Palladium-Catalyzed Coupling of Arylstannanes with Organic Sulfonates: A Comprehensive Study

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The effect of ligands and lithium chloride on the rates of the palladium catalyzed coupling between organic triflates and arylstannanes was studied. The dependence of the rate on the ligand is similar to the one previously reported for the coupling of vinylstannanes, but in the present case triphenylarsine is shown to be superior to both triphenylphosphine and tri(2-furyl)phosphine. The effect of added chloride is complex and varies depending on solvent and ligand used. Ortho-substituted arylstannanes tend to transfer alkyl moieties to a substantial extent , and therefore rates and efficiencies of aryl vs alkyl transfer were quantitated. When ortho substituents that are potentially coordinating to tin are used, no rate acceleration in the alkyl transfer process was observed, which is in contrast with two recently reported studies that suggest nucleophilic assistance at tin to be important in the transmetalation step. An important side reaction in the coupling of poorly reactive vinyltriflates and most aryltriflates is the Pd-induced homocoupling of the stannane to form biaryls. The experimental factors that control this process were evaluated.

Introduction

The Stille reaction can be best described as the palladium catalyzed coupling between organostannanes and unsaturated halides or sulfonates.[1] This synthetic method has gained increasing popularity among synthetic chemists[2] and the extension of this coupling reaction to include vinylic[3] and arylic[4] trifluoromethanesulfonates as electrophiles is especially important since these substrates can be conveniently made from readily available carbonyl compounds and phenols, respectively.

While olefinic stannanes smoothly participate in many Stille couplings, the coupling of arylstannanes is considerably more difficult.[1] Stille, for example, reported that this class of compounds does not couple with olefinic triflates, [3] while coupling with aryl triflates works well if extreme conditions (ca. 100 °C) are utilized.[4]

After initial reports that arylstannanes do indeed couple with some activated olefinic triflates derived from β-lactams,[5] we have demonstrated that *this coupling reaction can be successfully carried out at room temperature* on a variety of substrates, provided suitable ligands are employed (e.g. triphenylarsine or, in some cases, "ligandless" conditions).[6,7] Other investigators, employing traditional conditions, have reported failure to achieve this type of coupling.[8]

The aryl–aryl coupling reaction, on the other hand, has registered several applications and has been extended to other novel coupling partners such as aryl fluorosulfonates[9] and aryl *p*-fluorophenylsulfonates.[10] It has been noted, however, that ortho-substituted arylstannanes couple poorly,[11] and that in some cases alkyl transfer can effectively compete with the desired aryl transfer,[12] or completely override it.[13]

We have also detected considerable amounts of stannane homocoupling product in these reactions,[6] a reaction that has been encountered with olefinic stannanes as well,[14] and is mechanistically unexplained.

Ligands that dramatically accelerate the Stille coupling of olefinic stannanes were reported,[15] therefore it seemed worthwhile to investigate whether the same ligands may be used to facilitate the couplings of *arylstannanes*, and whether an inhibitory effect by free ligand may be present in these couplings also. It seemed reasonable that some mechanistic information could be derived from a thorough study of ligand effects in the aryl–aryl coupling. In addition, we wanted to explore and more fully document, from a kinetic standpoint, the reported retarding effect of ortho substituents on the aryltin in the coupling reaction, especially in relation to the very important issue of alkyl vs aryl transfer.

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(1) Recent reviews: Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. Also: Mitchell, T. N. *Synthesis* **1992**, 803.

(2) A survey of applications of transition metal-mediated cross-coupling reactions for the year 1992 shows that the Stille coupling accounts for over 50% of all cross-couplings reported. It is followed by the coupling of boron derivatives (the Suzuki reaction, see: Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314), with about a fourth of all couplings. Less popular appear to be couplings involving organozinc and Grignard reagents.

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Table I. Effect of Ligands and Halide on the Initial Rate of Coupling between Vinyl Triflate 1 and [*p*-(Trifluoromethyl)phenyl]tributyltin[a]

entry	ligand	Pd/L	halide (equiv)	rel k^b	% yield[c]
1	PPh_3	1:4	LiCl (3)	1.0 (0.12)	54
2	PPh_3	1:4	none	13.7[d]	7
3	TFP[e]	1:4	LiCl (3)	3.5	75
4	TFP	1:4	none	56[d]	8
5	TFP	1:4	LiCl (9)	3.5	ND[f]
6	(*o*-Tol)$_3$P	1:4	LiCl (3)	149	82
7	dppf	1:2	none	15[d]	15
8	[2,4,6-(MeO)$_3$C$_6$H$_2$]$_3$P	1:4	LiCl (3)	4.2	75
9	(*p*-MeO-C$_6$H$_4$)$_3$P	1:4	LiCl (3)	1.9	ND
10	$AsPh_3$	1:4	LiCl (3)	95	87
11	$AsPh_3$	1:4	none	58	83
12	$AsPh_3$	1:4	$ZnCl_2$	151	89
13	$AsPh_3$	1:6	LiCl (3)	76	88
14	$AsPh_3$	1:7	LiCl (3)	59	86
15	$AsPh_3$	1:8	LiCl (3)	52	90
16	$AsPh_3$	1:10	LiCl (3)	32	85
17	none	-	LiCl (3)	1480	69
18	none	-	none	56[d]	28

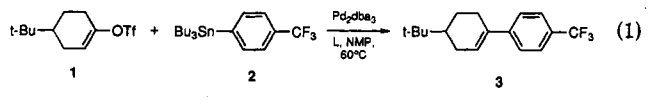
[a] Triflate and stannane were 0.11 M in NMP, with 2.5% Pd_2dba_3 (5% Pd) at 60 °C. [b] Observed rate constant for entry 1 was 4.3×10^{-5} min^{-1}. Standard deviation in brackets. [c] Determined by HPLC after 40 h at 60 °C. [d] Rate noticeably declined with time, and catalyst decomposition occurred. [e] Tri(2-furyl)phosphine. [f] ND = not determined.

What is the kinetic preference for aryl vs alkyl transfer under a variety of experimental conditions? Can this ratio be affected by the proper choice of ligands, or will very "fast" ligands (e.g. triphenylarsine) indiscriminately facilitate the coupling of both aryl and alkyl moieties?

Finally, while this work was in progress, two studies appeared, suggesting that in some special cases alkyl transfer can be accelerated by a coordinating moiety on the stannane.[16,17] These authors invoke nucleophilic assistance at departing tin as a mechanistic rationale; it was felt that it would be valuable to try to document this effect in quantitative terms. This report pinpoints the scope of the Stille reaction employing arylstannanes, and presents some mechanistic hypotheses based on the ligand effects, kinetic results, ^{31}P-NMR data, and a Hammett study.

Results

Coupling between Olefinic Triflates and Arylstannanes. The palladium-catalyzed coupling between triflate 1 and stannane 2 in 1-methyl-2-pyrrolidinone (NMP) at 60 °C was monitored by HPLC under a number of conditions (eq 1). The temperature was a suitable



1 2 3 (1)

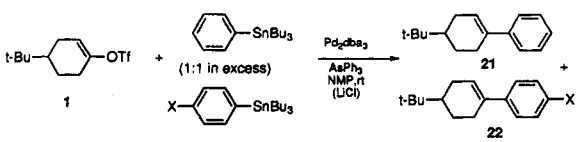
compromise that allowed us to measure rates for the "slow" ligands as well as the "fast" ones under otherwise identical conditions. Some of our key findings were reported previously.[6] In addition, we have explored the role of excess ligand on the reaction rate. Relative rates for this coupling were obtained by assuming first-order kinetics overall, as in a previous study[15] and are summarized in Table I.

Modest rate accelerations over PPh_3/LiCl were obtained with the previously recommended tri(2-furyl)phosphine (TFP)[5a] and tris(2,4,6-trimethoxyphenyl)phosphine[5c] (entries 3 and 8 vs 1), although final yields are better with these ligands than with PPh_3. Bidentate ligands are generally not particularly effective in the Stille reaction[15,18,19] and entry 7 confirms this fact. The best ligands in terms of both yields and initial rates are tri(*o*-tolyl)phosphine (entry 6) and $AsPh_3$ (entry 10). In addition, conducting the reaction without strong ligands (entry 17) furnished acceptable yields of product at an extremely rapid rate. The effect of chloride is more complex, and in most cases the reaction was not successful in its absence. Faster initial conversion was observed in the presence of PPh_3 (entry 2) or TFP (entry 4), but the reaction stopped at very low conversion due to catalyst instability. Large amounts of chloride (entry 5) did not produce any further effect over the customarily used 3 equiv. The reaction with $AsPh_3$, on the other hand, was rather insensitive to added chloride and worked well under all conditions (entries 10–12). Increasing the amount of ligand had a slight but noticeable retarding effect on the rate (entries 12–16). Finally, the "ligandless" conditions also appear to require chloride for optimum results (entries 17, 18).

From a preparative standpoint, the use of $AsPh_3$ as ligand or, in very hindered cases, the use of ligandless conditions, allow the coupling between olefinic triflates and a variety of arylstannanes to be carried out at room temperature with good to excellent results (Table II).

