Organometallic Catalysis

In Situ Generation of ArCu from CuF₂ Makes Coupling of Bulky Aryl Silanes Feasible and Highly Efficient

Juan delPozo, Juan A. Casares,* and Pablo Espinet*^[a]

Abstract: A bimetallic system of Pd/CuF₂, catalytic in Pd and stoichiometric in Cu, is very efficient and selective for the coupling of fairly hindered aryl silanes with aryl, anisyl, phenylaldehyde, *p*-cyanophenyl, *p*-nitrophenyl, or pyridyl iodides of conventional size. The reaction involves the activation of the silane by Cu^{II}, followed by disproportionation and transmetalation from the Cu^I(aryl) to Pd^{II}, upon which coupling takes place. Cu^{III} formed during disproportionation is reduced to Cu^I(aryl) by excess aryl silane, so that the CuF₂

Introduction

Compounds containing bulky aryls are interesting targets because they are found as components of many natural products.^[1] They find use in medicinal chemistry because they improve the lipophilicity and metabolic stability of drugs.^[2] Heterocoupling of bulky aryls can be achieved by using lithium,^[3] magnesium,^[4] or zinc derivatives,^[5] but these strongly basic reagents are less compatible with many functional groups, which severely narrows their scope of application. Suzuki-Miyaura reactions have been occasionally used,^[6] but voluminous boronic acids are very prone to protodeboronation, their manipulation is delicate,^[6,7] and Suzuki-Miyaura reactions involving transmetalation of bulky groups are extremely challenging: fine-tuning of the reaction and optimization for every substrate is usually needed. As a matter of fact, all reported examples rely on the use of bulky and electron-rich ligands, which can be expensive or are not readily available. Simpler efficient methodologies are still lacking.^[8] Moreover, recent reports on the mutagenic activity of boronic acids and esters might make them less attractive for industry.^[9]

The Hiyama reaction is a very interesting cross-coupling process because of the stability of the reagents, the high compatibility with functional groups, and the nontoxicity of the byproducts.^[10] Although the process can now be used for the synthesis of complicated molecules,^[11] it is much less popular than homologous Suzuki–Miyaura or Negishi reactions.^[12] A se-

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system is fully converted into Cu¹(aryl) and used in the coupling. Moreover, no extra source of fluoride is needed. Interesting size selectivity towards coupling is found in competitive reactions of hindered aryl silanes. Easily accessible [PdCl₂(IDM)(AsPh₃)] (IDM = 1,3-dimethylimidazol-2-ylidene) is by far the best catalyst, and the isolated products are essentially free from As or Pd (<1 ppm). The mechanistic aspects of the process have been experimentally examined and discussed.

rious limitation is that it is inefficient at coping with bulky groups. To the best of our knowledge, there are very few Hiyama coupling examples that deal with any hindered silanes or arylalkoxysilanes,^[13] and there is no precedent of using *ortho*-disubstituted aryl silanes. This lesser reactivity of silanes with bulky substituents is also observed in other processes, and is deemed to be due to steric hindrance.^[14] It was our purpose herein to find an efficient methodology to circumvent this problem and open up the Hiyama procedure to bulky aryl-silane derivatives.

Results and Discussion

Synthetic studies

Recently, we managed to achieve coupling of bulky and common aryls through the Stille reaction, by using gold(I) as a transmetalation cocatalyst. The use of linear gold complexes as "aryl carriers" in this bimetallic catalysis^[15] leads to a sequential Sn/Au/Pd bulky-aryl double transmetalation, in which either of the two steps is much less congested and has a lower transmetalation barrier than that of direct Sn/Pd transmetalation.^[16,17] In this research we found that, for the facilitation of transmetalation to Pd^{II} (Sn/Pd or Au/Pd), it was important that Pd should contain an ancillary ligand that was easy to displace; at the same time, to stabilize the Pd⁰ intermediate, good coordinating soft ligands should be available to coordinate to Pd. This led us to discover the excellent performance of [PdCl₂(IDM)(AsPh₃)] (IDM = 1,3-dimethylimidazol-2-ylidene), which is an asymmetric complex with one strong and one weak ligand that does not symmetrize to [PdCl₂(IDM)₂] and [PdCl₂(AsPh₃)₂] under the working conditions for that Au-cocatalyzed Stille process. Unfortunately, our attempts, at the be-

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ginning of this work, at extending this gold(I) cocatalysis to the Hiyama reaction have been unsuccessful.

In this context, copper looks a possible attractive alternative to gold.^[18] Although there is no direct parallelism of gold and copper, due to the richer variety of accessible oxidation states and coordination geometries for the latter, copper has been successfully used, for instance, as an additive for the cross-coupling of indolyls (in the form of stoichiometric Cu^l),^[19] or for the transmetalation of the alkyl group from 2-(2-hydroxyprop-2-yl)phenyl alkylsilanes (remarkably in a catalytic amount in the form of $[Cu(hfacac)_2]$; hfacac = hexafluoroacetylacetone).^[20] These reports did not address the transmetalation of bulky groups. There are also several studies of palladium-free systems in which transmetalation between organosilanes and copper takes place, always in the presence of fluoride salts.^[21-23] The palladium-free Hiyama reaction catalyzed by Cul, using CsF and P,N ligands, has been reported.^[24] However, chemical systems analogous to those mentioned above were, in our hands, inefficient for the cross-coupling of ortho-disubstituted arylsilanes.^[25] Eventually, in a methodical testing of palladium/copper systems with different copper additives and fluoride sources for the mesityl-aryl cross-coupling [Eq. (1) and Table 1], we found some interesting results. Several copper sources, under stoichiometric and substoichiometric conditions relative to the aryl halide, were tested and combined, or not, with different external fluoride sources.

