $[\mathbf{2}]_0$ = 0.2 mol L^{-1}, [**3a**] = 0.01 mol L^{-1}). The reactions of **2a** with isolated *trans*-$[PdR^1X(AsPh_3)_2]$ (X = halide) show rates Cl > Br > I. From these observations, the following mechanism is proposed: Oxidative addition of R^1X to PdL_n gives *cis*-$[PdR^1XL_2]$, which isomerizes rapidly to *trans*-$[PdR^1XL_2]$. This trans complex reacts with the organotin compound following a S_E2(cyclic) mechanism, with release of $AsPh_3$ (which explains the retarding effect of the addition of L), to give a bridged intermediate $[PdR^1L(\mu\text{-}X)(\mu\text{-}R^2)SnBu_3]$. In other words, an L-for-R^2 substitution on the palladium leads R^2 and R^1 to mutually cis positions. From there the elimination of $XSnBu_3$ yields a three-coordinate species *cis*-$[PdR^1R^2L]$, which readily gives the coupling product R^1-R^2.

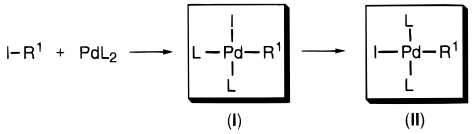
Introduction

The palladium-catalyzed cross-coupling of organotin reagents with organic electrophiles (Stille reaction) has become an attractive method in modern organic synthesis,[1] mainly due to the advantages of using trialkylorganotin species: They are readily available and quite air and moisture stable and tolerate many functional groups.[2] The broadly accepted mechanism is the catalytic cycle in Scheme 1.[1,3] Both the oxidative addition and the reductive elimination steps are supposed to be fast, compared to the Sn/Pd transmetalation,[4,5] which is the rate-determining step.[6,7] This proposal fits the observations that the reaction rate is zeroth order in electrophile (the oxidative addition must be fast) and first order in stannane.

Scheme 1



Scheme 2[a]



[a] R^1 = $C_6Cl_2F_3$, L = PPh_3.

We have proved recently that the oxidative addition of R^1I to PdL_2 is not as simple as it appears in Scheme 1. It gives first *cis*-$[PdR^1IL_2]$ (**I**), which then isomerizes to *trans*-$[PdR^1IL_2]$ (**II**) in a reaction autocatalyzed by both isomers (Scheme 2).[8]

(1) (a) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263−303. (b) Farina, V.; Roth, G. P. *Adv. Metalorg. Chem.* **1996**, *5*, 1−53. (c) Curran, D. P.; Hoshino, M. *J. Org. Chem.* **1996**, *61*, 6480−6481. (d) Mateo, C.; Cárdenas, D. J.; Fernández-Rivas, C.; Echavarren, A. M. *Chem. Eur. J.* **1996**, *2*, 1596−1606. (e) Roth, G. P.; Farina, V.; Liebeskind, L. S.; Peña-Cabrera, E. *Tetrahedron Lett.* **1995**, *36*, 2191−2194. (f) Mitchell, T. N. *Synthesis* **1992**, 803−815. (g) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033−3040. (h) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524. (i) Beletskaya, I. P. *J. Organomet. Chem.* **1983**, *250*, 551−564.

(2) Lee, A. S.-Y.; Dai, W.-C. *Tetrahedron* **1997**, *53*, 859−868, and references therein.

(3) (a) Farina, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995; Vol. 12, Chapter 3.4. (b) Brown, J. M.; Cooley, N. A. *Chem. Rev.* **1988**, *88*, 1031−1046.

(4) Studies on oxidative additions: (a) Amatore. C.; Jutand, A.; Suarez, A. *J. Am. Chem. Soc.* **1993**, *115*, 9531−9541. (b) Amatore, C.; Pflüger, F. *Organometallics* **1990**, *9*, 2276−2282. And references therein.

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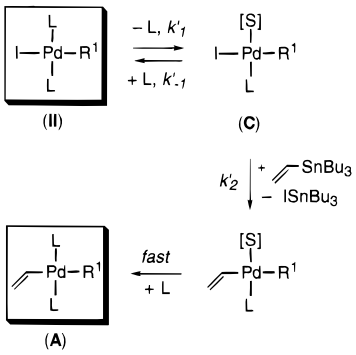
Scheme 3



Also, the transmetalation step (framed in Scheme 1) is still not well understood. Although there is no evidence, it is generally thought to preserve the trans configuration of complex **II** to give a *trans*-[$PdR^1R^2L_2$] complex (**A**), as it occurs in the case of main-group organometallic transmetalations.[9] Since the reductive elimination of R^1-R^2 is well established to occur on cis derivatives,[5] a fast isomerization of **A** to **B** needs to be postulated.

Attempts at gaining insight into the transmetalation step have shown that the addition of neutral ligand L retards the coupling,[1b,10,11] and this has been taken as an indication that L dissociation from **II** is a key step in the transmetalation. Thus, the mechanism in Scheme 3, involving a *dissociative X-for-R*^{2} substitution (X = I, Br) with preservation of the stereochemistry at the Pd, has been proposed for vinyl- and arylstannanes. It is assumed that **II** cannot undergo transmetalation, probably because it is too electron rich, and a ligand dissociation occurs previous to the transmetalation; it is the more coordinatively unsaturated species **C** (most likely having a coordinated solvent molecule, S) that is involved in the electrophilic substitution at tin.

This proposal is *qualitatively* consistent with the observations: The existence of a (fast) preequilibrium explains the retarding effect of L, whereas the (slow) transmetalation on **C** explains the first-order dependence on the stannane. However, it is stated in the literature[1b] that the equilibrium constant for the dissociation of **II** in Scheme 3 (for $R^1 = C_6H_5$, L = $AsPh_3$, THF at 323 K) is $K_{dis} = (k'_1/k'_{-1}) = 8.6 \times 10^{-4}$ mol L^{-1}. From this we calculate 40% dissociation in the experimental conditions,[12] a value impossible to accept.[13] Thus this mechanism is inconsistent with the quantitative results.

Alternatively, if the L dependence was attributed to the dissociation step in Scheme 3 being slow and rate determining, one would expect the process to be independent of the concentration and nature of the stannane, against what is observed.

Thus, the two plausible mechanisms initiated by a dissociation of L (whether fast or slow) are inconsistent with the data in the literature and must be discarded.

Other obscure points reveal that further studies are needed. In effect, it is not clear that the trans-to-cis isomerizations in [PdR_2L_2] complexes are fast. On the contrary, the theoretical paper usually cited to support this assumption states literally, "T-shaped *trans*-[PdR_2L], arising from dissociation of L in [PdR_2L_2], will encounter a substantial barrier to polytopal rearrangement to *cis*-[PdR_2L]".[5b] Actually, the isomerizations studied in isolated [PdR_2L_2] complexes are slow[5c] or extremely slow.[14] Thus, intermediates of the type *trans*-[$PdR^1R^2L_2$] (**A**) might be expected to be quite long-lived, but they have never been detected under catalytic conditions.[5g] *This warns, in our opinion, against a cursory acceptance of an I-for-R*^{2} *substitution with preservation of the configuration at the palladium.*

Finally, substitution reactions in palladium involving initial L dissociation are a rarity.[15] Since associative models are perfectly compatible with an eventual neutral ligand dissociation, they should not be discarded a priori on the basis of the observed L retarding effect. On the contrary, measurements of activation parameters, not available so far, seem convenient in order to better decide which mechanism is more consistent with the observations.