We attempted to find conditions that would lead, in each case, to effective coupling at room temperature. Typical unhindered triflates coupled smoothly in the presence of $AsPh_3$ as ligand (entries 1, 2, 5). In some cases, when more hindered triflates were used (notably entries 6 and 7), the reaction was sluggish in the presence of $AsPh_3$, and the coupling was more conveniently carried out under ligandless conditions. When LiCl was employed as an additive, its role was mainly as an inhibitor of stannane homocoupling (*vide infra*). Although it was also found to accelerate the cross-coupling reaction (Table I, entry 17, 18), in several cases (Table II, entries 4, 7, 8) its addition was found unnecessary and the reaction proceeded smoothly in the presence of Pd_2dba_3 alone. In one case (entry 5) where double bond isomerization was possible, we indeed detected essentially complete isomerization to the more stable of the two possible geometrical isomers.

Hammett Studies. In order to probe the electronic influence that the arylstannane exerts during the transmetalation step, a competition study was conducted. Two series of experiments were set up whereby 1 equiv of vinyl triflate 1 was cross-coupled with a molar excess of a 1:1 mixture of a para-substituted arylstannane and phenyltributyltin (eq 2). The two sets of experiments were



1 22 (2)

conducted under otherwise identical reaction conditions,

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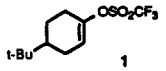
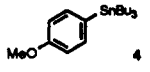
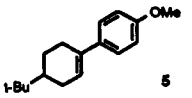
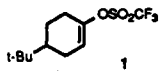
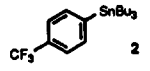
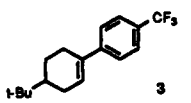
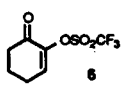
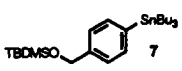
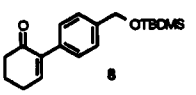
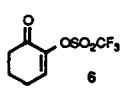
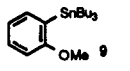
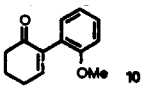
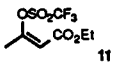
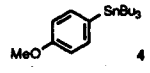
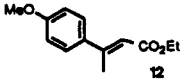
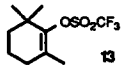
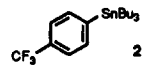
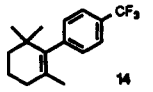
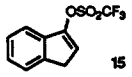
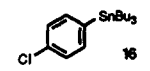
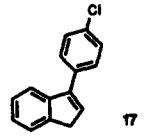
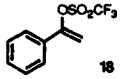
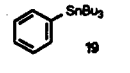
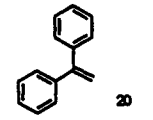
(19) Bidentate phosphines as ligands have, however, been described in the Stille reaction, e.g. see ref 12. Bidentate nitrogen ligands have also been reported: see Van Asselt, R.; Elsevier, C. J. *Organometallics* **1992**, *11*, 1999.

Table II. Generalized Coupling between Vinyl Triflates and Arylstannanes[a]

entry	triflate	stannane	conditions[a]	product	% yield
1	 1	 4	$Pd_2(dba)_3$, $AsPh_3$	 5	89
2	 1	 2	$Pd_2(dba)_3$, $AsPh_3$	 3	83
3	 6	 7	$Pd_2(dba)_3$, LiCl	 8	83
4	 6	 9	$Pd_2(dba)_3$	 10	77
5	 11	 4	$Pd_2(dba)_3$, $AsPh_3$	 12	72[b]
6	 13	 2	$Pd_2(dba)_3$, LiCl	 14	60
7	 15	 16	$Pd_2(dba)_3$	 17	68
8	 18	 19	$Pd_2(dba)_3$	 20	72

[a] All reactions in dry, degassed NMP at 24 °C. [b] Starting material was 100% *Z*, product was 95% *E*.

Table III. Competition Experiments (eq 2) for the Evaluation of Electronic Effects in the Stille Coupling of Vinyl Triflates with Arylstannanes, with and without LiCl

X	σ_p value	k_X/k_H (no LiCl)	k_X/k_H (3 equiv LiCl)
Me_2N	−0.83	89:11	69:31
MeO	−0.27	72:28	48:52
H	0	(50:50)	(50:50)
Cl	0.227	41:59	65:35
CF_3	0.54	38:62	62:38

with the exception of the use of LiCl in one set of reactions. The results of this study are illustrated in Table III and Figures 1 and 2.

The product ratios (**21**/**22**) are taken as a measure of the relative rates of the two competitive transmetalation reactions under study. It is clear that, in the case of the examples conducted in the absence of LiCl (Figure 1), a fairly good linear free energy relationship (plot of log k_X/k_H vs σ) exists (r^2 = 0.946) whereby the presence of an electron-releasing substituent on the arylstannane increases the reaction rate (ρ = −0.89). When the same competition reactions were conducted in the presence of 3 equiv of LiCl, a remarkable difference was seen. The plot of log k_X/k_H vs σ did not yield a linear Hammett relationship (Figure 2). Although other types of σ values were tried,[20] a linear relationship could not be obtained.

Coupling between Aryl Triflates and Tetrabutyltin. In the study of conditions that affect the partitioning between the aryl transfer reaction vs transfer of the (typically) "dummy" alkyl substituents (usually butyl), it

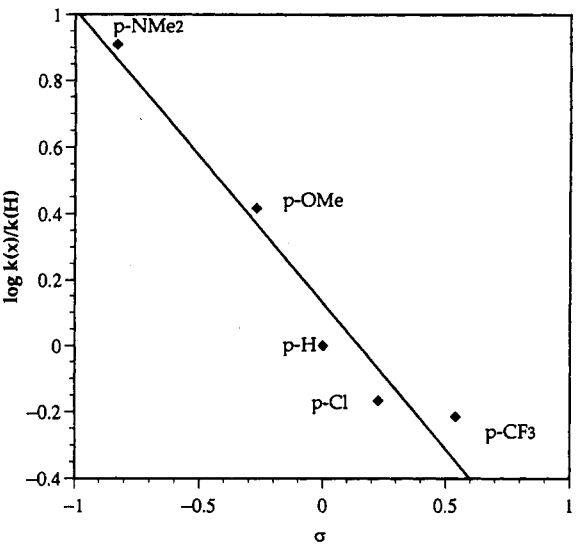
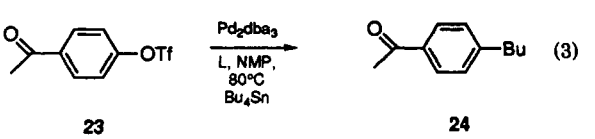


Figure 1. Hammett plot for the coupling between triflate **1** and aryltin derivatives *in the absence of LiCl* (Pd_2dba_3, $AsPh_3$, NMP, rt); ρ = −0.89 (r^2 = 0.954).

was decided to first explore the effect of several ligands on the rate of transfer of alkyl groups from tetrabutyltin (eq 3).



23 **24** (3)

It was also thought that the effect of ligands on the rate may shed some light on the mechanistic details of the

(20) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; J. Wiley: New York, 1972, p 144.

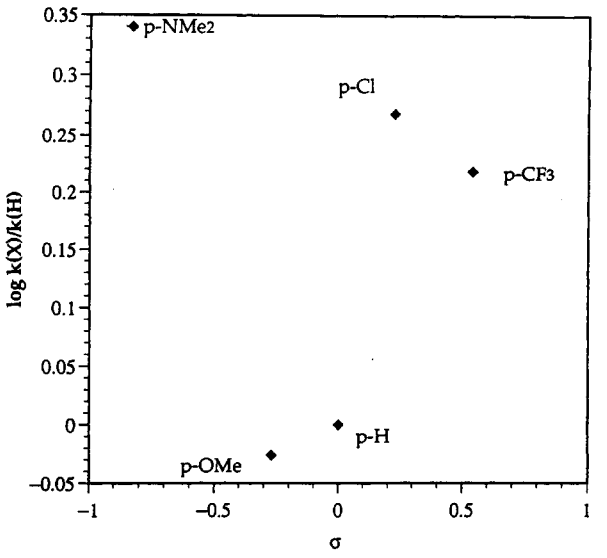


Figure 2. 2: Hammett plot for the coupling between triflate 1 and aryltin derivatives *in the presence of 3 equiv of LiCl* (Pd_2dba_3, $AsPh_3$,NMP, rt).

Table IV. Effect of Ligands and Halides on the Initial Rate of Coupling between Aryl Triflate 23 and Tetrabutyltin

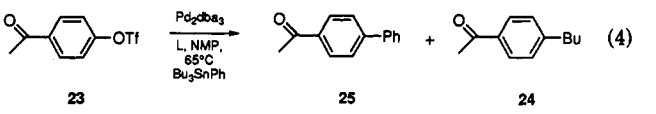
entry	ligand	Pd/L	halide (equiv)	rel k_{obs}[a]	% yield of 24 (recvd start. matl)[b]
1	PPh_3	1:4	LiCl (3)	1.0 (0.08)	3.5 (96.1)
2	PPh_3	1:6	LiCl (3)	0.31	1.3 (98.2)
3	PPh_3	1:4	none	34.0	81.8 (9.0)
4	PPh_3	1:8	none	35.1	82.3 (4.7)
5	PPh_3	1:4	LiCl (1)	1.1	1.4 (97.3)
6	dppp	1:2	none	27.2[c]	50 (36.1)
7	TFP[d]	1:4	LiCl (3)	2.8	91.8 (1.0)
8	TFP[d]	1:4	none	86[c]	4.0 (82.4)
9	$AsPh_3$	1:4	LiCl (3)	125 (18)	93.5 (1.0)
10	$AsPh_3$	1:6	LiCl (3)	120	>98 (<0.5)
11	$AsPh_3$	1:8	LiCl (3)	73	96.8 (2.8)
12	$AsPh_3$	1:10	LiCl (3)	67	>98 (<0.5)
13	$AsPh_3$	1:4	none	375[c]	33.0 (61.0)
14	$AsPh_3$	1:4	LiCl (1)	197[c]	75.5 (15.9)

[a] 0.13 M triflate and stannane, 1% Pd_2dba_3 (2% Pd) in NMP at 80 °C. Relative initial rate for entry 1 was 1.0×10^{-5} min^{-1} (std dev in parentheses). [b] Yield of product and starting material determined by HPLC after 40 h. [c] Rate substantially decreases with time, and catalyst decomposed. [d] Tri(2-furyl)phosphine.

transmetalation reaction of tetraalkyltins with Pd(II). Preliminary work had established that NMP is also an excellent solvent for this type of coupling and some ligand effects had been reported for the coupling of tetramethyltin.[15] Our new findings are summarized in Table IV.