Table 1. Experiments with different copper sources using [PdCl₂(AsPh₃)₂] as catalyst. Entry Cu source Cu [%] CsF Yield of p-CF₃C₆H₄Mes [%] 0 < 5 1 none ves 2 Cul 50 4 yes 3 Cu(OtBu) 100 0 no 4 CuF₂ 100 no 88 5 CuF₂·3H₂O 81 100 no Cu(OH)₂ 6 100 0 no 7 Cu(OAc)₂·H₂O 25 yes 25 8 Cu(OTf)₂ 25 25 yes 9 CuF₂ 25 17 yes

[a] Reaction conditions: $p-CF_3C_6H_4I$ (1 mol), MesSi(OEt)₃ (2 mol) in DMF at 110 °C for 24–48 h; 2 mol% [Pd] = [PdCl_2(AsPh_3)_2]; the specified amount of Cu promoter (mol% relative to $p-CF_3C_6H_4I$); 2 mol of CsF when specified. Termination of the reaction and yields were determined by integration of ¹⁹F NMR spectra. Mes = mesityl, Tf = trifluoromethanesulfonyl.



Copper(I) compounds CuI and Cu(OtBu), which we hoped would form CuMes and transmetalate Mes to Pd, gave poor results or were ineffective (Table 1, entries 2 and 3). In contrast, the reactions with stoichiometric amounts of CuF_2 proceeded in good yield (Table 1, entries 4 and 5) without added CsF. An oxygenated source of Cu^{II}, Cu(OH)₂, which is, in theory, good for the transfer, failed to work in the absence of fluoride (Table 1, entry 6). The addition of CsF activated the reaction of copper sources with labile anions (Table 1, entries 7 and 8), but could not make the process catalytic in copper. In all active conditions (Table 1, entries 4, 5, 7–9), the amount of p-CF₃C₆H₄I converted into p-CF₃C₆H₄Mes was stoichiometric relative to the amount of Cu^{II} used, or fairly close to it.

Thus, although we failed to find conditions for a process catalytic in copper (it is catalytic in Pd), a very interesting atomeconomic transformation that was stoichiometric in CuF_2 was found (Table 1, entry 4). The need for a stoichiometric amount of CuF_2 might appear to be a disadvantage, but, on the contrary, it has several advantages. As discussed below, it provides the exact amounts of Cu^IAr and fluoride needed for the reaction, which avoids the need for any other source of fluoride typically used in Hiyama couplings (e.g., CsF or (NBu₄)F). Moreover, CuF_2 is of similar cost or cheaper (per F atom) than other fluoride sources, and is easier to handle than, for instance, very hygroscopic (NBu₄)F.

Anhydrous CuF₂ is a moderately hygroscopic white solid that leads to the green complex CuF₂·3H₂O when hydrated. The latter as a copper additive (Table 1, entry 5) also gave an excellent cross-coupling yield; this shows that the reaction is fairly compatible with water, although it produced about 10% of the homocoupled biphenyl F₃CC₆H₄C₆H₄CF₃ (a byproduct not easy to separate) and a larger amount of MesH through the hydrolysis of the silane. In contrast, under optimized conditions with anhydrous CuF₂, the cross-coupling product F₃CC₆H₄Mes could be easily purified by extraction with diethyl ether and filtration through a short pad of silica gel.^[25]

Other palladium precatalysts were checked (Table 2) in model reaction 1, with CuF_2 as a promoter, to optimize the reaction. The formation of $F_3CC_6H_4C_6H_4CF_3$ was eliminated (Table 2, entry 5) or highly diminished (Table 2, entry 8) with the most efficient catalysts.

A blank experiment without Pd catalyst confirmed that CuF_2 alone did not activate the cross-coupling process. Remarkably, for catalysts bearing bulky ligands (Table 2, entries 1 and 2), which were very efficient in other instances, almost no reaction

	Pd precatalyst	Yield R ¹ –R ² [%]	Other R ² R ² /R ² H [%]		
1	$[Pd(OAc)_2] + 2 equiv Xphos (1)$	12	66/0		
2	[PdCl ₂ (IPr)(3-Clpy)] (2)	< 5	70/0		
3	$[PdCl_2(AsPh_3)_2]$ (3)	87	5/7		
4	$[PdCl_2(dppf)]$ (4)	88	5/5		
5	[PdCl ₂ (IDM)(AsPh ₃)] (5)	>98	0/0		
6	[PdCl ₂ (IDM)(3-Clpy)] (6)	87	10/0		
7	$[{PdCl(\mu-Cl)(IDM)}_2]$ (7)	81	9/0 ^[b]		
8	[PdCl ₂ (PPh ₃) ₂] (8)	96	2/0		
[a] Reaction conditions: [Pd] (2 mol%), CuF ₂ (1 mol), p -CF ₃ C ₆ H ₄ I (1 mol), MesSi(OEt) ₃ (2 mol) in DMF at 110 °C for 24–48 h. R ¹ = Mes; R ² = p -CF ₃ C ₆ H ₄ . [b] 10% unreacted ArI and some black Pd are observed. Termination of					

[b] 10% unreacted Arl and some black Pd are observed. Termination of the reaction and yields were determined by integration of ¹⁹F NMR spectra. 3-Clpy=3-chloropyridine, dppf=1,1'-bis(diphenylphosphino)ferrocene.

Chem. Eur. J. 2016, 22, 4274 – 4284



was observed, whereas other palladium precatalysts were very efficient for the cross-coupling process (Table 2, entries 3–8).^[26] Unsurprisingly, from our previous experience with stannanes,^[16] the mixed complex **5** showed excellent performance (Table 2, entry 5).