In the same paper where they proposed the formation of a three-coordinate intermediate as the general mechanism for the transmetalation with organotin compounds, Louie and Hartwig remarked, "Moreover, dissociative ligand substitution typically occurs by initial loss of the covalent ligand that is being replaced. It is striking that transmetalation reactions involving organotin reagents are dissociative and even more unusual that it is a dative spectator ligand that undergoes dissociation".[10] These puzzling questions disappear in the light of an associative ligand substitution of L (which is not an spectator ligand anymore) as the rate-determining step. Thus, we have considered the alternative cycle proposed in Scheme 4, which in our opinion solves all the inconsistencies just analyzed. Differently from the proposals in the literature, the transmetalation involves an associative L-for-R^2 substitution, which gives directly a cis R^1/R^2 rather than a trans R^1/R^2 arrangement in **IV**, and therefrom the cis T-shaped **V**, from which the coupled product will immediately be eliminated.

Our proposal is consistent with the observations in the literature and is supported by a detailed kinetic study of the Stille coupling between 1-iodo-3,5-dichlorotrifluorobenzene ($C_6Cl_2F_3I$) and vinyl- or 4-methoxyphenyltributyltin, catalyzed by *trans*-[$Pd(C_6Cl_2F_3)I(AsPh_3)_2$]. Furthermore, it offers a plausible picture of the kind of bonding interactions leading from the reagents to the products (see later) and eliminates the need for unlikely fast trans-to-cis isomerization after the transmetalation step.

(5) Studies on reductive eliminations: (a) Ozawa, F.; Fujimori, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1986**, *5*, 2144−2149. (b) Tatsumi, K.; Hoffmann, R.; Yamamoto, A.; Stille, J. K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1857−1867. (c) Ozawa, F.; Ito, T.; Nakamura, Y.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1868−1880. (d) Moravski, A.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4182−4186. (e) Loar, M. K.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4174−4181. (f) Ozawa, F.; Ito, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1980**, *102*, 6457−6463. (g) Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933−4941. (h) Komiya, S.; Albright, T. A.; Hoffmann, R.; Kochi, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 7255−7265.

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

(7) For transmetalation with platinum complexes, see: (a) Eaborn, C.; Odell, K. J.; Pidcock, A. *J. Chem. Soc., Dalton Trans.* **1978**, 357−368. (b) Eaborn, C.; Odell, K. J.; Pidcock, A. *J. Chem. Soc., Dalton Trans.* **1979**, 758−760. (c) Deacon, G. B.; Gatehouse, B. M.; Nelson-Reed, K. T. *J. Organomet. Chem.* **1989**, *359*, 267−283.

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

(9) Parshall, G. W. *J. Am. Chem. Soc.* **1974**, *96*, 2360−2366.

(10) Louie, J.; Hartwig J. F. *J. Am. Chem. Soc.* **1995**, *117*, 11598−11599.

(11) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585−9595.

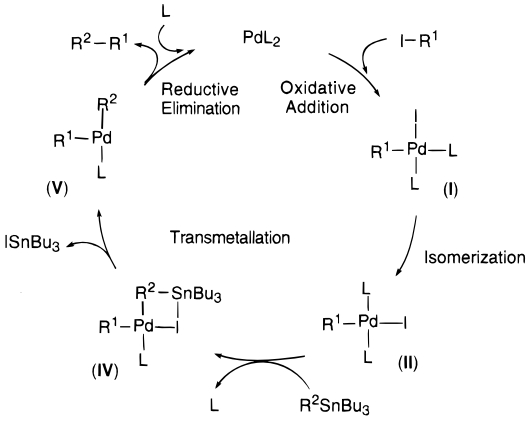
(12) Reference 1b, p 10, gives a dissociation constant at 50 °C in THF: $K_{dis} = 8.6 \times 10^{-4}$ mol L^{-1}. The catalyst concentration was $[Pd]_{total} = 3.2 \times 10^{-3}$ mol L^{-1}: The concentration of three-coordinate *trans*-[$PdPhI(AsPh_3)$] can be calculated from $K_{dis} = [PdPhI(AsPh_3)][AsPh_3]/[PdPhI(AsPh_3)_2] = x^2/[Pd]_{total} - x$. This gives $[PdPhI(AsPh_3)] = x = 1.3 \times 10^{-3}$ mol L^{-1}, corresponding to 40% dissociation.

(13) For instance, for complexes *cis*-[PdR_2L_2] (R = C_6F_5, $C_6F_3Cl_2$; L = tetrahydrothiophene, an easily dissociable ligand), we have estimated the dissociation of L as 0.13% for a solution 8×10^{-4} mol L^{-1} in the complex. See ref 14b.

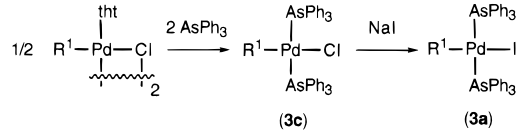
(14) (a) Minniti, D. *Inorg. Chem.* **1994**, *33*, 2631−2634. (b) Casado, A. L.; Casares, J. A.; Espinet, P. *Organometallics* **1997**, *16*, 5730−5736.

(15) Cross, R. J. *Adv. Inorg. Chem.* **1989**, *34*, 219−292.

Scheme 4



Scheme 5[a]

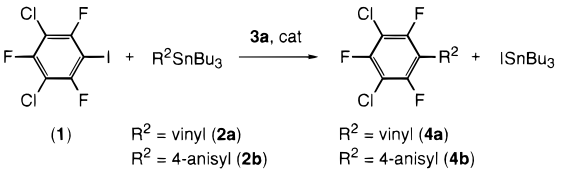


[a] $R^1 = C_6Cl_2F_3$, tht = tetrahydrothiophene.

Results

Preparation of the Catalyst. The catalyst *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**) was prepared in quantitative yield as shown in Scheme 5.[16] Under the standard conditions used in catalytic couplings (10^{-2} mol L^{-1} in THF at 323 K), no detectable dissociation was found by ^{19}F NMR.[17]

Catalytic Studies. The couplings of $C_6Cl_2F_3I$ (**1**) with R^2-$SnBu_3$ (R^2 = CH═CH_2, **2a**; or C_6H_4-4-OCH_3, **2b**) catalyzed by **3a** were monitored by ^{19}F NMR (eq 1, Figure 1). The



(1)

products $R^2C_6Cl_2F_3$ (R^2 = CH═CH_2, **4a**; or C_6H_4-4-OCH_3, **4b**) were formed in up to 95% yield (~1% of ($C_6Cl_2F_3$)$SnBu_3$ (**2c**) was also detected after long reaction periods). Vinyltributyltin **2a** reacts much faster than 4-methoxytributyltin, **2b**. Both couplings are retarded by addition of $AsPh_3$. The catalyst **3a** was the only organopalladium(II) species detected under catalytic conditions.[18]

Kinetic Studies. The couplings of $C_6Cl_2F_3I$ (**1**) with **2a** or **2b** were followed by monitoring the disappearance of **1** by ^{19}F NMR. The reactions followed first-order kinetics, providing straight lines $\ln([\mathbf{1}]_0 - [\mathbf{1}]) = k_{obs}t$.[19] Since the concentration of **1** is stoichiometrically linked to that of **2a**,**b**, the consummation of the latter necessarily obey a first-order law as well. The use of **3a** (the actual transmetalation catalyst) allows us to make measurements from the beginning, as it eliminates the delays needed in other cases, when the catalysts are formed in situ from Pd(0) precursors.[1,11] Some decomposition to Pd(0) (less than 10% mol after 50−60% conversion) was observed in couplings with **2a** carried out without addition of free $AsPh_3$. This affected the linearity of the plots, and in these cases, we measured the initial reaction rate r_0 (= −d[**2a**]/dt), from which first-order constants were estimated as $k_{obs} = r_0/[\mathbf{2a}]_0$ (see Experimental Section).