Once again, rate gains were modest when we switched from PPh_3/LiCl (entry 1) to TFP (entry 7), although the yield improved. $AsPh_3$ displayed initial rates that were 2 orders of magnitude higher than the ones with PPh_3, in analogy with the coupling of olefinic triflates and aryltins. The effect of chloride was, however, quite different. With PPh_3, the deletion of chloride substantially increased the initial rate (entry 3) and produced a stable catalyst, capable of bringing the reaction to near completion. While the reaction in the presence of chloride was further inhibited by free ligand (entries 1, 2), the reaction without chloride was completely insensitive to excess ligand (entries 3, 4). With $AsPh_3$, however, 3 equiv of LiCl were found necessary to achieve complete conversion, no chloride or just 1 equiv leading to premature catalyst decomposition (entries 13, 14). In the presence of chloride, a small but consistent drop in rate was observed with $AsPh_3$ when increasing the concentration of the ligand (entries 9–12). TFP was also unable to stabilize the catalyst without added chloride (entry 8), while a bidentate ligand (entry 6) gave acceptable rates but, once again, unsatisfactory catalyst stability in the absence of chloride. From a preparative standpoint, essentially quantitative conversion to **24** can be obtained using $AsPh_3$ as ligand in the presence of 3 equiv of lithium chloride.

Coupling of Aryl Triflates with Arylstannanes. The effect of ligands, chloride, and solvent on the rates of aryl and butyl transfer from phenyltributyltin to triflate **23** (eq 4) were next examined. Once again, a temperature



23 **25** **24**

(65 °C) was selected that would allow us to conveniently carry out couplings with PPh_3 and $AsPh_3$ under the same conditions.

The results are shown in Table V. The reaction was carried out in an atmosphere of argon, obtained with three cycles of vacuum/argon at ambient temperature. Efforts were made in each entry to account for every product of the reaction, and the mass balance was close to 100% in most cases.

The coupling rate in the presence of PPh_3/LiCl in NMP was extremely slow at 65 °C, but nevertheless gave a 74% yield of biaryl in 40 h. Some butyl transfer product was also isolated and the ratio of phenyl vs butyl transfer in this simple unhindered system is a surprisingly low 12:1. A much faster rate was obtained with $AsPh_3$ as ligand (entry 5) and appreciable amounts of butyl transfer (6%) were detected. The reaction with PPh_3 was once again faster without LiCl, although slightly lower yields were obtained. Here the yield of **24** was only 2%, but some biphenyl, the product of stannane homocoupling, was detected. Deleting lithium chloride also accelerated the coupling in the presence of $AsPh_3$ (entry 6), producing only 1% of **24**. Here the incomplete conversion is due to extensive formation of biphenyl (16%), which consumed much of the arylstannane.

Running the reaction in dioxane, reported by Stille to be a superior solvent for these couplings, gave generally slower conversions and consistently produced more biphenyl (entries 3, 4, 8, 9). Interestingly, and in complete contrast with the results in NMP, the reaction in dioxane did not appreciably proceed without chloride (entries 4, 9). Thus, coupling in dioxane, although quite selective for aryl transfer, is plagued by the formation of biaryl in the presence of chloride and catalyst instability in the absence of chloride. Finally (entry 10), the fastest rates were obtained under "ligandless" conditions, which afforded also fairly good selectivity of aryl vs butyl transfer. One must also note that, in general, the ratio of aryl vs alkyl transfer products reflects fairly closely the initial rates of group transfer, but in some cases the ratio of the initial rates is slightly different from the final product ratio.

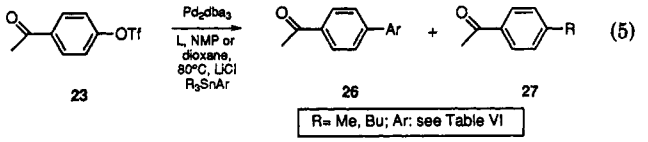
The effect of substituents on the aryltin moiety vs rate was next examined in NMP or dioxane using the optimum conditions ($AsPh_3$, LiCl). The reaction was carried out at 80 °C, although some of these couplings can easily be done at 25–50 °C, because ortho-substituted aryltins coupled

Table V. Effect of Ligands, Solvent, and Chloride on the Initial Rate of Phenyl and Butyl Transfer in the Coupling between Aryl Triflate 23 and Phenyltributyltin[a]

entry	ligand (solvent)	Pd/L	halide (equiv)	$10^3 k_{obs}$ phenyl transfer (min^{-1})	$10^3 k_{obs}$ butyl transfer (min^{-1})	% yields[b] (start. mater; biaryl; 24)	ratio 25/24[c]
1	PPh_3 (NMP)	1:4	LiCl (3)	<0.03[d]	<0.03	6.0; 73.8; 6.1	12
2	PPh_3 (NMP)	1:4	none	1.4 (0.15)[d]	0.045	35.4; 61.3; 2.2	28[e]
3	PPh_3 (dioxane)	1:4	LiCl (3)	<0.03[d]	<0.03	14.9; 80.9; 2.1	38[f]
4	PPh_3 (dioxane)	1:4	none	0.13[d]	<0.03	93.0; 6.4; 0	–
5	$AsPh_3$ (NMP)	1:4	LiCl 93)	3.9 (0.2)	0.25	1.8; 91.8; 6.1	15
6	$AsPh_3$ (NMP)	1:4	none	7.3	0.08	14.6; 80.5; 1.0	80[g]
7	$AsPh_3$ (NMP)	1:8	LiCl (3)	3.5	0.22	0; 87.7; 6.3	14
8	$AsPh_3$ (dioxane)	1:4	LiCl (3)	1.7 (0.2)	0.065	34.4; 55.5; 2.5	22[h]
9	$AsPh_3$ (dioxane)	1:4	none	2.1	ND	87.5; 11.0; <0.5	–
10	none (NMP)	–	LiCl (3)	23	1.5	0; 83.4; 5.6	15

[a] Triflate and stannane were 0.125 M in NMP or dioxane, with 1% Pd_2dba_3 (2% Pd) at 65 °C. [b] Determined by HPLC after 40 h. [c] Ratio of final products (HPLC). [d] Catalyst unstable, decomposed prematurely. [e] Also produced biphenyl (5%). [f] Biphenyl, 15%. [g] Biphenyl, 16%. [h] Biphenyl, 36%. [i] Biphenyl, 12%.

much more sluggishly at lower temperatures and rates could not be measured (eq 5).



(5)

Table VI shows the rate constants for aryl vs alkyl transfer with a number of different stannanes. Efforts were made to isolate all products and in many cases we were able to account for >95% of the mass balance. In some cases both HPLC and isolated yields are reported for comparison, while in some entries only HPLC yields are reported. Biaryls were isolated by chromatography and further purified by recrystallization. The melting points generally matched the values reported in the literature, with the exception of compound **36**, which sharply melted at a much higher temperature than reported.[21]

When comparing the rates of butyl transfer using tetrabutyltin and phenyltributyltin, respectively (entry 1 and 2), one can see that these are essentially the same, at least in NMP under our conditions. Trimethyltin derivatives are used sometimes in synthesis because they afford faster rates of aryl transfer than the bulkier tributyltin counterparts.[1] Entry 3 shows that such kinetic advantage is very small, while methyl transfer is 10 times faster than butyl transfer, therefore leading to substantial amounts of toluene derivative **28**.

Also measured were the coupling rates in dioxane (entry 4), where methyl transfer is much slower, leading to better selectivity. Poor yield was observed due to competitive biaryl formation in this solvent. An alkyl substituent in the ortho-position of the aryltin (entry 5) slows down the aryl transfer reaction by a factor of ca. 20, but does not affect the alkyl transfer process, which now becomes clearly competitive.

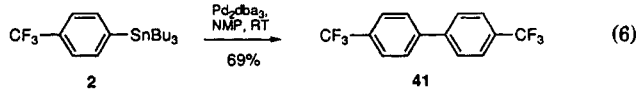
An ortho substituent that is potentially coordinating to tin (entry 7 vs 6) also leads to large amounts of butyl transfer, but not because the butyl transfer reaction is accelerated; it is clearly the aryl transfer reaction that is disfavored vs phenyltributyltin. Other stannanes confirm this trend. While an aldehyde group in the ortho position slows down the aryl coupling by more than 1 order of magnitude (entry 8), a methoxy substituent (entry 9) has only a minor effect on the aryl transfer rate and leads to the expected biaryl in good yield. Coordinating arms such as the (dimethylamino)methyl (entry 10), used by Brown[17] to accelerate coupling in a related system, only lead to butyl transfer, albeit in low yield, and not because of kinetic acceleration, but because the aryl transfer reaction is exceedingly slow here. Even the highly constrained 1-(dimethylamino)-8-(tributylstannyl)naphthalene (entry 11), which has been shown to feature an unusual pentacoordinate tin center,[18] fails to show the acceleration that would be expected based on Brown's results. In fact, no coupling is observed at all.