It might seem that Pd complexes with any other weak ligand instead of AsPh₃ could be used if arsine is to be avoided, but this is not quite true: the use of 3-Clpy in place of AsPh₃ (Table 2, entry 6) affords poorer results. Similarly, (μ -Cl)₂[PdCl(IDM)]₂, which probably splits in DMF to give [PdCl₂(IDM)(DMF)], gives worse results accompanied by catalyst decomposition that leaves 11% Arl unreacted (Table 2, entry 7). Thus, the ancillary weak ligand has some effect, which is discussed in the section on mechanistic considerations. For the moment, we concentrate on some steric effects with synthetic consequences that are clear from the very direct comparison between the excellent performance of [PdCl₂(IDM)(AsPh₃)] (5) and the fairly good performance of [PdCl₂(IDM)(3-Clpy)] (6) against the poor results of the electronically related PEPPSI catalyst [PdCl₂(IPr)(3-Clpy)] (2). The three complexes have an easy leaving ligand and an imidazol-2-ylidene carbene that remains strongly coordinated to palladium along the process, but the steric requirements of the two carbenes, IDM and IPr, are very different (Figure 1). The commonly



Figure 1. Carbene ligands in entries 5 and 6 (left) and 2 (right) of Table 2.

accepted understanding of reductive elimination suggests that eventually cross-coupling should take place via a palladium [PdMes(C₆H₄CF₃)(carbene)] intermediate. The results in Table 2 show that, in our reaction involving a poor Cu¹ nucleophile,^[27] the formation of this tri-coordinate intermediate and the subsequent transition state is critically dependent on the steric factors of all coordinated groups:^[28] a smaller ancillary carbene ligand, IDM, is more compatible with the participation of the bulky aryl Mes group than a bulkier carbene ligand, *i*Pr–carbene (Table 2, entries 5 and 6 versus 2). The same problem must affect the bulky ^tBuXphos ligand (Table 2, entry 1) more than PPh₃ (Table 2, entry 8). The better or worse steric compatibility of coupling groups and ligands of diverse sizes dominates the transmetalation rate and the feasibility of the subsequent coupling step.

The requirement of steric compatibility is also clearly seen in the following stoichiometric syntheses reported in the literature: the stoichiometric reaction of PhSi(OEt)₃ with the isolated complex [Pd(*p*-CNC₆H₄)F(PPh₃)₂], has been reported to yield easily *p*-CNC₆H₄Ph and FSi(OEt)₃,^[29] by direct exchange of Ph for F. In contrast, all our attempts to react bulkier MesSi(OEt)₃ with the isolated complex [Pd(*p*-CF₃C₆H₄)F(PPh₃)₂] failed (see the Experimental Section).

In our initial tests of possible catalysts, we did not consider the common catalyst $[PdCl_2(PPh_3)_2]$, misled by our previous ex-

periences showing that 1) in the gold cocatalyzed Stille reaction of bulky groups, $[PdCl_2(IDM)(AsPh_3)]$ behaved very well, but $[PdCl_2(PPh_3)_2]$ performed extremely slowly, as expected from the use of a strong ligand that is not easy to release during transmetalation;^[16] and 2) we are aware that PPh₃ coordinates strongly to Cu¹, whereas AsPh₃ does not.^[30] Therefore, we were concerned about possible detrimental interactions of copper and PPh₃. However, when we tried $[PdCl_2(PPh_3)_2]$ (Table 2, entry 8), we were surprised and delighted to see that it performed almost as well as $[PdCl_2(IDM)(AsPh_3)]$.

To explore the scope of the process in Equation (2), the reactivity of other differently substituted bulky arylalkoxysilanes as nucleophiles was studied, with the best catalyst, **5**, and, for some reactions, with **8**. The cross-coupling results are gathered in Table 3. The excellent performance of **5** towards bulky



[a] Reaction conditions: **5** (2 mol%); 1:1:2CuF₂/R²I/R¹Si(OEt)₃, in DMF at 110°C for 24–48 h. [b] Byproducts for the reaction in entries 1a and 2 [c] Yield (% from R²I) determined by ¹⁹F NMR spectroscopy. [d] Catalyst **8** was used instead of **5**. [e] 1 mol of CuF₂ was substituted for 2 mol of CsF. [f] Yield determined by GC-MS with biphenyl as an internal standard. [g] R²Br was used instead of R²I. [h] Yield of isolated product.



groups was found to be quite general, whereas **8** turned out to be somewhat less or much less efficient in other couplings (see entries 2, 3, 6, and 11 in Table 3). Catalyst **5** is extremely efficient and quite general, as discussed below. It might appear that its composition (two different ligands, one of them AsPh₃) corresponds to a highly contaminant and not easily accessible catalyst, but it is very easy to make in two steps from simple precursors,^[16b] and the isolated cross-coupling reaction products analyzed by inductively coupled plasma mass spectrometry (ICP-MS) show that the palladium or arsenic concentrations in the product are <1 μ g g⁻¹ (see the Supporting Information for details).

$$R^{1}Si(OEt)_{3}+R^{2}I \xrightarrow{CuF_{2}} R^{1}-R^{2}$$

$$(2)$$

As shown in Table 3, the reactions with **5** as a catalyst afford excellent yields for the coupling of mesityl and naphthyl derivatives (entries 3–5), which do not work under normal Hiyama protocols. The good result obtained for 2,4,6-triisopropyltris(ethoxy)silane (Table 3, entry 6) is noteworthy when considering the extreme bulkiness of this substrate. Suzuki–Miyaura couplings with the much more reactive boronic counterpart usually fail for similarly bulky aryls.^[6] It is also worth noting that the procedure with CuF₂ tolerates equally well electron-withdrawing (Table 3, entries 5, 6, and 9) and -donating (Table 3, entries 7 and 8) substituents. Sensitive groups that are difficult to access otherwise, such as phenylaldehyde, pyridyl, *p*-cyanophenyl, and *p*-nitrophenyl (Table 3, entries 9–13), can be effectively coupled.