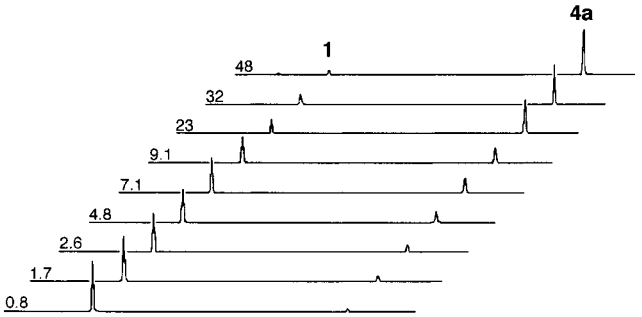


Figure 1. ^{19}F NMR (282 MHz, F^4 region) spectra sequence (intervals in hours) of the coupling of $C_6Cl_2F_3I$ (**1**, 0.2 mol L^{-1}) with (CH_2═CH)$SnBu_3$ (**2a**, 0.2 mol L^{-1}) catalyzed by *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**, 0.01 mol L^{-1}) and $AsPh_3$ (0.02 mol L^{-1}), in THF at 322.6 K. The product is $C_6Cl_2F_3$(CH═CH_2) (**4a**).

The kinetic results obtained from catalytic couplings between **1** and **2a** in THF at 322.6 K have been analyzed as follows in order to obtain the experimental rate law.

1. Kinetic Order with Respect to the Reagents. In agreement with previous results in the literature,[1b,g,10,11] the reaction rate is clearly independent of the electrophile concentration, [**1**]: A similar value $r_0 = 6.8 \times 10^{-5}$ mol L^{-1} s^{-1} ($k_{obs} = 3.4 \times 10^{-4}$ s^{-1}) was found for [**1**] = 0.1 or 0.2 mol L^{-1} (with [**2a**] = 0.2 mol L^{-1}, [**3a**] = 0.01 mol L^{-1} in THF at 322.6 K). Hence, the overall first order observed is assigned to [**2a**] and reveals a behavior typical of the Stille reaction. Thus, an experiment using [**2a**] = 0.092 mol L^{-1} (other conditions the same as before) resulted in $r_0 = 3.2 \times 10^{-5}$ mol L^{-1} s^{-1} ($k_{obs} = 3.5 \times 10^{-4}$ s^{-1}).

2. Retardation by Addition of Free Neutral Ligand. The reaction rate is minus first order with respect to [$AsPh_3$] (the slope of ln(k_{obs}) vs ln[$AsPh_3$] is −1.1). Then, a good linear dependence k_{obs}^{-1} vs [$AsPh_3$] is observed, with a slope (4.31 ± 0.17) × 10^6 mol^{-1} L s in THF at 322.6 K (Figure 2).

3. Catalyst Activity. The kinetic order with respect to the catalyst concentration [**3a**] was determined in the presence of added $AsPh_3$ (0.02 mol L^{-1}). The slope of ln(k_{obs}) vs ln[**3a**] is 1.0, indicating a first-order dependence with respect to [**3a**]. Accordingly, the experimental values fit very well a straight line k_{obs} vs [**3a**], the slope being (1.16 ± 0.05) × 10^{-3} mol^{-1} L s^{-1} (Figure 3a).

Numerical analysis of the kinetic data leads to the rate law given in eq 2, with $a = (2.32 \pm 0.09) \times 10^{-5}$ s^{-1} and $b = (6.9$

$$r_{obs} = k_{obs}[\mathbf{2a}] = \frac{a[\mathbf{3a}]}{[AsPh_3] + b}[\mathbf{2a}] \qquad (2)$$

(16) Espinet, P.; Martinez-Ilarduya, J. M.; Pérez-Briso, C.; Casado, A. L.; Alonso, M. A. *J. Organomet. Chem.* **1998**, *551*, 9−20.

(17) The integration of the signals agreed with that of the added internal standard, 1,3,5-$C_6Cl_3F_3$, and no shift was observed upon successive additions of $AsPh_3$. This discounts the existence of an appreciable percentage of the three-coordinate **C** in fast equilibrium with **3a**. In that case, the observed chemical shifts of a solution of **3a**, would be those averaged between **C** and **3a**, but with an appreciable value for K_{eq}, they should move noticeably toward those of **3a** upon addition of $AsPh_3$, following the displacement of the equilibrium. Thus, the percentage of dissociation must be very small.

(18) When **3a** was replaced by *trans*-[$PdCl_2$($AsPh_3$)$_2$], the latter gave quantitatively **3a** in a short time.

(19) A selection of kinetics and mechanisms books is given: (a) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: Singapore, 1995. (b) Jordan, R. B. *Reaction Mechanisms of Inorganic and Organometallic Systems*; Oxford University Press: New York, 1991. (c) Katakis, D., Gordon, G. *Mechanisms of Inorganic Reactions*; John Wiley & Sons: New York, 1987. (d) Wilkins, R. G. *Kinetics and Mechanism of Reactions of Transition Metal Complexes*, 2nd ed.; VCH: New York, 1991.

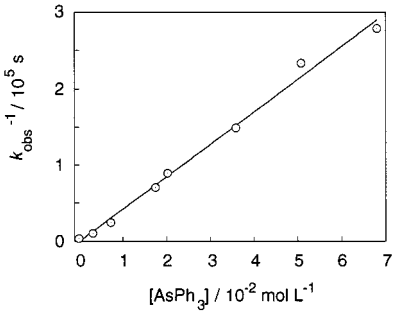


Figure 2. Retarding effect of the addition of $AsPh_3$ on the coupling of $C_6Cl_2F_3I$ (**1**, 0.2 mol L^{-1}) and $(CH_2{=}CH)SnBu_3$ (**2a**, 0.2 mol L^{-1}) catalyzed by *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**, 0.01 mol L^{-1}) in THF at 322.6 K.

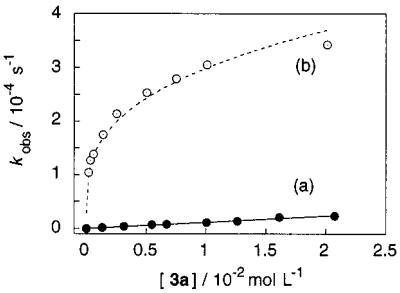


Figure 3. k_{obs} vs [**3a**] plot for the coupling of $C_6Cl_2F_3I$ (**1**, 0.2 mol L^{-1}) and $(CH_2{=}CH)SnBu_3$ (**2a**, 0.2 mol L^{-1}) catalyzed by *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**) in THF at 322.6 K: (a) with $AsPh_3$ (0.02 mol L^{-1}); (b) without $AsPh_3$.

$\pm$ 0.3) $\times$ 10^{-4} mol L^{-1}. The same value of coefficient *a* was obtained from Figure 2 and from Figure 3a, supporting the consistency of our data.[20]

Although it is not relevant to the catalytic conditions, where ratios L:Pd > 2:1 are used, it can be noted that in absence of added $AsPh_3$ (L:Pd = 2:1) the increase of rate with the catalyst concentration is not linear (Figure 3b).[21]

4. Activation Parameters. The temperature dependence of the rate was examined within the range 295−328 K (lower temperatures gave very low rates, difficult to measure; the upper limit is imposed by the boiling point of the solvent). Eyring plots (Figure 4) provided the apparent activation parameters given in Table 1.[19,22] The apparent activation entropy $\Delta S^{\ddagger}_{obs}$ is very negative (ranging from −56 to −155 J K^{-1} mol^{-1}) regardless of the presence or not of added neutral ligand $AsPh_3$, the type of organotributyltin reagent, or the solvent used.[23] This result suggests an associative rate-controlling step.