Finally, little effect is seen on the aryl transfer reaction when introducing electron-withdrawing or -donating substituents (entries 12, 13) on the aryltin moiety. A slight effect was noted on the transfer of butyl groups. Electron-rich aromatic moieties slightly accelerate the butyl transfer reaction (entries 9, 13), while the opposite effect is seen with an ortho electron-withdrawing group (entry 8).

In order to compare the measured ortho effect on the tin moiety with the steric effect of ortho groups on the aryl triflate, the experiments shown in Scheme I were performed. The rate constants measured for the two processes show that a methyl group ortho to the triflate moiety slows down the coupling by a factor of only ca. 3 under the present conditions.

Aryl Stannane Homocoupling. Since products that formally arise from an oxidative homocoupling of the aryltin were often isolated in some of our cross-coupling reactions, attempts were made to induce this homocoupling reaction in the absence of the triflates under a variety of conditions in order to determine the experimental parameters affecting this side reaction.

When [*p*-(trifluoromethyl)phenyl]tributyltin (**2**) was simply stirred at rt in NMP in the presence of a catalytic amount of Pd_2dba_3, an 80% yield of biaryl **41** was detected by HPLC, and the crystalline compound was isolated in 69% yield (eq 6 and Table VII, entry 1).

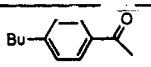
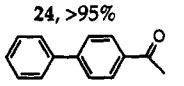
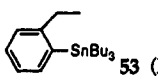
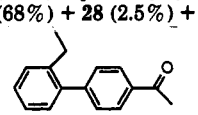
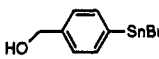
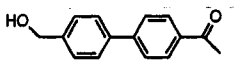
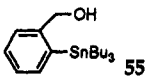
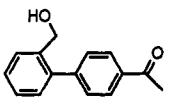
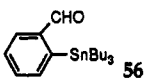
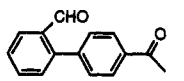
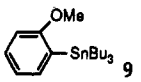
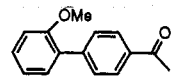
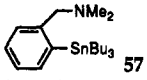
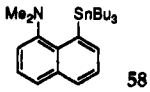
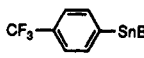
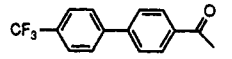
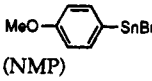
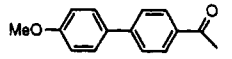


(6)

When monitored by ^{119}Sn NMR spectroscopy, smooth and complete disappearance of the peak due to **2** (δ −40.3) was accompanied by appearance of a single peak at δ 77.2, identical with isolated hexabutyltin oxide ($Bu_3SnOSnBu_3$). This indicates that the reaction involves an oxidation at tin and, since oxygen is a likely candidate as the oxidizing agent, the role of O_2 was studied. Kinetics of homocoupling were measured (monitoring product formation by reversed-phase HPLC) at 40 °C in NMP in the presence of air.

(21) Dasgupta, R.; Kanjilal, P. R.; Patra, S. K.; Sarkar, M.; Ghatak, U. R. *Tetrahedron* **1985**, *41*, 5619.

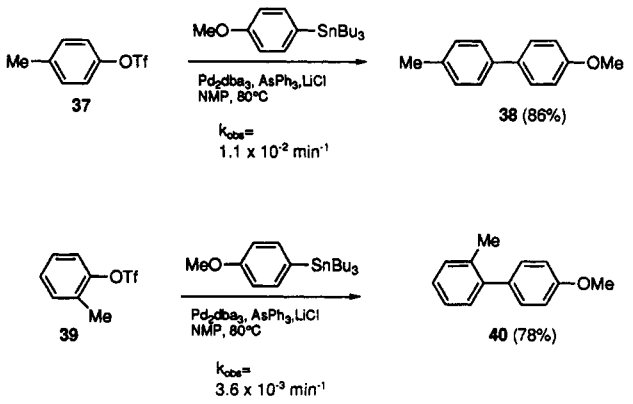
Table VI. Effect of Aryltin Structure on the Rate of Transfer of Aryl vs Alkyl Groups in the Pd(0)-Catalyzed Coupling with Aryl Triflate 23

entry	stannane (solvent)	10^3k_1 aryl transfer (min^{-1})[a]	10^3k_2 alkyl transfer (min^{-1})[a]	k_1/k_2	products and yields[b]
1	Bu_4Sn (NMP)	-	1.2	-	
2	$PhSnBu_3$ (19) (NMP)	40.5	1.1	37	**24**, >95%  + **24**, 4% (5%) **25**, 82% (90%)
3	$PhSnMe_3$ (NMP)	53.1	10.5	5	**25** (74%) + *p*-MeC_6H_4COMe (**28**) (21%)
4	$PhSnMe_3$ (dioxane)	6.6	0.10	66	**25** (68%) + **28** (2.5%) + Ph–Ph (27%)
5	 **53** (NMP)	1.8	1.0	1.8	 **29**, 46% + **24**, 27% + start. matl, 20%
6	 **54** (NMP)	37.1	1.2	31	 **30**, 76% + **24**, 6% + *p*-HO-C_6H_4COMe (**31**, 10%) + start. matl, 6%
7	 **55** (NMP)	1.9	0.9	2.1	 **32**, 50% + **24**, 24% + **31**, 21%
8	 **56** (NMP)	3.0	0.15	20	 **33**, 25% (72%) + **24** (4%)
9	 **9** (NMP)	18.2	1.8	10	 **34**, 88% (90%) + **24**, 10% (9%)
10	 **57** (NMP)	*c*	0.05, <0.01[d]	-	**24** (6%) + start. matl (16%) + **31** (45%)
11	 **58** (NMP)	*c*	<0.01	-	start. matl (49%) + **31** (39%)
12	 **2** (NMP)	28.5	1.2	23	 **35** (89%) + **24** (9%)
13	 **4** (NMP)	38.2	3.2	12	 **36** (92%) + **24** (7%)

[a] Rates measured by HPLC vs standard solutions. Conditions: 0.11 M **1** and stannane in NMP (or dioxane) at 80 °C with 1% Pd_2dba_3 (2% Pd) and 8% $AsPh_3$ with 3 equiv LiCl. [b] Yields refer to isolated material (chromatography); yields in brackets refer to HPLC quantitation. [c] No aryl coupling product could be detected. [d] This experiment was carried out in the absence of LiCl. Only 2% yield of **4** was detected.

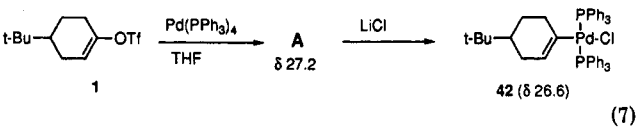
Since rates in some cases appreciably dropped after the first 5–10 turnovers, only initial rates were measured. A good fit was obtained by assuming kinetics to be first order in stannane (Figure 3). When the reaction mixture was carefully degassed (Table VII, entry 4), the initial rate constant was negatively affected and the reaction essentially stopped at 23% conversion. The tin-containing product was exclusively, once again, the tin oxide. It appeared from these results that traces of oxygen were still present in the "degassed" solution, and they were causing the limited amount of conversion. It was found that as many as *six freeze-thaw cycles* were necessary to exclude oxygen from the solution. This completely shut off the reaction (entry 5). The reaction rate was negatively affected by radical scavengers (entry 3), but evidently the scavenger was consumed and the reaction proceeded almost to completion. A more profound effect was exerted by lithium chloride and $AsPh_3$ which, acting in synergy, substantially slowed down the reaction (entries 2, 6, 7). The reaction did not proceed at 40 °C in the absence of palladium (using radical initiators like AIBN) or with palladium in combination with "strong" donors like PPh_3 (data not shown). Finally, the reaction was not sensitive to electronic factors, since (*p*-methoxyphenyl)tributyltin

Scheme I



underwent homocoupling at almost the same rate as **2** (entry 8). No other products were detected in these reactions and in each case unreacted stannane accounted for the remainder of the mass balance (HPLC, NMR evidence).

NMR Studies. In order to establish whether the transmetalation is the rate-determining step in these couplings, as in the related couplings of iodoarenes with vinyltins,[15] we monitored the oxidative addition step by $^{31}P\{^1H\}$-NMR under stoichiometric conditions. We began by essentially repeating Stille's study[3] with vinyl triflate **1** in anhydrous THF. In all our experiments triphenylphosphine oxide (TPPO) served as an internal standard (δ 22.7 in THF, δ 25.1 in NMP vs external H_3PO_4), in order to compensate for some drifting of the observed chemical shifts. When $Pd(PPh_3)_4$ in THF (br s, δ ca. 20) was treated with LiCl (3 equiv), a smaller second peak appeared (δ 27.1), presumably due to a Pd(0)Cl adduct.[22] Addition of **1** (exactly 1 equiv or an excess) led immediately to a spectrum consisting only of two sharp singlets (in addition to TPPO), one due to PPh_3 (δ −6) and another, at δ 26.6 which, in analogy with Stille, can be assigned to species **42**. If, however, no LiCl was used in the experiment, the signal due to $Pd(PPh_3)_4$, upon addition of **1**, slowly shifted and sharpened, to finally yield (4 h) a singlet at δ 27.2, representing an unknown species **A** (eq 7). No



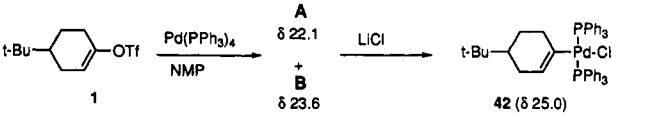
(7)

signal for free PPh_3 was seen here. Addition of excess LiCl gave **42** and free PPh_3. These experiments are essentially in agreement with Stille's results, except for some differences in δ values between the two studies.