Although the yield of desired cross-coupling product R^1-R^2 is very good for the bulky arylalkoxysilanes, as found initially for MesSi(OEt)₃ (virtually quantitative yield, as determined by NMR spectroscopy; Table 3, entries 3–11), it is noticeably lower for aryls of conventional size (Table 3, entries 1 and 2). This apparently surprising behavior makes sense when examination of the products reveals (Table 3, entries 1 and 2) that this lower yield is mostly due to a loss of coupling selectivity to produce a significant percentage of R^1-R^1 and R^2-R^2 homocoupling products. In fact, the use of CsF instead of CuF₂ in Table 3, entry 1b improved the yield of PhC₆H₄CF₃. This confirms that CsF succeeds at cross-coupling arylalkoxysilanes of conventional bulk, whereas CsF fails and CuF₂ is required when the coupling involves a bulky arylalkoxysilane.

The formation of homocoupling products with arylalkoxysilanes of conventional bulk is easily explained by assuming that the bimetallic copper-mediated Hiyama process also facilitates undesired transmetalations that eventually generate homocoupling products.^[31] Thus, when the arylalkoxysilane has a conventional size, all [PdR¹R²(L)], [PdR²R²(L)], and [PdR¹R¹(L)] transition states are kinetically accessible and can generate R¹–R², R²–R², and R¹–R¹, respectively.^[32] However, when R¹ is bulky, the formation of [PdR¹R¹(L)] is made inaccessible at some point of the process (as discussed below) and the rate of formation of R^1-R^1 drops to zero. The positive consequence of this is that the reaction becomes very selective in favor of the heterocoupling product.

In principle, a fine combination of R^1 , R^2 , and L groups should allow for tuning of selectivity of the reactions controlled by the kinetic accessibility of the corresponding [PdR¹R²(L)] intermediate. For instance, a smaller ligand might allow for further improvement of the reaction in Table 3, entry 6. Similarly, competitive reactions coupling differently sized arylalkoxysilanes should show selectivity of the bulky alkoxysilane towards the less encumbered intermediate.

As a proof of principle, the two competitive reactions shown in Scheme 1 were studied on three groups with different nucleophilicities. It is worth remembering that nucleophilicity of a reagent is a rate concept that is influenced by electronic factors (a property of the nucleophile alone) and by steric factors



Scheme 1. Relative selectivity of naphthyl versus 2-Me-mesityl and naphthyl versus mesityl coupling with 5 or 8 as catalyst. Reaction conditions are given in Table 3.

(a property determined by the steric compatibility of the nucleophile and electrophile). In the absence of serious hindrance, the electronic factors dominate, but, in the case of congested transition states, steric hindrance plays an important role. For the groups involved, the order of steric hindrance on the reactive carbon atom is mesityl > Me-naphthyl > naphthyl. The order of the electronic component of nucleophilicity towards transmetalations is clearly Me-naphthyl > naphthyl, and probably mesityl \approx naphthyl.^[33] The size of the ligands on the Pd catalyst (which will eventually be the electrophile during the catalytic cycle) is PPh₃ > IDM.

For the case of 2-Me-naphthyl versus naphthyl, in the absence of steric effects, one could expect to find a ratio of A/Bof < 1. However, the ratio with catalyst **5** is 1.1; this shows that the unfavorable steric effect of the Me substituent in 2-Menaphthyl is slightly greater than its favorable electronic effect. Moreover, upon changing the catalyst to **8**, the difference in rate increases to 1.64:1; this nicely supports the hypothesis that a bulkier electrophile (the catalyst) enhances the influence of the steric component of the nucleophile. Along the same



lines, comparing two reagents with a higher steric difference (mesityl vs. naphthyl) exaggerates the steric factor and also the influence of the size of the ligand. The A/C ratio changes from 12:1 with 5 to 18:1 with 8, and provides interesting selectivity to these competitive couplings. These experiments show how much the size influences the nucleophilicity of these Si reagents (and their corresponding Cu¹ intermediates), which is a determining factor for processes in which the reaction has to proceed through critically crowded species.

The stringent reaction conditions used in the syntheses (DMF at 110 °C for 24–48 h) are responsible for some side reactions from the arylalkoxysilane. Thus, if CuF_2 and $MesSi(OEt)_3$ are heated in DMF at 110 °C for 48 h in the absence of any Pd catalyst or aryl iodide, full consumption of the silane is observed, along with the formation of Mes–H, MesOEt, and Mes–Mes (only traces). These products are likely to come from hydrolysis of a copper organometallic intermediate (in the case of Mes–H), or reductive elimination from Cu^{III} (see below) in the case of MesOEt. These side products, which are not specified in Table 3, are the reason for the need to use an excess of the arylalkoxysilane.

Up to now, we have shown that the so far inaccessible coupling of bulky silyl derivatives with the Hiyama protocols can be made accessible in bimetallic catalysis with **5** (or, occasionally **8**) and stoichiometric CuF_2 instead of other fluoride sources (different steric conditions of the reagents might require other ligand optimizations). The process is not convenient for small aryls, for which classical Hiyama conditions are much better. Now we consider some mechanistic aspects of this bimetallic process that explain the performance observed.