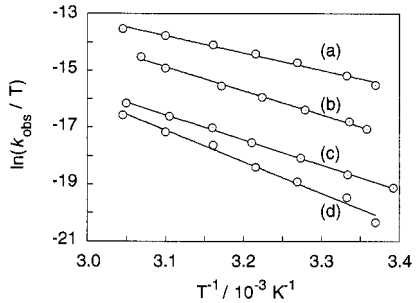


Figure 4. Eyring plots for the coupling of $C_6Cl_2F_3I$ (**1**, 0.2 mol L^{-1}) and R^2SnBu_3 (**2**, 0.2 mol L^{-1}) catalyzed by *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**, 0.01 mol L^{-1}): (a) THF, R^2 = vinyl; (b) PhCl, R^2 = vinyl; (c) THF, R^2 = 4-anisyl; (d) THF, R^2 = vinyl, [$AsPh_3$] = 0.02 mol L^{-1}.

Table 1. Apparent Activation Parameters for the Coupling of $C_6Cl_2F_3I$ (**1**, 0.2 mol L^{-1}) with R^2SnBu_3 (**2**, 0.2 mol L^{-1}) Catalyzed by *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**, 0.01 mol L^{-1})

R^2	solvent	$\Delta H^{\ddagger}_{obs}$/kJ mol^{-1}	$\Delta S^{\ddagger}_{obs}$/J K^{-1} mol^{-1}
vinyl	THF	50 ± 2	−155 ± 7
vinyl[a]	THF	91 ± 4	−56 ± 15
vinyl	PhCl	70.0 ± 1.7	−104 ± 6
4-anisyl	THF	72.8 ± 1.1	−100 ± 3

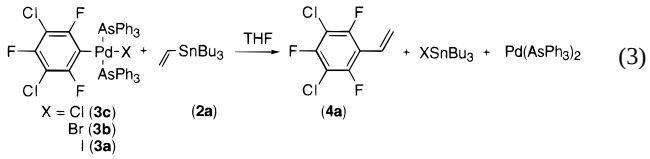
[a] With [$AsPh_3$] = 0.02 mol L^{-1}.

Table 2. Reactions of *trans*-[Pd($C_6Cl_2F_3$)X($AsPh_3$)$_2$] (0.01 mol L^{-1}) and $(CH_2{=}CH)SnBu_3$ (**2a**, 0.2 mol L^{-1}) at 20 °C in THF: Conversion (%) to $CH_2{=}CH{-}C_6Cl_2F_3$ (**4a**)

X (complex)	% after 2.3 h	% after 10 h
I (**3a**)	20	37
Br (**3b**)	58	92
Cl (**3c**)	90	100
Cl (**3c**)[a]	51	100

[a] With [$AsPh_3$] = 0.02 mol L^{-1}.

Reactions of Isolated Organopalladium(II) Complexes with Organotributyltins. The influence of the halide on the transmetalation rate was studied on reactions using isolated palladium complexes. Reactions of *trans*-[Pd($C_6Cl_2F_3$)X($AsPh_3$)$_2$] (X = I, **3a**; Br, **3b**; Cl, **3c**) with $(CH_2{=}CH)SnBu_3$ (**2a**) in a 1:20 ratio (similar to that used in catalytic reactions) gave the coupled product $CH_2{=}CH{-}C_6Cl_2F_3$ (**4a**) and were monitored at similar times in order to have an approximate estimation of their relative rates (eq 3). The rate depended on



(3)

X in the order Cl > Br > I (Table 2), and the reactions were retarded by addition of $AsPh_3$.

Discussion

The experiments carried out on isolated perhalophenylpalladium(II) reaction intermediates support that the transmetalation is the rate-determining process of the coupling cycle (Scheme 4), as expected for a typical Stille reaction. In effect, [Pd(C_6-

(20) Note that the imprecision in the intercept in Figure 2, (−2 ± 6) × 10^3 s, is higher than the value measured (in fact a negative intercept makes no physical sense). Thus the *b* coefficient has been calculated from those of *a* and k_{obs} = (3.37 ± 0.04) × 10^{-4} s^{-1} measured in the absence of added $AsPh_3$.

(21) Under these conditions (L:Pd = 2:1), the kinetic order in respect to [**3a**] is 0.27 (Figure 3b). This order is only apparent. The nonlinear behavior probably comes from the fact that in the absence of added $AsPh_3$ the concentration of $AsPh_3$ arising from dissociation (otherwise negligible) must be considered and is not fixed but varies with the concentration of **3a** (we have studied a similar phenomenon before in ref 14b). Moreover, this dissociation must lead to the formation of other catalytic species (such as iodo-bridged dimers; see ref 10), contributing to the catalysis. This effect has never been noticed before, probably because generally an excess of neutral ligand is used in catalytic couplings (see ref 1). However, Scott and Stille[1g] already noticed that the reaction rate did not increase linearly with the amount of palladium added for higher concentrations of Pd and attributed this to "increased concentration of free phosphine in solution, catalyst aggregation, or change in the catalytic species in solution").

(22) The activation parameters given in the Table 1 cannot be assigned to any elemental step at this point (see Discussion). For this reason we refer to them as "apparent".

(23) To detect any solvent participation in the reaction, PhCl was checked, in addition to the widely used THF; note that both solvents have the same polarity (E_T = 98.8 kJ mol^{-1}), hence similar solvation effects, but PhCl is a much worse donor: (a) Catalán, J.; López, V.; Pérez, P.; Martín-Villamil, R.; Rodriguez, J.-G. *Liebigs Ann. Chem.* **1995**, 241−252. (b) Jensen, W. B. *Chem. Rev.* **1978**, *78*, 1−22. (c) Gutmann, V. *Coord. Chem. Rev.* **1976**, *18*, 225−255.

$Cl_2F_3)(CH{=}CH_2)L_2$] could not be detected in transmetalation experiments at moderate temperature (eq 3), suggesting that the reductive elimination occurs fast once the transmetalation has taken place. *trans*-[Pd($C_6Cl_2F_3$)I($AsPh_3$)$_2$] (**3a**) was the only organopalladium(II) intermediate detected along the catalytic couplings of $C_6Cl_2F_3I$ (**1**) with R^2SnBu_3 (R^2 = CH=CH_2, **2a**; C_6H_4-4-OCH_3, **2b**) (eq 1); hence the oxidative addition step and the subsequent cis-to-trans isomerization (Scheme 4) are also faster than the transmetalation.[24] The kinetic zeroth order in electrophile **1** agrees with this. Consequently, the kinetic results of the catalytic runs can be properly assigned to the transmetalation step.

The true complexity of the rate law (eq 2) reveals the concurrence at the transmetalation process of a set of elemental steps. The mechanistic interpretation establishes that the elemental composition at the transition state is [**2a** + **3a** − $AsPh_3$].[19a] In other words, the interaction between **2a** and **3a** takes place with release of one molecule of $AsPh_3$. We will consider the two general pathways by which $AsPh_3$ can be released from **3a**: before or during the interaction with the stannane. We will refer to them as dissociative or associative transmetalation, respectively.