When phenyltributyltin (2 equiv) was added neat and the solution of **42** and PPh_3 was heated at 50 °C overnight, no reaction was observed. We should note that even small amounts of Pd(0) species would be easy to detect, since they extensively broaden the signal due to free PPh_3. The oxidative addition step is therefore much faster than the transmetalation step, at least under these conditions.

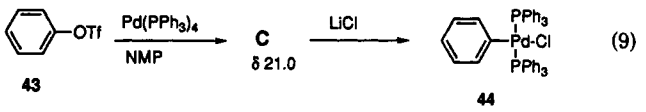
When the above experiments were repeated in NMP (eq 8) in the presence of LiCl, species **42** was formed as before (δ 25.0, TPPO shifted to δ 26.2 due to the effect of LiCl).

In the absence of LiCl, in contrast with the THF experiment, *two* sharp singlets were produced *immediately* (δ 22.1 and 23.6), the one at δ 23.6 (species **B**) slowly increasing in intensity with time at the expense of the other signal.



(8)

Addition of excess LiCl caused the immediate disappearance of the signal at δ 22.1 with concomitant formation of **42** (δ 25.0). The signal at δ 23.6 did not change or disappear even upon mild warming (40 °C) or prolonged (24 h) periods at rt. More drastic conditions caused deterioration of the spectrum.



(9)

When we carried out similar experiments with aryl triflate **43** (eq 9), it became obvious that oxidative addition is much slower with **43** than with vinyl triflate **1**. For example, in NMP with LiCl present, **43** gave, after 30 min at rt, only traces of **44** (δ 24.6), which was identified by comparison with an authentic sample prepared by oxidative addition of $Pd(PPh_3)_4$ to chlorobenzene.[23] Heating at 40 °C for 1 h was necessary to drive the reaction to completion. Very sluggish also was the reaction without LiCl. A sharp singlet for the oxidative addition product (labeled **C**) was observed at δ 21.0, and once again the reaction took ca. 1 h at 40 °C to reach completion. Addition of excess chloride to this solution immediately and cleanly led to **44**. Addition of excess phenyltributyltin and heating at 50 °C failed to produce, once again, any traces of products, showing that in this case also the oxidative addition is much faster than the transmetalation.

The oxidative addition was slower in THF than in NMP. Only traces of **44** were observed after 1 h at 40 °C, and the reaction was only ca. 50% complete after 18 h at this temperature (0.02 M Pd, 0.04 M triflate), while in the absence of LiCl no clearcut oxidative addition was detected: no reaction was observed at rt, and complete decomposition to elemental palladium resulted from heating at 40 °C overnight.

Discussion

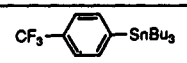
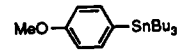
Our data clearly show that the palladium-catalyzed coupling of arylstannanes with organic triflates is a synthetically useful process that takes place at room temperature or slightly above it, provided one chooses a suitable catalytic system, involving "soft" palladium ligands or, in some cases, "ligandless" conditions.

The data presented in this paper are consistent with the simplified mechanistic rationale presented in Scheme II. The NMR results under stoichiometric conditions suggest that oxidative addition is a fast step, readily taking place at room temperature for vinyl triflates and at 40 °C for aryl triflates, while no transmetalation takes place at these temperatures at least when employing PPh_3 as a ligand. It is therefore very unlikely, contrary to a recent

(22) Amatore, C.; Azzabi, M.; Jutand, A. *J. Organomet. Chem.* **1989**, *363*, C41.

(23) Coulson, D. R. *J. Chem. Soc., Chem. Commun.* **1968**, 1530.

Table VII. Effect of Additives on the Observed Rate Constant and Yield of Homocoupling of Arylstannanes in the Presence of 1.5% Pd_2dba_3 in NMP at 40 °C under O_2[a]

entry	stannane	additives	10^2k_{obs} (min^{-1})[b]	HPLC conversion, % (24 h)[c]
1		none	1.1	80
2		LiCl (3 equiv)	0.40	82
3		LiCl (3 equiv); BHT (0.25 equiv)	0.23	81
4		LiCl (3 equiv); argon (3 cycles)[a]	0.35	23
5		LiCl (3 equiv); argon (6 cycles)[a]	<0.01	traces (<5)
6		LiCl (3 equiv); $AsPh_3$ (12%)	0.018	27
7		$AsPh_3$ (12%)	0.26	49
8		LiCl (3 equiv)	0.91	70

[a] Reactions were carried out under a slight positive pressure of oxygen, except for entries 4 and 5, where an argon atmosphere was established by carrying out three to six freeze-thaw cycles. [b] Initial rate determined by HPLC. In all cases when LiCl was used, first-order kinetics were observed for at least one half-life; in other cases the initial rate dropped quickly with time. [c] Yield determined after all catalyst had decomposed (no further conversion). Unreacted stannane accounts for remainder of the material balance.

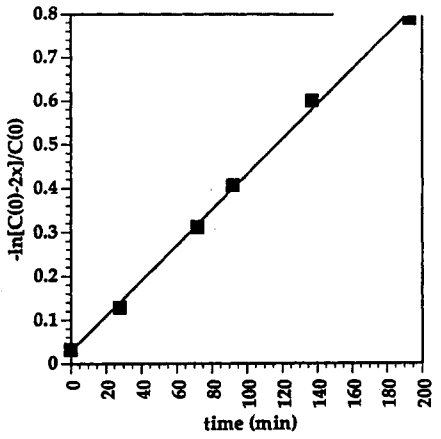
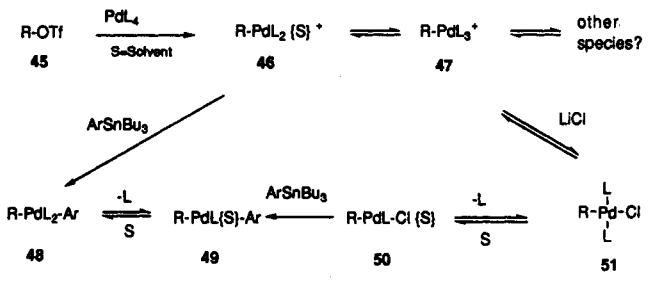


Figure 3. 3: Homocoupling of [*p*-(trifluoromethyl)phenyl-]tributyltin (50 mM) in the presence of Pd_2dba_3 (1.5%), LiCl (3 equiv) in NMP at −40 °C under an O_2 atmosphere. Initial rate: 4.0 ×

Scheme II



proposal,[11] that oxidative addition can be rate-limiting. The reductive elimination step is usually also regarded as a fast step.[1] The effect of softer ligands ($AsPh_3$), which lead to much faster coupling rates, is therefore interpreted as an accelerating effect on the transmetalation step.

As to the nature of the species produced by the oxidative addition in the absence of chloride, on the other hand, it is impossible to be precise at this stage. Chen[24] has isolated the oxidative addition product between aryl sulfonates and Pd(0) and has described the product as $ArPdL_2OSO_2R$, but in solution the triflate anion is unlikely to be coordinated to palladium(II),[25] and therefore, depending on the solvent, **46** or **47** (as shown by Stang[26] in the analogous Pt complexes) are likely candidate for the species observed by NMR. The experiment in NMP actually suggests that *two oxidative addition products* are formed in this case, and therefore it is likely that other species, in addition to the ones shown, are present in NMP solution. One or more of them may be catalytically active. In THF, on the other hand, the sluggishness of the oxidative addition of Pd(0) to aryl triflates may explain the failure of these couplings in ethereal solvents in the absence of chloride.

The NMR experiments show that oxidative addition is faster with vinyl triflates than with their aryl counterparts. This may be due to the formation of an olefinic–Pd(0) complex on the pathway to insertion, as proposed by Stang for the Pt(0) analog.[26] The formation of such a complex presumably lowers the barrier for insertion in the C–O bond. In the presence of chloride, the only species detected is identified as **51**.

Both from the kinetic experiments and from the Hammett studies, it is evident that *at least two mechanistically distinct pathways exist for the transmetalation reaction.* It appears that only in highly polar solvents such as NMP can the coupling take place without added chloride. The Hammett study shown in Figure 1 shows that in the transition state a substantial amount of positive charge is born by the aryl ring, i.e. carbon–palladium bond-making precedes carbon–tin bond-breaking. A second mechanism is obviously available to the stannane when LiCl is present. Such a mechanism involves, as clearly shown by the kinetic influence of free ligand, ligand dissociation from **51** to yield intermediate **50**, a formally neutral species, which undergoes transmetalation *via* a transition state that apparently places a partial negative charge on the benzene ring, *i.e.* in this case it is carbon–tin bond breaking that predominates over carbon–palladium bond-making. The Hammett plot in Figure 2 is consistent with this picture and demonstrates that the overall coupling is accelerated both by electron-withdrawing and -releasing substituents on the aryl ring of the stannane. A reasonable interpretation of this phenomenon is in terms of two competing mechanisms having opposite electronic requirements,[27] as shown in Scheme II. We note that a related competition study by Stille[28] employing acyl chlorides and benzylic stannanes yielded a slightly positive ρ, in clear contrast with our study, showing that the transmetalation in the Stille reaction is actually a complex family of reactions, in which electronic effects can substantially vary depending on the experimental conditions.