Mechanistic studies and considerations

With the evidence provided so far, two pathways are possible for the Hiyama coupling, depending on how the nucleophilic moiety R^1 reaches the palladium cycle (Scheme 2): *i*) directly from the Si reagent in the conventional process (which requires an ionized source of F^-); or *ii*) via CuR¹, which is formed stoichiometrically in situ in the CuF₂-mediated noncatalytic steps of the process. The conversion of CuF₂ into CuR¹ requires a change in the oxidation state of copper. Sufficiently bulky R¹ groups will have essentially zero rate in pathway *i*, and conse-



Scheme 2. Simplified picture of direct Hiyama (*i*) and Cu-mediated (*ii*) catalysis. Ligand exchanges (L/L'/DMF) are possible.

quently will require CuF_2 as a reagent to follow pathway *ii*. In this case, other fluoride sources can be spared. Pathway *ii* is slow (therefore high temperature and long times are required), but efficient for heterocoupling on palladium. In the case of conventional R¹ groups, which heterocouple well in pathway *i* by using sources of ionic fluoride, the presence of undesired homocoupling products when CuF_2 is used suggests that CuF_2 is not a good source of ionized F⁻ and it is unable to make pathway *i* efficient; this also supports that, in pathway *ii*, there is some reversibility of Cu^1/Pd^{II} transmetalation, giving rise to undesired transmetalations that are the source of R²–R² and, at least in part, R¹–R¹.^[31] From now on, we focus our attention on pathway *ii*.

The palladium-catalyzed cycle that closes the coupling process can be read in a rather conventional way,^[10] and we have already discussed above how the coupling rates depend on the size of the groups to be coupled, as well as on the coordinating strength and size of the ancillary ligands. The ancillary ligands can influence every step of this cycle. For instance, phosphines can slow down the transmetalation, compared with AsPh₃; the stability of the Pd⁰ intermediate, which is critical for the protection of the catalyst working under harsh conditions, and the barrier to oxidative addition depend also on these ligands. Consequently, it is not surprising that the nature of the ligands (also the weak ones) has a direct effect on the efficiency of the reaction.

Can we propose a reaction scheme for the noncatalytic part of the process and a plausible mode of reaction of CuF₂ that is consistent with all products and byproducts observed? Fortunately, studies available in the literature and experiments discussed below allow us to obtain a convincing picture of this noncatalytic part of the reaction. In this respect, there are reports in the literature of Cu^{II} fluorides reacting with organosilicon compounds. For instance, Lam et al. reported the use of Cu(OAc)₂ + NBu₄F to promote the coupling of amines with arylsilanes.^[22] Several other results in the literature strongly suggest that the disproportionation of Cu^{II} organometallic compounds is fast and is the usual fate of these complexes under anaerobic conditions.^[34] There are also examples that show that the reductive elimination from Cu^{III} is usually easy and fast.^[35] Recently, Nebra and Grushin studied the reaction of [CuF₂(bipy)(H₂O)]·2H₂O with CF₃SiMe₃,^[23] and concluded very convincingly that the transmetalation of CF_3 to copper was followed by disproportionation of Cu^{II}, leading to a reversible equilibrium between Cu^I+Cu^{III} and Cu^{II} species that could be observed because CF₃--CF₃ coupling is not feasible.

We have obtained further mechanistic hints of this disproportionation from experiments with CuF_2 and pentafluorophenyltris(ethoxy)silane.^[36] Thus, a suspension of CuF_2 was stirred in the absence of Pd catalyst with $(C_6F_5)Si(OEt)_3$ (3 equiv) in DMF for 24 h at RT. After this time, the ¹⁹F NMR spectrum of the reaction mixture (Figure S1 in the Supporting Information) showed signals corresponding to the Cu¹ complex $[Cu(C_6F_5)(DMF)_n]$,^[37] along with decafluorobiphenyl and C_6F_5H (originating from hydrolysis). The presence of decafluorobiphenyl suggests that two nonbulky C_6F_5 groups are preferentially transferred to Cu¹¹ (Scheme 3), which, by disproportiona-



	$2 \operatorname{Cu}^{II}F_2 + 4 (\operatorname{C}_6F_5)\operatorname{Si}(\operatorname{OEt})_3 \longrightarrow 2 \operatorname{Cu}^{II}(\operatorname{C}_6F_5)_2 + 4 \operatorname{FSi}(\operatorname{OEt})_3$
	2 $Cu^{II}(C_6F_5)_2 \longrightarrow Cu^{I}(C_6F_5) + Cu^{III}(C_6F_5)_3$
_	$Cu^{III}(C_6F_5)_3 \longrightarrow Cu^I(C_6F_5) + C_6F_5 - C_6F_5$
Sum.:	2 Cu ^{II} F ₂ + 4 (C ₆ F ₅)Si(OEt) ₃ \rightarrow 2 Cu ^I (C ₆ F ₅) + C ₆ F ₅ -C ₆ F ₅ + 4 FSi(OEt) ₃

Scheme 3. Products formed in the reactions of CuF_2 with $(C_6F_5)Si(OEt)_3$ as a model for regular-size arylalkoxysilane (the reactions are stoichiometrically adjusted; the proportions used in the experiments can differ). DMF acting as a probable ligand for some species is omitted for simplification.

tion,^[38] leads to complexes $[Cu(C_6F_5)_3(DMF)]$ and $[Cu(C_6F_5)(DMF)_n]$. The latter is the nucleophile that conveys R¹ to the Pd cycle in Scheme 2. The possible alternative product of oxidation, C₆F₅OEt, is not observed, which is consistent with easier transmetalation of two fluoroaryl groups to copper and subsequent fast coupling. $[Cu(C_6F_5)(DMF)_n]$ is additionally formed in the reduction of $[Cu(C_6F_5)_3(DMF)]$, which produces the observed homocoupling product decafluorobiphenyl, so that, in theory, all CuF₂ is stoichiometrically transformed into CuR^1 , at the expense of consuming 50% of $R^1Si(OEt)_3$ to give C₁₂F₁₀ (Scheme 3).