In the so far accepted model, the dissociation of $AsPh_3$ precedes the interaction with the stannane. This has been drawn in Scheme 3 (in our case $R^1 = C_6Cl_2F_3$ and L = $AsPh_3$). If we consider the dissociation to be rate determining, application of the steady-state approximation leads to eq 4.

$$r_{obs,ss} = k_{obs,ss}[\mathbf{2a}] = \frac{k'_1k'_2[\mathbf{3a}]}{k'_{-1}[AsPh_3] + k'_2[\mathbf{2a}]}[\mathbf{2a}] \qquad (4)$$

For a very low concentration of $AsPh_3$ (as is the case in the absence of added $AsPh_3$), eq 4 is simplified to $r_{obs,ss} \approx k'_1[\mathbf{3a}]$, a rate expression zeroth order with respect to [**2a**], contrary to the first-order dependence observed experimentally (eq 2). Moreover, the reaction rate becomes mathematically independent of the organotributyltin used, contrary to the marked differences observed between vinyltin and phenyltin compounds. Therefore, the mechanistic assumption leading to eq 4 is to be discarded.

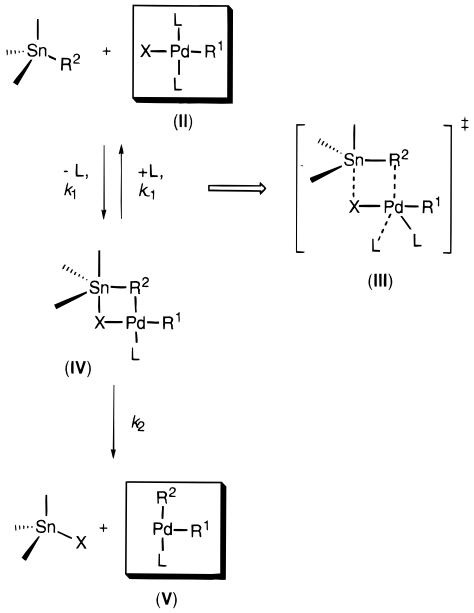
Alternatively, if we consider a fast dissociation,[1b,10,11] eq 5 is obtained applying the preequilibrium model,[19b] with $K_{dis} = k'_1/k'_{-1}$.

$$r_{obs,pe} = k_{obs,pe}[\mathbf{2a}] = \frac{k'_2K_{dis}[\mathbf{3a}]_{total}}{K_{dis} + [AsPh_3]}[\mathbf{2a}] \qquad (5)$$

Equation 5 agrees with the rate law (eq 2) and data treatment gives $k'_2 = 1.8 \times 10^{-1}$ s^{-1} and $K_{dis} = 1.3 \times 10^{-4}$ mol L^{-1} (at 322.6 K in THF). Since the concentration of catalyst added was $[\mathbf{3a}]_{total} = 10^{-2}$ mol L^{-1}, the value of K_{dis} indicates that 12% of catalyst **3a** should be dissociated as **C** (or its corresponding solvated complex) in the absence of added $AsPh_3$. This high dissociation should be detectable by ^{19}F NMR, but the expected effects were not observed.[17] Hence the three-coordinate intermediate **C** is not formed in significant concentration, and the preequilibrium dissociative model is also unsatisfactory.

(24) In fact, the coupling rate of **1** and **2a** catalyzed by *trans*-[Pd($C_6Cl_2F_3$)I(PPh_3)$_2$] (10^{-2} mol L^{-1}) in THF at 322.6 K is $(9.9 \pm 0.4) \times 10^{-6}$ s^{-1}: Casado, A. L. Ph.D. Thesis, Universidad de Valladolid, Spain, March 1998. Under the same conditions, the isomerization rate of *cis*-[Pd($C_6Cl_2F_3$)I(PPh_3)$_2$] to *trans*-[Pd($C_6Cl_2F_3$)I(PPh_3)$_2$] is $(1.49 \pm 0.09) \times 10^{-3}$ s^{-1}, i.e., ~150 times faster (the isomerization limits the formation of *trans*-[Pd($C_6Cl_2F_3$)I(PPh_3)$_2$] and the oxidative addition is faster; see ref 8).

Scheme 6[a]



[a] $R^1 = C_6Cl_2F_3$, L = $AsPh_3$, X = halide.

Consequently, *the two possible models for a dissociative transmetalation, are inconsistent with the observations.*

We propose the associative transmetalation pathway shown in Scheme 6, which leads to the transformation *trans*-**II** → *cis*-**V** via L-for-R^2 substitution at the coordination plane. A nucleophilic attack of the Pd-coordinated halide to the organotin compound makes the palladium center more electrophilic and the C_α atom of R^2 more nucleophilic, assisting the electrophilic attack of Pd to give the activated complex **III**, from which L is released.,[14b,25,26] Since associative substitutions via pentacoordinate palladium occur with preservation of the stereochemistry at the palladium,[15] intermediate **IV**, as well as the three-coordinate **V**, must necessarily have R^2 in the position of the leaving $AsPh_3$, i.e., cis to R^1. Then, **V** can readily eliminate the coupling product $R^1{-}R^2$ without the need for further (and comparatively slow) dissociation or isomerization steps that must be proposed in the so far accepted mechanism (Scheme 1).

Applying the steady-state approximation to our associative transmetalation model (Scheme 6), eq 6, with $k_1 = 0.034$ mol^{-1} L s^{-1} and $k_2/k_{-1} = 6.9 \times 10^{-4}$ mol L^{-1}, is obtained (see Appendix; numeric values given hold for X = I, in THF at 322.6 K), which also agrees with the experimental rate law (eq 2).

$$r_{obs,ss} = k_{obs,ss}[\mathbf{2a}] = \frac{k_1k_2[\mathbf{3a}]}{k_{-1}[AsPh_3] + k_2}[\mathbf{2a}] \qquad (6)$$

(25) Both the ability of tin(IV) to increase its coordination number and the formation of single-bridged compounds are well documented in the following reviews: (a) Davies, A. G. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995. Vol. 2, Chapters 6.4 and 6.5. (b) Harrison, P. G. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon: Oxford, U.K., 1987, Vol. 3, Chapter 26.3.4. (c) Davies, A. G.; Smith P. J. Chapter 11.4.4.2 In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, U.K., 1982; Vol. 2, Chapter 11.4.4.2.

(26) For R-bridging structures observed by X-ray diffraction, see: (a) Usón, R.; Forniés, J.; Falvello, L. R.; Tomás, M.; Casas, J. M.; Martín, A.; Cotton, F. A. *J. Am. Chem. Soc.* **1994**, *116*, 7160−7165. (b) Usón, R.; Forniés, J.; Tomás, M.; Casas, J. M.; Cotton, F. A.; Falvello, L. R.; Feng, X. *J. Am. Chem. Soc.* **1993**, *115*, 4145−4154. (c) Usón, R.; Forniés, J.; Tomás, M.; Casas, J. M.; Navarro, P. *J. Chem. Soc., Dalton Trans.* **1989**, 169−172. (d) Usón, R.; Forniés, J.; Tomás, M.; Casas, J. M. *Organometallics* **1988**, *7*, 2279−2285.

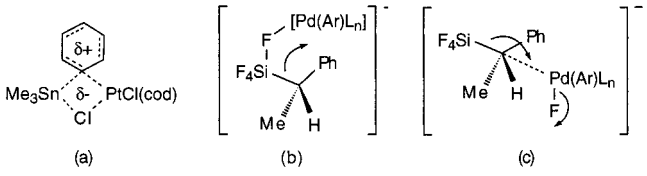


Figure 5. Activated complex models for transmetalation with stannanes and silanes, as proposed in refs 7a and 30.