(24) Chen, Q. Y.; He, Y. B. *Chin. J. Chem.* **1990**, *5*, 451.
(25) Lawrance, G. A. *Chem. Rev.* **1986**, *86*, 17.
(26) Stang, P. J.; Kowalski, M. H.; Schiavelli, M. D.; Longford, D. *J. Am. Chem. Soc.* **1989**, *111*, 3347.
(27) Schreck, J. O. *J. Chem. Ed.* **1971**, *48*, 103.
(28) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129.

Two competing pathways were also shown in the transmetalation involving olefinic stannanes,[15] where a π complex between Pd(II) and the stannane was proposed as an intermediate. Although an η^2 aryltin–Pd(II) complex appears possible,[29] the similarity of the ligand effects observed in the coupling af aryltins and tetrabutyltin (Tables IV and V) suggests a similar pathway for the two couplings, i.e. no prior complexation with the stannane appears necessary to justify our results.

Two roles for added chloride in the coupling of triflates appear reasonable: first, stabilization of the oxidative addition product, *i.e.* **51** (in the absence of chloride intermediates **46** and/or **47** may be too unstable to complete a catalytic cycle). Second, nucleophilic assistance at departing tin may be needed for successful transmetalation. This proposal appears strengthened by the recent work of Vedejs[16] and Brown,[17] who have shown that potential intramolecular coordination of the tin atom speeds up the transmetalation.

The data shown in Table VI illustrates that potentially coordinating groups on the arylstannane do not accelerate the transfer of alkyl groups, but merely slow down, presumably by steric interaction, the aryl transfer process. Therefore, at least under our conditions, the effect described by Brown is not operational, while we have not examined the Vedejs system. Our data suggest that intramolecular nucleophilic assistance at departing tin may not be a generally important phenomenon in the Stille reaction. One major difference between the studies under consideration may be the use of highly polar solvents in our work, while ethereal solvents were used by Brown. Substitution reactions at tin are accelerated by NMP (vs THF)[30] as NMP may serve in assisting the departing tin. We have already shown that when no chloride is used, the tin-containing product in these couplings is the Bu_3Sn-OTf/NMP adduct.[31] Further studies are needed to clarify these points.

All our data point to the coordinating ability at Pd(0) as the key role for chloride ion. Indeed, while couplings of vinyltins appear to require chloride in NMP when PPh_3 or TFP are the ligands, with $AsPh_3$ no chloride appears required (Tables I and II). Stabilization of intermediates **46** and **47** may be provided by the solvent. The better stabilizing effect of NMP vs THF is in agreement with its better donicity.[25]

The coupling of ortho-substituted aryltins (Table VI) shows that an *o*-alkyl substituent slows down the coupling rate substantially, such that butyl transfer can become competitive, although butyl transfer was observed as a side reaction in every case. The observed rates correlate well with the steric bulk of the ortho group (*e.g.* methoxy is much smaller than ethyl).[32] While the use of dioxane leads to better transfer selectivity, the coupling rate is definitely slower in this solvent, and the large proportion of homocoupling argues against the use of dioxane in these couplings. As shown by the ligand effects in the butyl transfer reaction (Table IV), although $AsPh_3$ greatly speeds up the transmetalation reaction, the selectivity of the aryl transfer (vs butyl) is not markedly affected by this ligand. The use of trimethyltin derivatives, on the other hand, should be avoided in these couplings, as substantial amounts of methyl coupling products were observed.

Finally, the homocoupling reaction needs a brief comment. This reaction may well be of synthetic value, given the simplicity of the conditions employed. In the present case it is an unwanted side reaction, and we show that it can be prevented by addition of chloride and more coordinating ligands. Mechanistically, the reaction may be initiated by oxidative addition of the very reactive "ligandless" Pd in the C–Sn bond of the aryltin, a documented reaction for Pt(0) complexes.[33] Oxidation of the putative $RPd–SnBu_3$ species involves O_2 and seems to have a radical component, as shown by the experiment with BHT; this presumably complex step may be followed by transmetalation with a second stannane moiety to yield, after reductive elimination, the observed biaryl. NMR monitoring of the reaction failed to record any intermediates in the reaction. Although we are unable to propose a detailed mechanism for the oxidation process, we have shown that oxygen does not merely oxidize a tin-containing end-product (e.g. $Bu_3Sn–SnBu_3$), but is intimately involved in the key step of the catalytic cycle.

Conclusions

Our results extend the previously observed ligand effects in the palladium coupling between electrophiles and olefinic stannanes[15] to the important class of arylstannanes. The reportedly difficult vinyl–aryl and aryl–aryl couplings can now be performed at room temperature or slightly above for unhindered stannanes even with very bulky triflates, provided soft ligands or no ligands are used. We recommend the use of triphenylarsine as the optimum ligand in these reaction, in conjunction with the convenient source of Pd(0), Pd_2dba_3. Both reagents are commercially available and easy to handle without particular precautions. Major side reactions can be the alkyl transfer reaction, especially with ortho-substituted aryltins, and the homocoupling reaction of the stannanes. The latter can be prevented by very careful degassing or, more practically, by using lithium chloride and $AsPh_3$ as a palladium ligand, in conjunction with a slight excess of the stannane.

The proposed role of intramolecular coordination at tin in the transition state, an effect recently proposed in the literature, was not confirmed by our kinetic studies. While such an effect may occur in certain situations, our data cast doubt on its generality.

Experimental Section

Reactions were carried out under argon using oven-dried (130 °C) glassware. Anhydrous dioxane and 1-methyl-2-pyrrolidinone were obtained from Aldrich and degassed prior to use. Anhydrous THF and diethyl ether were obtained by distillation from sodium/benzophenone. Nuclear magnetic resonance spectra were obtained on a Bruker WM-360 instrument. In the ^{31}P-NMR spectra, positive shifts are downfield of 85% phosphoric acid. In the ^{119}Sn-NMR spectra, positive shifts are downfield vs tetramethyltin. Mass spectra were obtained in the chemical ionization mode on a Finnigan 4500 instrument, using isobutane as the ionizing gas, and in the FAB mode on a Kratos MS50RF instrument, using *m*-nitrobenzyl alcohol as the matrix. HPLC monitoring and determination of rate constants were carried out in analogy with previous studies.[15] The vinyl triflates and the aryl triflates were prepared according to the literature.[3,4] All ligands were commercially available (Aldrich) except tri(2-

(29) See: Li, C. S.; Cheng, C. H.; Liao, F. L.; Wang, S. L. *J. Chem. Soc., Chem. Commun.* **1991**, 710 and refs therein.
(30) Harpp, D. N.; Gingras, M. *J. Am. Chem. Soc.* **1988**, *110*, 7737.
(31) Farina, V.; Baker, S. R.; Benigni, D. A.; Hauck, S. I.; Sapino, C. *J. Org. Chem.* **1990**, *55*, 5833.
(32) Taft, R. W. *J. Am. Chem. Soc.* **1952**, *74*, 3120.
(33) Butler, G.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1978**, *144*, C23.

furyl)phosphine[34] (mp 63–4 °C from benzene/hexane) and tri(2,4,6-trimethoxyphenyl)phosphine,[35] which were made by the literature procedure.

The following arylstannanes were prepared according to literature procedures: (2-methoxyphenyl)tributyltin (9),[36] [2-(hydroxymethyl)phenyl]tributyltin (55),[37] [2-[(dimethylamino)-methyl]phenyl]tributyltin (57),[38] [8-(dimethylamino)-1-naphthyl]tributyltin (58),[39] (4-methoxyphenyl)tributyltin (4),[40] [4-(trifluoromethyl)phenyl]tributyltin (2),[36] (4-chlorophenyl)tributyltin (16).[41] The other stannanes were either obtained from Aldrich or prepared by the procedures that follow.

[4-(Dimethylamino)phenyl]tributyltin (52). A solution of 4-bromo-*N*,*N*-dimethylaniline (1.446 g, 7.22 mmol) and tributyltin chloride (2.10 mL, 7.74 mmol) in anhydrous THF (10 mL) was slowly added (45 min) to a suspension of magnesium turnings (0.220 g, 9.13 mmol) in THF (5 mL). The reaction was initiated by adding a few drops of ethylene dibromide. The yellow slurry that resulted was stirred at room temperature overnight. The reaction was quenched with saturated aqueous ammonium chloride (100 mL) and thoroughly extracted with ethyl acetate. The organics were dried on sodium sulfate and filtered. Evaporation in vacuo and reverse-phase flash chromatography (C-18, acetonitrile)[42] afforded the stannane (1.450 g, 49%) as a colorless liquid in analytically pure form. This stannane was rapidly decomposed to dimethylaniline on contact with acid or silica gel: ^{1}H-NMR ($CDCl_3$) δ 7.29 (d, J = 7.8 Hz, 2H), 6.73 (d, J = 7.8 Hz, 2H), 2.92 (s, 6H); 1.52–0.84 (m, 27H). MS 411 (^{120}Sn). Anal. Calcd for $C_{20}H_{37}NSn$: C, 58.56; H, 9.09; N, 3.41. Found: C, 58.65; H, 9.12; N, 3.20.