Before we consider the singularities in the case of bulky arylsilanes, it is interesting to comment on some other experiments (given in the Supporting Information) that support some of the group exchanges proposed in the Cu/Si reactivity schemes.

The reaction of CuF₂(bipy)-3H₂O in DMF,^[23] with excess $(C_6F_5)Si(OEt)_3$, produces quantitatively Cu(C₆F₅)(bipy) plus decafluorobiphenyl and some C₆F₅H (Figure S2 in the Supporting Information). It was also confirmed that this Cu(C₆F₅)(bipy) complex worked as an efficient nucleophile (as proposed in Scheme 2, path *ii*) in the model cross-coupling reaction shown in Equation (3).

$$\begin{array}{c} Cu(C_6F_5)(bipy) & \underline{DMF} & CuBr(bipy)(PPh_3) \\ + & + \\ Pd(C_6F_5)Br(PPh_3)_2 & Pd(C_6F_5)_2(PPh_3)(DMF) \end{array}$$
(3)

Similarly, Cu(Mes)(bipy) can be generated in situ by treating CuF₂(bipy)·3 H₂O with an excess of (Mes)Si(OEt)₃. When a preformed solution of this organometallic in DMF is transferred to a flask containing $[Pd(C_6H_4CF_3)I(PPh_3)_2]$ and heated to 110 °C for 1 h, the quantitative formation of Mes-C₆H₄CF₃ is observed [Eq. (4)]. This experiment confirms that a Cu¹ organometallic transmetalates effectively the bulky aryl to the palladium catalyst.

We could also verify that complexes of Cu^IF were easily arylated by arylalkoxysilanes, whether bulky or small, in DMF at room temperature [Eq. (5)].^[39] The corresponding $CuR^{1}(PPh_{3})_{3}$ complexes generated in situ transmetalate effectively C_6F_5 or Mes to the palladium catalysts $[Pd(C_6F_5)Br(PPh_3)_2]$ and $[Pd(C_6H_4CF_3)I(PPh_3)_2]$, respectively (Figure S3 in the Supporting Information).

CuF(PPh ₃) ₃ ·2 MeO	H DMF 🔪	CuR ¹ (PPh ₃) ₃ + FSi(OEt) ₃	(5)
3 R ¹ Si(OEt) ₃	R^1 = Mes, C_6F_5	2 R ¹ H + 2 (MeO)Si(OEt) ₃	(3)

Returning to the analysis of Scheme 3, half of the $R^1Si(OEt)_3$ reagent is consumed as the reducing agent, which means that, in practice, the amount of $R^1Si(OEt)_3$ acting as nucleophile is in only a 1:1 ratio to the electrophile and not 2:1 as apparently suggested by the reaction conditions. Because under the reaction conditions some $R^1Si(OEt)_3$ is unavoidably hydrolyzed, in practice the arylalkoxysilane can easily become the limiting reagent in the reaction, and this explains the appreciable amount of homocoupling products in entries 1 and 2 in Table 3. In fact, monitoring the reaction by ¹⁹F NMR spectroscopy reveals that these side products start to form when $R^1Si(OEt)_3$ is already scarce or has been totally consumed. Because this problem only happens when R^1 has a conventional size (see below the analysis for the case of bulky aryls), the classic Hiyama reaction should be utilized for these aryls.

It is fortunate that the CuF₂-promoted reaction has the great bonus of being suitable for MesSi(OEt)₃ and similar bulky arylalkoxysilanes. These compounds cannot be used to reduce CuF₂ through the mechanism in Scheme 3 for the simple reason that putative Cu^{III} or Cu^{III} intermediates with two Mes groups are severely hindered. In fact, GC-MS analyses of the reaction products of the reactions in entries 7–11 of Table 3 reveal, in all cases, the formation of a main byproduct, MesOEt, which suggests that at some time during the reaction coupling must take place from an intermediate containing a CuMes(OEt) moiety.^[40] As already mentioned, the elimination of aryl ethers from Cu^{IIII} is a well-known process (Chan–Lahm–Evans reaction),^[41] and this alternative for Cu^{III} reduction is proposed in Scheme 4, which shows a plausible set of equations leading to the products observed.

Clearly, the exact nature of the fluorosilane participating in each occasion is not defined (it could even change along the reaction as the F/OEt proportion changes), but the need for the disproportionation of Cu^{II} and reductive coupling from Cu^{III}

2 Cu ^{II} F ₂ + 2 MesSi(OEt) ₃ → 2 Cu ^{II} MesF + 2 FSi(OEt) ₃
2 Cu ^{ll} MesF — Cu ^{lll} MesF ₂ + Cu ^l Mes
$Cu^{III}MesF_2 + FSi(OEt)_3 \longrightarrow Cu^{III}Mes(OEt)F + F_2Si(OEt)_2$
Cu ^{III} Mes(OEt)F
$Cu^{I}F + MesSi(OEt)_{3} \longrightarrow Cu^{I}Mes + FSi(OEt)_{3}$
um.: 2 Cu ^{II} F ₂ + 3 MesSi(OEt) ₃ \longrightarrow 2 Cu ^I Mes + MesOEt + 2 FSi(OEt) ₃ + F ₂ Si(OEt) ₂

Scheme 4. Products formed in the reactions of CuF_2 with $MesSi(OEt)_3$ as a model of bulky arylalkoxysilanes (the reactions are stoichiometrically adjusted; the proportions used in the experiments can differ). DMF acting as a probable ligand for some species is omitted for simplification.

Chem.	Eur.	J.	2016.	22.	4274 – 4284	

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are solidly supported by the observation of MesOEt and the stoichiometry of the reactions, which fully transform each initial mol of Cu^{II} into 1 mol of CuMes.