As k_1 depends on the nature of the organotin reagent, different coupling rates are to be expected for different organotributyltins, even for $[AsPh_3] = 0$ (in such case $r_{obs,ss} = k_{obs,ss}[\mathbf{2a}] = k_1[\mathbf{3a}][\mathbf{2a}]$). In fact, the observed rate is vinyl > phenyl.[27]

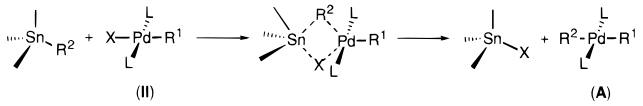
Although the interpretation of apparent activation parameters is not simple in such a multistep reaction,[22] the very large negative values for the apparent $\Delta S^{\ddagger}_{obs}$ (Table 1, obtained from the composite rate constant k_{obs}) found in all cases examined are in agreement with the associative mechanism proposed. This entropy argument also rules out solvent (THF) participation in the $AsPh_3$ replacement (at least as the main pathway), which should produce only a small increase in order in the transition state.[19d] Moreover, the activation entropy found in chlorobenzene is also negative, although this solvent is much worse ligand than THF.[28]

Changes of the halogen atom X are expected to produce little effect on the activation entropies of the processes concerned; hence, the variation in rates observed for the transmetalation of *trans*-$[Pd(C_6Cl_2F_3)X(AsPh_3)_2]$ (Table 2) must be related to changes in activation entalpy. These are probably associated with a high activation enthalpy for the pentacoordination of the Pd atom. In fact the **II** → **IV** transformation corresponds, with little variation, to the rate-determining step of an associative substitution in Pd complexes.[15] The nucleophilic attack of the atom of the R^2 group (entering ligand) on the electrophilic Pd complex must be facilitated as the Pd complex becomes more electrophilic and the C_α more nucleophilic (predicting a rate variation Cl > Br > I, as observed).[29]

The mechanism in Scheme 6 is a variation of the so-called S_E2(cyclic) ligand replacement.[15] Thus, for the arylation of $[PtX_2L_2]$ complexes using aryltrimethylstannanes, four center-activated complexes (Figure 5a) have been suggested.[7a] Moreover, Hatanaka and Hiyama have proposed similar activated complexes for the palladium-catalyzed coupling of organosilicon compounds with the aid of fluoride ion: This coupling can course with retention or with inversion of configuration, depending on the temperature and the solvent. For the reaction occurring with retention of the configuration, the cyclic transition state (Figure 5b) was proposed, whereas an S_E2(open) mechanism would be operating when the reaction courses with inversion (Figure 5c).[30]

The S_E2(cyclic) mechanism implies retention of the configuration at C_α. Unfortunately, the effect on the stereochemistry of the Pd complex was disregarded, and the effect of added ligand was not studied in refs 7 and 30, where a direct X-for-R^2 substitution is implied (Scheme 7). Note that this kind of substitution would lead to a trans arrangement of the two R groups after transmetalation and should be little sensitive to the addition of L, which remains coordinated. On the contrary, our proposal explains the dependence on L observed and produces immediately the cis arrangement needed for fast R^1-R^2 coupling.[31]

Scheme 7



Finally, some comments about the influence of the neutral ligands, L, can be made in light of our mechanism. It is known from the literature that there is an inverse relationship between ligand donicity and transmetalation rate.[11] The Stille reaction runs up to 3 orders of magnitude faster with ligands of modest donicity ($AsPh_3$) than with good donors (PPh_3). This seemed to support the dissociative proposal because the former should dissociate more readily. But they will be more easily displaced also in an associative substitution process. Moreover, the electrophilicity of the palladium complex will be higher with L ligands of low donicity, and this will make the activated complex **III** more accessible. Furthermore, the L ligands must move to equatorial positions in **III** for the substitution to occur. Hence, if L ligands with similar net donicities are compared, it is reasonable that the transmetalation should be favored by those better π acceptors, as they have a stronger preference for the equatorial sites in d^8 bpt complexes.[32]

On the other hand, it seems that there is no clear correlation between rate and the steric parameters of L,[1b] contrary to the expectations for an initial L dissociation, which should be favored for increasing steric requirement of L. In the mechanism in Scheme 6, the influence of increasing the bulkiness of L is more difficult to predict since this will destabilize the ground and the transition states less differently than when these are four- and three-coordinated (as in the dissociative mechanism). Bulkier ligands will probably make more difficult the access to **III**, but at the same time they will favor the dissociation to **IV**. Thus, in a concerted process, a less clear influence can be expected. Note, however, that coming to very bulky ligands, a dramatic change in behavior has been reported: For the transmetalation of the dimeric complex $[PdArBrL]_2$ (Ar = *p*-Tol; L = P(*o*-Tol)$_3$) with trialkyltin aryls, the rate depends on the square root of the concentration of dimer and is not affected by the addition of L. This is consistent with a dissociative mechanism.[10] The scheme proposed in the literature for this mechanism can be accommodated to an S_E2(cyclic) model as shown in Scheme 8.

Conclusions

The studies presented here concern the conditions most commonly used for the Stille reaction, involving the use of aryl or vinyl halides in solvents of moderate donicity, palladium complexes with monodentate ligands of normal steric bulk, and ratios L:Pd > 2:1. The mechanism proposed in Scheme 4 fits all the observations made on the reaction, either stoichiometric or catalytic. First, it depicts the fact that the oxidative addition

(27) It must be noted that in order to produce the transmetalation, R^2 must become bridging ligand using its C_α. This does not discount an initial π-coordination of R^2 helping the bimolecular interaction, when possible (R^2 = vinyl, alkynyl). This kind of coordination has been proposed by Farina et al.[11] and would account for two facts observed for vinyl derivatives: (i) A faster reaction rate and (ii) the formation of Heck coupling byproducts in some cases; see: (a) Liao, J.-H.; Kanatzidis, M. G. *J. Am. Chem. Soc.* **1990**, *112*, 7399−7400. (b) Kikukawa, K.; Umekawa, H.; Matsuda, T. *J. Organomet. Chem.* **1986**, *311*, C44−C46.

(28) For THF complexes of Pd(II), see: Usón, R.; Forniés, J. *Adv. Organomet. Chem.* **1988**, *28*, 219−297.

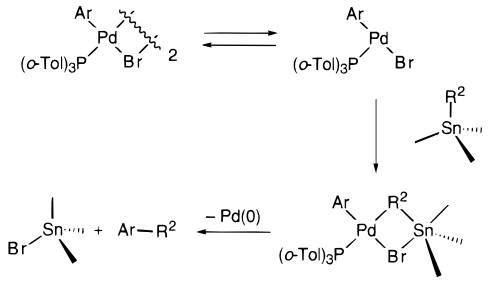
(29) For a dissociative ligand substitution, the converse trend should be expected, as the dissociation of L should be the more difficult (hence K_{dis} in eq 5 should be the smaller) the more electronegative the halide.

(30) Hatanaka, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1990**, *112*, 7794−7796.

(31) Pitifully, neglect of the coordination sphere of the metal is quite common in the literature of metal-catalyzed organic transformations. We hope that this paper will serve to draw attention on its mechanistic relevance in some cases.

(32) Rossi, A. R.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 365−374.