(2-Ethylphenyl)tributyltin (53). It was prepared as above in 68% yield. It was purified by fractional distillation: colorless liquid, bp 129–33 °C/0.1 mm; ^{1}H-NMR ($CDCl_3$) δ 7.38–7.10 (m, 4H), 2.60 (q, 2H), 1.55–0.84 (m, 30H); MS 396 (^{120}Sn). Anal. Calcd for $C_{20}H_{36}Sn$: C, 60.78; H, 9.18. Found: C, 60.81; H, 8.78.

[(4-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-phenyl]tributyltin (7). *p*-Bromobenzyl alcohol (4.801 g, 0.0256 mol), imidazole (4.703 g, 0.0690 mol), and *t*-butyldimethylsilyl chloride (4.400 g, 0.0292 mol) in anhydrous NMP (40 mL) were stirred for 72 h at room temperature. Standard workup gave *p*-bromobenzyl alcohol *tert*-butyldimethylsilyl ether in very pure form (7.741 g, 100%). This bromide (1.370 g, 4.54 mmol) was dissolved in anhydrous ether (20 mL) and treated at -30 °Cwith *n*-BuLi (1.6 M in hexane, 3.50 mL, 5.60 mM). The solution was allowed to reach room temperature over 2 h and recooled to 0 °C, and then tributyltin chloride (1.25 mL, 4.54 mM) was added neat by syringe. After an overnight period at room temperature, workup (ethyl acetate/saturated aqueous ammonium chloride) gave a crude oil, which was purified by reverse phase flash chromatography (C-18, 25% dichloromethane in acetonitrile):[42] yield 1.764 g (76%) of a clear colorless liquid; ^{1}H-NMR ($CDCl_3$) δ 7.42 (br d, 2H), 7.26 (br d, 2H), 5.72 (s, 2H), 1.60–0.85 (m, 36H), 0.04 (s, 6H); MS 512 (^{120}Sn). Anal. Calcd for $C_{25}H_{48}$-OSiSn: C, 58.71; H, 9.46. Found: C, 59.09; H, 9.55.

[4-(Hydroxymethyl)phenyl]tributyltin (54). The above stannane (1.056 g, 2.06 mmol) in anhydrous THF (5 mL) was treated with acetic acid (0.5 mL) and tetrabutylammonium fluoride (1 M in THF, 4 mL) for 3 h at room temperature. Workup with ethyl acetate and saturated aqueous sodium bicarbonate gave a crude oil, which was purified by flash chromatography (silica gel, 5–10% ethyl acetate/hexane), to afford a colorless liquid (632 mg, 77%): ^{1}H-NMR ($CDCl_3$) δ 7.45 (d, J = 7.8 Hz, 2H), 7.31(d, J = 7.8 Hz, 2H), 4.66 (d, J = 6.0 Hz, 2H), 1.56–0.84 (m, 28H); MS 398 (^{120}Sn). Anal. Calcd for $C_{19}H_{34}OSn$: C, 57.46; H, 8.63. Found: C, 57.61; H, 8.50.

(2-Formylphenyl)tributyltin (56). A solution of 1,3-dimethyl-2-phenylimidazolidine (1.05 g, 6 mM) and TMEDA (2.7 mL, 18 mM) in dry diethyl ether (40 mL) was treated with *n*-butyllithium (1.6 M in hexanes, 11.2 ml, 18 mM) under an argon atmosphere. The reaction was allowed to stir for 7 h at ambient temperature then was quenched with tributyltin chloride (4.8 mL, 18 mM). After stirring 10 min, the solution was partitioned between 1 N HCl (50 mL) and ether (50 mL) and the resulting mixture was stirred for 30 min. The organic fraction was dried ($MgSO_4$) and concentrated to give a crude oil, which was purified by reverse-phase flash chromatography[42] (C-18, acetonitrile). This furnished 1.60 g (71%) of the desired product as a colorless oil: 1H-NMR ($CDCl_3$) δ 9.98 (s, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.56–7.49 (m, 2H), 1.55–0.83 (m, 27H); MS 396 (^{120}Sn). Anal. Calcd for $C_{19}H_{32}SnO$: C, 57.75; H, 8.16. Found: C, 58.12; H, 8.17.

Palladium-Catalyzed Coupling between Olefinic Triflates and Arylstannanes. 1-(4-Methoxyphenyl)-4-*tert*-butylcyclohex-1-ene (5). Triflate 1 (262.8 mg, 0.918 mmol), triphenylarsine (23 mg, 0.0734 mmol), and Pd_2dba_3 (8.3 mg, 0.0184 mmol Pd) were dissolved in anhydrous degassed NMP (5 mL), and (after the purple color was discharged (5 min)) (4-methoxyphenyl)tributyltin (430 mg, 1.083 mmol) in NMP (2 mL) was added. After 16 h at room temperature, the solution was treated with 1 M aqueous KF solution (1 mL) for 30 min, diluted with ethyl acetate, and filtered, and the filtrate was extensively washed with water. Drying, followed by evaporation, gave a crude oil, that was purified by reverse phase flash chromatography (C-18, 10% dichloromethane in acetonitrile):[42] yield 201 mg (89%) of a white solid; recrystallization gave white needles (methanol), mp 78–9 °C; ^{1}H-NMR ($CDCl_3$) δ 7.32 (d, J = 9.0 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 6.04 (m, 1H), 3.80 (s, 3H), 2.54–2.19 (m, 3H), 2.02–1.89 (m, 2H), 1.39–1.22 (m, 2H), 0.91 (s, 9H); MS 244 (M^+). Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.58; H, 9.85.

1-[4-(Trifluoromethyl)phenyl]-2,6,6-trimethylcyclohex-1-ene (14). Triflate 13 (123 mg, 0.452 mmol), lithium chloride (58 mg, 1.368 mmol), and Pd_2dba_3 (4.2 mg, 0.00904 mmol Pd) were dissolved in anhydrous degassed NMP (2 mL). After 5 min, [4-(trifluoromethyl)phenyl]tributyltin (220 mg, 0.505 mmol) in NMP (1 mL) was added, and the solution was stirred at room temperature for 15 h. Workup as above and reverse-phase flash chromatography[42] (C-18, acetonitrile) gave 14 as a colorless oil: yield 73 mg (60%); ^{1}H-NMR ($CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 2.06 (t, J = 6.3 Hz, 2H), 1.80–1.65 (m, 2H), 1.60–1.50 (m, 2H) 1.26 (s, 3H), 0.91 (s, 6H); HRMS calcd for $C_{16}H_{19}F_3$ (M^+) 268.1439, found 268.1445. Anal. Calcd for $C_{16}H_{19}F_3$: C, 71.62; H, 7.14. Found: C, 71.39; H, 7.09.

1-[4-(Trifluoromethyl)phenyl]-4-*tert*-butylcyclohex-1-ene (3). Prepared in 83% isolated yield by the same procedure used for 5. Purified by reverse phase flash chromatography[42] (30% dichloromethane in acetonitrile): white needles (methanol) mp 84–5 °C; ^{1}H-NMR ($CDCl_3$) δ 7.53 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 6.21 (m, 1H), 2.51–2.22 (m, 3H) 2.03–1.94 (m, 2H) 1.41–1.23 (m, 2H), 0.91 (s, 9H); HRMS calcd for $C_{17}H_{21}F_3$ (M^+) 282.1595, found 282.1597. Anal. Calcd for $C_{17}H_{21}F_3$: C, 72.31; H, 7.49; F, 20.19. Found: C, 72.22; H, 7.68; F, 19.79.

2-[4-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-phenyl]cyclohex-2-enone (8). Prepared in 83% yield by the same procedure used for 14. Purified by flash chromatography (silica gel, 10% ethyl acetate/hexane): white solid (cold MeOH), mp 57–8 °C; ^{1}H-NMR ($CDCl_3$) δ 7.31–7.21 (m, 4H), 7.02 (t, J = 4.3 Hz, 1H), 4.71 (s, 2H), 2.62–2.51 (m, 4H), 2.15–2.05 (m, 2H), 0.94 (s, 9H), 0.10 (s, 6H); HRMS calcd for $C_{19}H_{28}O_2Si$ 317.1937, found 317.1938. Anal. Calcd for $C_{19}H_{28}O_2Si$: C, 72.10; H, 7.92. Found: C, 72.01; H, 7.80.

2-(2-Methoxyphenyl)cyclohex-2-enone (10). Prepared in 77% yield by the method used for 14, but omitting LiCl. Purified by flash chromatography (silica gel, 25% ethyl acetate/hexane). Semisolid pale yellow mass: mp ca. 30 °C; ^{1}H-NMR ($CDCl_3$) δ 7.32–6.88 (m, 5H), 3.76 (s, 3H), 2.61–2.50 (m, 4H), 2.15–2.09 (m, 2H); HRMS calcd for $C_{13}H_{15}O_2$ (MH^+) 203.1072, found 203.1065. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.01; H, 6.69.