Very interestingly, at variance with Scheme 3, because the reduction of Cu^{III} produces Mes–OEt instead of Mes–Mes, only 25% of initial MesSi(OEt)₃ plays the role of the reducing agent, which changes the electrophile/nucleophile stoichiometry of the reaction to 1:1.5. This lower consumption of MesSi(OEt)₃ maintains a higher concentration of it until the end of the process, despite some hydrolysis, and prevents competition from homocoupling processes.

The formation of the second molecule of CuMes also finds a different origin in Scheme 4 than that in Scheme 3, namely, the direct arylation of a CuF intermediate. This is supported by a parallel experiment in which, reacting $[CuF(PPh_3)_3]$ -2 MeOH instead of CuF₂ for the experiment defined in Table 3, entry 5, gives MesC₆H₄CF₃ in 83% yield and does not produce Mes— OEt. This suggests that Cu^IF is able to undergo direct Cu^I/Si transmetalation to give R¹Cu. It also reveals that Mes—OEt formed as a byproduct in Equation (2) and Table 3 is produced on a different oxidation state of Cu.

Conclusions

A bimetallic synthetic procedure involving Si/Cu/Pd aryl transfers has been developed to make the Hiyama reaction useful for the coupling of bulky arylalkoxysilanes. It uses CuF₂ as the only stoichiometric source of the two important reagents required for the two aryl transmetalation steps in the reaction, namely, fluoride, for the initial Si to Cu transmetalation step, and Cu^I, for transmetalation from Cu(aryl) to Pd. The quantitative reduction of Cu^{II} to Cu^I occurs through the disproportionation of Cu^{\parallel} to $Cu^{\parallel} + Cu^{\parallel}$ and subsequent reduction of Cu^{\parallel} to Cu^l. Interestingly, by using Pd catalysts that are very simple to prepare from readily available materials, the reaction affords excellent yields and has a wide scope of application. The reaction is compatible with active functional groups such as aldehydes or pyridine, which, for hindered substrates, often fail with other cross-coupling alternatives. Moreover, the reaction shows size selectivity and offers the possibility of tuning for selective size competing couplings.

Experimental Section

General methods

All reactions were carried out under N₂ or Ar. Anhydrous DMF was purchased from Alfa Aesar. Prior to its use, it was degassed by freeze–pump–thaw cycles and stored over 3 Å molecular sieves for a week. All other solvents used were dried by standard techniques.^[42] NMR spectra were recorded on a Bruker AV 400 instrument equipped with a VT-100 variable-temperature probe, or on a Varian 500-MR spectrometer. Chemical shifts are reported in ppm from tetramethylsilane (¹H), CCl₃F (¹⁹F), or 85 % H₃PO₄ (³¹P), with positive shifts downfield, at ambient probe temperature, unless otherwise stated. The temperature for the NMR probe was calibrated by using ethylene glycol (T > 300 K) and methanol (T < 300 K) as temperature standards.^[43] In the ¹⁹F and ³¹P spectra measured in non-deuterated solvents, a coaxial tube containing [D₆]acetone was used for the lock ²H signal. GC-MS analyses were performed on a Thermo-Scientific DSQ II GC/MS Fows GL instrument. Combustion CHN analyses were made on a Perkin-Elmer 2400 CHN microanalyzer. Unless specified otherwise, all compounds used were purchased from commercial sources and used without further purification. Compounds 3,^[44] 8,^[45] [PdCl₂(IDM)₂],^[46] [PdCl₂(AsPh₃)(IDM)],^[16b] PEPPSI,^[48] **4**,^[47] $trans-[Pd(C_6F_5)(Br)(PPh_3)_2],^{[49]}$ trans- $[Pd(C_{6}H_{4}CF_{3})(I)(PPh_{3})_{2}],^{[50]}$ *trans*-[Pd($C_6H_4CF_3$)(F)(PPh₃)₂],^[51] [CuF₂(bipy)]·3 H₂O (bipy = 2,2'-bipyridine),^[52] Cl-Si(OEt)₃,^[53] and 1-[2- $(diphenyl phosphino) phenyl] - \textit{N,N-} dimethyl methanamine^{[54]}$ were made by methods reported in the literature. Particularly, anhydrous CuF₂ was purchased from Alfa Aesar, Ph-Si(OEt)₃ was purchased from Aldrich, and $(\mathsf{C}_6\mathsf{F}_5)\mathsf{Si}(\mathsf{OEt})_3$ from Fluorochem. The rest of the silanes were synthesized according to the procedure described herein. LiCl used for these syntheses was dried under vacuum at 250 °C overnight.

Synthesis of bulky (aryl)triethoxysilanes

Bulky (aryl)triethoxysilanes were prepared by treating Si(OEt)₄ with the corresponding LiCl-activated organomagnesium reagent,^[55] according to the procedure published by DeShong et al., with excellent yields.^[56] Individual yields and NMR spectroscopy details are given in the Supporting Information.

Synthesis of the activated bulky aryl Grignard reagents

A three-necked flask was charged with dry LiCl (2.9 g, 0.065 mol), Mg turnings, and an I_2 crystal, and set under an N_2 atmosphere. I_2 was sublimated with a heat gun, and released from the flask under a strong current of nitrogen, with the aim of activating the magnesium turnings. Once all iodine was released, THF (10 mL) was added by means of a syringe. A solution of the corresponding Ar–Br was added dropwise to the mixture at reflux (0.065 mol in THF (50 mL)) by using an addition funnel. Once the addition was finished, the reaction was monitored by TLC until full consumption of the aryl bromide was achieved (usually 20 h).