Scheme 8



gives a cis compound, which isomerizes rapidly to the trans isomer. From the latter, an associative ligand substitution produces L-for-R^2 exchange. This leads directly to a T-shaped three-coordinate *cis*-[PdR^1R^2L] species from which irreversible R^1-R^2 elimination must be fast, simplifying noticeably the course of the mechanism after the transmetalation step. The dependence of the transmetalation rate on the addition of L, on the halide, and on the tin derivative is also understood on the basis of this associative transmetalation. For all these reasons, the associative model for the Stille reaction is more adequate than the dissociative so far accepted.

However, one should be careful not to consider our proposal as the only possible mechanism for the Stille reaction. In very different conditions (e.g., very coordinating solvents, very bulky ligands, chelating ligands, or lack of halide in the system) other mechanisms might be competing with or replacing the one just discussed. For instance, a case has been reported recently where the stannane seems to react directly with the palladium(0) complex.[33] Also, our mechanism predicts retention of configuration at the carbon, which has been observed in some reactions,[34] but inversion has been reported in other cases.[6] This stresses the idea that other reaction conditions deserve mechanistic studies on their own.

Finally, a unified view seems to be merging for the transmetalations to palladium, whether with Sn (Stille), with silicon fluoride-assisted (Hiyama), and possibly with other transmetallating agents: The reactions occurring with retention of configuration most likely proceed in all cases by an S_E2(cyclic) L-for-R replacement at the Pd center. It is plausible that an S_E2(open) mechanism (as suggested by Hiyama in Si) can also be operating for the Stille coupling in those cases where inversion has been observed (using the very coordinating solvent mixture HMPA−THF). Further studies are in progress to explore these aspects.

Experimental Section

The reactions involving organolithium or organomagnesium reagents were carried out under N_2. Commercial $ClSnBu_3$, $AsPh_3$, and vinylmagnesium bromide (1 M solution in THF) were used without further purification. The solvents were purified using standard methods. $C_6Cl_2F_3I$ (**1**),[8] *trans*-[$PdCl_2(AsPh_3)_2$],[35] [$Pd_2(C_6Cl_2F_3)_2(\mu\text{-}Cl)_2(tht)_2$],[16] and (4-methoxyphenyl)magnesium iodide (from 4-bromoanisole and magnesium turnings)[2] were prepared as reported in the literature.

Infrared spectra (cm^{-1}) were recorded on a Perkin-Elmer FT-IR 1720 X spectrometer. Combustion analyses were made on a Perkin-Elmer 2400 CHN microanalyzer. Mass spectra were taken on a Hewlett-Packard 5980 spectrometer (70 eV, EI). ^1H, $^{13}C\{^1H\}$, ^{19}F, and $^{119}Sn\{^1H\}$ NMR spectra were run on a Bruker ARX-300 spectrometer equipped with a VT-100 variable-temperature probe; chemical shifts are reported in ppm from $SiMe_4$ (^1H, ^{13}C), CCl_3F (^{19}F) in $CDCl_3$, or net $SnMe_4$ (^{119}Sn) at room temperature.

R^2SnBu_3: R^2 = CH=CH_2 (2a), C_6H_4-4-OCH_3 (2b). To a solution below 0 °C of vinylmagnesium bromide (14.0 mmol) in diethyl ether (60 mL) $ClSnBu_3$ (3.48 mL, 12.8 mmol) was slowly added. The mixture was stirred overnight while it reached room temperature. The resulting white suspension was hydrolyzed with aqueous $NaHCO_3$, washed with water (2 × 30 mL), and dried over $MgSO_4$. The diethyl ether solution was evaporated to give a pale yellow oil which was vacuum-distilled yielding a colorless liquid **2a** (3.45 g, 85%): $^{119}Sn\{^1H\}$ NMR (0.2 mol L^{-1} in THF/ClPh) δ −48.96/−49.27 (s). **2b** was similarly prepared from (4-methoxyphenyl)magnesium iodide in 71% yield. The rest of spectroscopic data are similar to those reported.[2]

***trans*-[Pd($C_6Cl_2F_3$)Cl($AsPh_3$)$_2$] (3c).** To a stirred suspension of [$Pd_2(C_6Cl_2F_3)_2(\mu\text{-}Cl)_2(tht)_2$] (100 mg, 0.116 mmol) in acetone (10 mL) was added $AsPh_3$ (150 mg, 0.488 mmol). After some seconds, white **3c** precipitated. The mixture was stirred for 1 h, and the solvent evaporated. The solid was then washed with diethyl ether and air-dried (yield 209 mg, 94%): IR (KBr) 1436 (vs), 1400 (vs), 1078 (m), 1046 (m), 1034 (m), 777 (s), 739 (vs), 692 (vs), 480 (s), 460 (m), 331 (m), 314 (m); ^1H NMR ($CDCl_3$) δ 7.7−7.6 (m, 2C*H*), 7.5−7.3 (m, 3C*H*); ^{19}F NMR ($CDCl_3$/THF) δ −90.62/−86.82 (s, 2F^2), −120.27/−116.89 (s, F^4). Anal. Calcd for $C_{42}H_{30}As_2Cl_3F_3Pd$: C, 52.86; H, 3.17. Found: C, 52.65; H, 3.35.

***trans*-[Pd($C_6Cl_2F_3$)X($AsPh_3$)$_2$]: X = I (3a), Br (3b).** To a colorless solution of **3c** (110 mg, 0.115 mmol) in acetone/CH_2Cl_2 (4/4 mL) was added an excess of NaX (0.20 mmol). The yellow mixture formed was stirred for 1 h and then evaporated to dryness. The residue was extracted in CH_2Cl_2 (5 mL) and evaporated again. The yellow solid was washed with diethyl ether/*n*-hexane and vacuum-dried. **3a** (93%): IR (KBr) 3073 (m), 1482 (m), 1436 (vs), 1403 (vs), 1047 (m), 775 (m), 735 (vs), 691 (vs), 481 (s), 467 (s), 335 (s), 322 (s); ^1H NMR ($CDCl_3$) δ 7.58 (m, 2C*H*), 7.5−7.3 (m, 3C*H*); ^{19}F NMR ($CDCl_3$/THF/ClPh) δ −91.81/−87.60/−87.32 (s, 2F^2), −120.02/−116.72/−115.50 (s, F^4). Anal. Calcd for $C_{42}H_{30}As_2Cl_2F_3IPd$: C, 48.24; H, 2.89. Found: C, 48.12; H, 2.97. **3b** (89%): IR (KBr) 3055 (m), 1482 (m), 1435 (vs), 1404 (vs), 1047 (m), 778 (m), 737 (vs), 693 (vs), 483 (s), 471 (s); ^1H NMR ($CDCl_3$) δ 7.58 (m, 2C*H*), 7.5−7.3 (m, 3C*H*); ^{19}F NMR ($CDCl_3$/THF) δ −91.01/−86.82 (s, 2F^2), −120.15/−116.81 (s, F^4). Anal. Calcd for $C_{42}H_{30}As_2BrCl_2F_3Pd$: C, 50.51; H, 3.03. Found: C, 50.45; H, 3.16.