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Ethyl 3-(4-Methoxyphenyl)-2-butenoate (12). Prepared in 72% yield by the method used for **5**. Purified by flash chromatography (silica gel, 5% ethyl acetate/hexane). It was judged to be a 95:5 E/Z mixture by NMR. The major isomer displayed a strong NOE between the olefinic hydrogen (δ 6.09) and the two ortho aromatic hydrogens (δ 7.43): colorless liquid, bp 155–160 °C/4 mm (lit.[43] 156–8 °C/3 mm); ^{1}H-NMR ($CDCl_3$) δ 7.43 (m, 2H), 6.87 (m, 2H), 6.09 (q, J = 1.2 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 2.54 (d, J = 1.2 Hz, 3H), 1.29 (t, J = 7.2 Hz, 3H); MS 221 (MH^+), 175.

1-(4-Chlorophenyl)indene (17). Prepared in 68% isolated yield by the same procedure used for **5** with the omission of the triphenylarsine ligand. Purified by flash chromatography (silica gel, hexanes) to give the desired product as a waxy solid: mp 61–62 °C; ^{1}H-NMR ($CDCl_3$) δ 7.56–7.52 (m, 4H), 7.44–7.41 (m, 2H), 7.34–7.25 (m, 2H), 6.58 (t, 1H, J= 2.1 Hz), 3.51 (d, 2H, J = 2.1 Hz). Anal. Calcd for $C_{15}H_{11}Cl$: C, 79.62; H, 4.90. Found: C, 79.59; H, 4.97.

1,1-Diphenylethylene, (20). Prepared in 72% isolated yield by the same procedure used for **5** with the omission of the triphenylarsine ligand. Purified by flash chromatography (silica gel, hexanes) to give the desired product as a colorless oil. The ^{1}H-NMR spectrum was identical to that of a commercial sample (Aldrich).

General Procedure for the Competition Experiments. A flame-dried flask containing NMP (3.5 mL) was degassed using five vacuum/argon cycles and left under a positive argon atmosphere. To this solvent was then added Pd_2dba_3 (3.2 mg, 0.0035 mM) and then, after 2 min, triphenylarsine (8.5 mg, 0.028 mM). If the competition experiment required the presence of LiCl (44.5 mg, 1.05 mM), it was introduced at this point. To the above reaction mixture was added a solution of triflate **1** (100 mg, 0.35 mM) in NMP (0.5 mL). After 5 min a solution of phenyltributylstannane (192.7 mg, 0.52 mM) and the competing arylstannane (0.52 mM) in NMP (0.5 mL) was added. The resulting solution was allowed to stir at ambient temperature for 24 h. The reaction was then diluted with ethyl acetate (25 mL) and washed with water (4 × 10 mL). The organic fraction was dried ($MgSO_4$) and concentrated to give a a mixture of the two coupling products as a crude oil. Product ratios were determined on the crude oil using the ^{1}H-NMR signal ($CDCl_3$) for the vinylic proton, and ratios were calculated from the integration values.

Synthesis of Biaryls by Palladium-Catalyzed Coupling of Aryl Triflates with Arylstannanes. 4'-Phenylacetophenone (25). Triflate **23** (308.4 mg, 1.15 mmol), triphenylarsine (28.2 mg, 0.0920 mmol), Pd_2dba_3 (10.5 mg, 0.0230 mmol Pd), and lithium chloride (146 mg, 3.44 mmol) were placed in a dry flask and stirred in anhydrous degassed NMP (5 mL) for 10 min. Phenyltributyltin (0.450 mL, 1.38 mmol) was then added neat by syringe, and the solution was stirred at room temperature for 70 h. Addition of 1 M aqueous KF (2 mL), with stirring for 30 min, and dilution with ethyl acetate was followed by filtration. The filtrate was extensively washed with water, dried, and evaporated. Flash chromatography (silica, 10% ethyl acetate in hexane) gave **25** as a white solid (185 mg, 82%), identical (NMR, mp) to a commercial sample (Fluka).

Biaryl **29** was obtained by the above procedure, but at a reaction temperature of 80 °C. Purified by flash chromatography (silica, 5% ethyl acetate in hexane): yield 46% of a colorless oil; ^{1}H-NMR ($CDCl_3$) δ 8.00 (d, J = 7.9 Hz, 2H), 7.40 (d, J = 7.9 Hz, 2H), 7.32–7.25 (m, 4H), 2.63 (s, 3H), 2.57 (q, J = 7.1 Hz, 2H), 1.05 (t, J = 7.1 Hz, 3H); MS 225 (MH^+). Anal. Calcd for $C_{16}H_{16}O$: C, 85.75; H, 7.19. Found: C, 85.48; H, 7.02.

Biaryl **30** was obtained as above in 76% yield. Purified by flash chromatography (gradient 10–50% ethyl acetate in hexane): white crystals (hexane), mp 179–80 °C; ^{1}H-NMR ($CDCl_3$) δ 8.02 (d, J = 8.6 Hz, 2H), 7.66 (d, J = 8.6 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 4.76 (d, J = 5.7 Hz, 2H), 2.63 (s, 3H), 1.68 (t, J = 5.7 Hz, 1H); HRMS calcd for $C_{15}H_{15}O_2$ (MH^+) 227.1072, found 227.1070. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.69; H, 6.21.

Biaryl **32** was obtained as above in 50% yield. Purified by flash chromatography (gradient 10–50% ethyl acetate in hexane): white needles (hexane), mp 65–7 °C; ^{1}H-NMR ($CDCl_3$) δ 8.00 (m, 2H), 7.58–7.26 (m, 6H), 4.59 (d, J = 5.7 Hz, 2H), 2.64 (s, 3H), 1.60 (t, J = 5.7 Hz, 1H); MS (MH^+) 227. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.67; H, 6.12.

Biaryl **33** was isolated in 25% yield by the above procedure. Purified by flash chromatography (gradient 10–20% ethyl acetate in hexane): colorless oil; ^{1}H-NMR ($CDCl_3$) δ 9.95 (s, 1H), 8.06–8.01 (m, 4H), 7.65 (m, 1H), 7.53–7.41 (m, 3H), 2.65 (s, 3H); MS 225 (MH^+). Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.33; H, 5.40. Found: C, 80.07; H, 5.36.

Biaryl **34** was isolated in 88% yield by the above procedure. Purified by flash chromatography (silica, 10% ethyl acetate in hexane): white needles (MeOH), mp 105–6 °C; ^{1}H-NMR ($CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.37–7.30 (m, 2H), 7.06–6.97 (m, 2H), 3.81 (s, 3H), 2.62 (s, 3H); HRMS calcd for $C_{15}H_{14}O_2Na$ (MNa^+) 249.0892, found 249.0884. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.62; H, 6.22.

Biaryl **35** was isolated in 89% yield by the above procedure. Purified by flash chromatography (silica, 10% ethyl acetate in hexane): white solid (MeOH), mp 120–1 °C; ^{1}H-NMR ($CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 2H), 7.71–7.66 (m, 6H), 2.64 (s, 3H). Anal. Calcd for $C_{15}H_{11}F_3O$: C, 68.17; H, 4.20. Found: C, 67.43; H, 4.13. HRMS calcd for $C_{15}H_{12}F_3O$ (MH^+) 265.0840, found 265.0834.

Biaryl **36** was isolated in 92% yield by the above method. Purified by flash chromatography (silica, 10% ethyl acetate in hexane): white solid (MeOH), mp 153–4 °C (lit.[21] mp 81–2 °C); ^{1}H-NMR ($CDCl_3$) δ 7.99 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 2.62 (s, 3H); MS 227 (MH^+). Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.31; H, 6.26.

Biaryl **38** was isolated in 86% yield by the above method. Purified by flash chromatography (silica, 5% ethyl acetate in hexane): white solid, mp 105–7 °C (lit.[44] mp 108 °C); ^{1}H-NMR ($CDCl_3$) δ 7.50–7.42 (m, 4H), 7.20 (d, J = 8.2 Hz, 2H), 6.95 (d, J = 8.2 Hz, 2H), 3.83 (s, 3H), 2.37 (s, 3H); MS 199 (MH^+). Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.62; H, 7.12.

Biaryl **40** was isolated in 78% yield by the above method. Purified by flash chromatography (silica gel, 2–4% ethyl acetate in hexane) as a colorless oil. NMR slightly deviates from literature values:[45] ^{1}H-NMR ($CDCl_3$) δ 7.25–7.20 (m, 6H), 6.93 (d, 2H), 3.84 (s, 3H), 2.26 (s, 3H); HRMS calcd for $C_{14}H_{15}O$ (MH^+) 199.1123, found 199.1121. Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.85; H, 6.93.

Homocoupling of Aryltins. 4,4'-(Bis(trifluoromethyl)biphenyl (41). [4-(Trifluoromethyl)phenyl]tributyltin (117.3 mg, 0.269 mmol) in dry *non-degassed* NMP (5 mL) was treated with Pd_2dba_3 (3.7 mg, 0.0081 mmol Pd) at room temperature for 48 h. Addition of 1 M aqueous KF with stirring for 30 min, dilution (EtOAc), and filtration were followed by evaporation of the filtrate and purification by flash chromatography (silica gel, hexane) to furnish 27 mg (69%) of **41** as a white solid: mp (MeOH) 90–2 °C (lit.[46] 91–2 °C); MS 291 (MH^+).

4,4'-Dimethoxybiphenyl was obtained similarly in 59% isolated yield and was identical (NMR, mp) to a commercial sample (Aldrich).

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