Isolation of $R^2C_6Cl_2F_3$ from Catalytic Reaction Mixtures: R^2 = CH=CH_2 (4a), C_6H_4-4-OCH_3 (4b). After evaporation of the solvent (THF), product **4a** was vacuum-distilled (70 °C, 3 mm) as a colorless liquid (80% isolated yield): d 1.19. IR (NaCl) 2928 (m), 1610 (s), 1463 (vs), 1451 (vs), 1411 (vs), 1219 (s), 1081 (s), 991 (s), 936 (s), 860 (s), 801 (s); ^1H NMR ($CDCl_3$) δ 6.61 (dd, $^{3,trans}J_{HH}$ = 18.0 Hz, $^{3,cis}J_{HH}$ = 11.9 Hz, CH_{gem}), 6.06 (d, $^{3,trans}J_{HH}$ = 18.0 Hz, CH_{cis}), 5.69 (d, $^{3,cis}J_{HH}$ = 11.9 Hz, CH_{trans}); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 154.94 (ddd, $^1J_{CF}$ = 253.9 Hz, $^4J_{CF}$ = 9.2 Hz, $^4J_{CF}$ = 4.2 Hz, *C*F^2), 153.77 (dt, $^1J_{CF}$ = 251.9 Hz, $^4J_{CF}$ = 5.5 Hz, *C*F^4), 123.22 (td, $^4J_{CF}$ = 7.9 Hz, $^6J_{CF}$ = 2.5 Hz, *C*H$_2$), 121.60 (td, $^3J_{CF}$ = 17.3 Hz, $^5J_{CF}$ = 2.3 Hz, *C*H), 112.62 (td, $^2J_{CF}$ = 16.5 Hz, $^4J_{CF}$ = 4.6 Hz, *C*-vinyl), 107.29 (ddd, $^2J_{CF}$ = 24.9 Hz, $^2J_{CF}$ = 21.0

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Hz, $^4J_{CF}$ = 3.9 Hz, *C*-CF); ^{19}F NMR ($CDCl_3$/THF/ClPh) δ −115.41/−112.21/−111.50 (d, $^4J_{FF}$ = 2.4 Hz, 2*F*^{2}), −113.29/−110.62/−109.57 (t, $^4J_{FF}$ = 2.4 Hz, *F*^{4}); MS *m*/*z* (%) 226 (50) [M$^+$], 191 (41), 156 (100), 105 (25). Anal. Calcd for $C_8H_3Cl_2F_3$: C, 42.33; H, 1.33. Found: C, 42.27; H, 1.32. **4b**: After evaporation of the solvent (THF), the residue was treated with diethyl ether and a saturated aqueous KF solution. After vigorous stirring, $FSnBu_3$ separated as a white solid. The diethyl ether phase was separated, dried over $MgSO_4$, and evaporated to dryness. The residue was chromatographed (silica gel/hexane) giving a white solid, which was recrystallized from pentane at −28 °C (white needles, 95%): mp 98−99 °C; IR (KBr) 2941 (m), 2839 (m), 1613 (s), 1522 (s), 1445 (vs), 1408 (vs), 1255 (vs), 1186 (s), 1053 (vs), 1034 (s), 795 (vs), 565 (m), 526 (m); ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 2C*H*), 7.14 (m, 2C*H*), 3.87 (s, C*H*$_3$); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 160.09 (s, *C*-OMe), 154.34 (ddd, $^1J_{CF}$ = 249.7 Hz, $^4J_{CF}$ = 8.3 Hz, $^4J_{CF}$ = 4.4 Hz, *C*F^2), 153.80 (dt, $^1J_{CF}$ = 250.6 Hz, $^4J_{CF}$ = 5.3 Hz, *C*F^4), 131.30 (s, *C*H), 118.87 (s, *C*-$C_6Cl_2F_3$), 114.07 (s, *C*H), 116.09 (td, $^2J_{CF}$ = 20.1 Hz, $^4J_{CF}$ = 4.4 Hz, *C*-Ph), 107.34 (ddd, $^2J_{CF}$ = 25.6 Hz, $^2J_{CF}$ = 21.0 Hz, $^4J_{CF}$ = 3.3 Hz, *C*CF), 55.22 (s, *C*H$_3$); ^{19}F NMR ($CDCl_3$/THF) δ −115.69/−112.18 (dt, $^4J_{FF}$ = 2.4 Hz, $^5J_{FH}$ = 1.3 Hz, 2*F*^{2}), −113.64/−111.39 (t, $^4J_{FF}$ = 2.4 Hz, *F*^{4}); MS *m*/*z* (%) 306 (78) [M$^+$], 263 (69), 193 (100). Anal. Calcd for $C_{13}H_7Cl_2F_3O$: C, 50.85; H, 2.30. Found: C, 50.84; H, 2.36.

Kinetics on Palladium-Catalyzed Couplings of $C_6Cl_2F_3I$ (1) with Organotributyltins (2a,b). NMR tubes (5 mm) were charged with **1** (39.2 ± 0.1 mg, 120.0 ± 0.3 mmol) and suitable amounts of palladium catalyst **3a**, $AsPh_3$, and organotributyltin **2a,b**. The samples were dissolved under N_2 at room temperature (293 K) in THF (or PhCl) to a fixed volume of 600 ± 5 μL, charged with an acetone-d_6 capillary for NMR lock, and placed into a thermostated probe (±0.2 K; the temperature was measured by an ethylene glycol standard method). Concentration−time data were then acquired from ^{19}F NMR signal areas of **1** and the products (**4a,b**), and fitted to equation $\ln([\mathbf{1}]_0 - [\mathbf{1}]) = k_{obs}t$ to get first-order constants k_{obs} (standard deviations are also given). Alternatively, when no good first-order rates were achieved (couplings with **2a** in absence of added $AsPh_3$), first data points (up to 10% of conversion) were fitted to the following second-degree Taylor equation $[\mathbf{1}] = a_0 + a_1t + a_2t^2$, where a_1 gives the initial reaction rate in mol L^{-1} s^{-1} ($a_1 = r_0 = -\mathrm{d}[\mathbf{1}]/\mathrm{d}t = -\mathrm{d}[\mathbf{2a}]/\mathrm{d}t$). Since the reaction rate *r* is first order in **2a** and zeroth order in **1** (eq 2), the first-order constants can be estimated in these cases as $k_{obs} = r_0/[\mathbf{2a}]_0$.

Reactions of Organopalladium(II) Complexes and Organotributyltins. Samples containing 0.01 mol L^{-1} in palladium complex and 0.2 mol L^{-1} in the corresponding organotributyltin, prepared as above-described, were allowed to react at 20 °C (thermostated bath). The reaction products were analyzed by ^{19}F NMR at the reported intervals of time.

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Supporting Information Available: Values of the first-order rate constant k_{obs} for the coupling of $C_6Cl_2F_3I$ (**1**, 0.2 mol L^{-1}) with R^2SnBu_3 (**2a,b**, 0.2 mol L^{-1}) catalyzed by *trans*-[$Pd(C_6Cl_2F_3)I(AsPh_3)_2$] (**3a**) under different experimental conditions (1 page, print/PDF). See any current masthead page for ordering information and Web access instructions.

Appendix: Derivation of the Kinetic Eq 6. The steady-state concentration of intermediate **IV** (Scheme 6, X = I), and the reaction rate, are given in eqs 7−9.

$$\mathrm{d}[\mathbf{IV}]/\mathrm{d}t = k_1[\mathbf{2a}]\,[\mathbf{3a}] - k_{-1}[\mathbf{IV}][\mathrm{AsPh_3}] - k_2[\mathbf{IV}] = 0 \quad (7)$$

$$[\mathbf{IV}] = \frac{k_1[\mathbf{2a}][\mathbf{3a}]}{k_{-1}[\mathrm{AsPh_3}] + k_2} \quad (8)$$

$$r_{obs,ss} = k_2\,[\mathbf{IV}] \quad (9)$$

$$r_{obs,ss} = k_{obs,ss}[\mathbf{2a}] = \frac{k_1k_2[\mathbf{3a}]}{k_{-1}[\mathrm{AsPh_3}] + k_2}[\mathbf{2a}] \quad (6)$$

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