Reaction of the Grignard reagent with Si(OEt)₄

A separate flask containing Si(OEt)₄ (0.19 mol) in THF (50 mL) was cooled to $-30\,^\circ\text{C}.$ The solution of Br–Mg–Ar-LiCl was cannulated dropwise to the flask containing Si(OEt)₄. When the addition was finished, the reaction was allowed to warm to RT and stirred for 8 h. To ensure that the reaction was complete, the mixture was heated at reflux overnight. The reaction was then quenched with a saturated solution of NH₄Cl (40 mL) and the organic layer was decanted. The aqueous layer was extracted with Et_2O (3×50 mL). All organic layers were combined, washed with brine (2×100 mL), and dried over MgSO₄. The solvent was removed under reduced pressure to obtain a yellowish oil. All (aryl)triethoxysilanes were purified by distillation under vacuum (1 mbar). The excess of (SiOEt)₄ was recovered at 90 °C, whereas the pure (aryl)triethoxysilane was obtained at about 160°C as an oil. For (2,4,6-triisopropylphenyl)triethoxysilane, a special procedure was used; see the Supporting Information.

Synthesis of the palladium complexes

[PdCl₂(IDM)(3-Clpy)] (6): This palladium complex was synthesized according to the reported synthesis of $[PdCl_2(IDM)(py)]$ (py = pyridine) by using 3-Clpy as a solvent instead of py.^[57] ¹H NMR (500 MHz, CDCl₃): δ =9.05 (dd, J=2.4, 0.6 Hz, 1 H), 8.95 (dd, J=5.5,

Chem. Eur. J. 2016, 22, 4274 – 4284



1.4 Hz, 1H), 7.78 (ddd, J=8.2, 2.4, 1.3 Hz, 1H), 7.33 (ddd, J=8.2, 5.5, 0.7 Hz, 1H), 6.90 (s, 2H), 4.14 ppm (s, 6H); ¹³C NMR (126 MHz, CDCl₃): δ =150.2, 149.1, 147.8, 138.1, 124.8, 123.1, 37.9 ppm; elemental analysis calcd (%) for C₁₀H₁₂Cl₃N₃Pd: C 31.04, H 3.13, N 10.86; found: C 31.28, H 3.11, N 11.02.

[{PdCl(μ-Cl)(IDM)}₂] (7): In air, a flask was charged with PdCl₂ (36 mg, 0.186 mmol) and [PdCl₂(IDM)₂] (68.4 mg, 0.186 mmol). The mixture of solids was heated at reflux for 36 h in acetone (50 mL). The solution was filtered through a pad of Celite. The crude product and pad were washed with abundant boiling acetone (3× 20 mL). The solvent was removed until 2 mL of acetone remained. At this volume, fine orange crystals started to form. Slow addition of hexane (30 mL) led to the formation of an orange solid (76 mg, 75%), which was filtered and dried under vacuum. ¹H NMR (500 MHz, CDCl₃): δ =6.89 (s, 2H), 4.19 ppm (s, 6H);¹³C NMR (126 MHz, CDCl₃): δ =141.1, 123.4, 38.1 ppm; elemental analysis calcd (%) for C₁₀H₁₆Cl₄N₄Pd₂: C 21.96, H 2.95, N 10.24; found: C 22.12, H 3.01, N 10.43.

General procedure for the palladium-catalyzed Hiyama cross-coupling reactions promoted by Cu–F complexes

The organic products obtained in the catalytic cross-coupling reactions were common products and reported elsewhere. In all cases, the NMR chemical shifts matched those reported in the literature. GC-MS analyses were used in all cases to confirm the expected molecular weight and structure. For NMR spectroscopy parameters, see the Supporting Information.

Optimization of the Cu source (Table 1)

A screw-capped Schlenk flask was charged with the appropriate amount of the Cu salt and the fluoride promoter specified in each entry of Table 1. The solids were stored under an N₂ atmosphere in a flask equipped with a magnetic stirrer bar. Under a strong current of N₂, a separately prepared stock solution (1 mL) in DMF, containing I–Ph–CF₃ (0.061 mmol), and MesSi(OEt)₃ (0.12 mmol), and **3** (0.0012 mmol), was transferred by syringe. The flask was heated at 110 °C until completion of the reaction or specified time. All reactions were monitored by ¹⁹F NMR spectroscopy of samples taken under an N₂ atmosphere. Yields of the reactions in Table 1 were determined by integration of the ¹⁹F NMR spectra. The products could also be isolated after chromatography on silica gel with hexane as the eluent.

Optimization of the Pd source (Table 2)

A screw-capped Schlenk flask was charged with the appropriate amount of Pd catalyst (0.0012 mmol; and 0.0024 mmol of XPhos for entry 1) specified in each entry of Table 2 and CuF₂ (0.061 mmol) was weighed in air as fast as possible. The solids were stored under an N₂ atmosphere in a flask equipped with a magnetic stirrer bar. Under a strong current of N₂, a separately prepared stock solution (1 mL) in DMF, containing I–Ph–CF₃ (0.061 mmol), and Mes–Si(OEt)₃ (0.12 mmol) of, was transferred by syringe. The flask was heated at 110 °C until completion of the reaction or specified time. All reactions were monitored by ¹⁹F NMR spectroscopy of samples taken under an N₂ atmosphere. Yields of reactions given in Table 2 were determined by integration of ¹⁹F NMR spectra. The products were isolated after chromatography on silica gel with hexane as the eluent.

Copper-promoted Hiyama coupling of I–Ar with various Ar-Si(OEt) $_3$ (Table 3)

Stock solutions were used to add accurate quantities of all reagents. If they were added independently, identical results were obtained. A screw-capped Schlenk flask was charged with CuF₂ (0.061 mmol) weighed in air as fast as possible. The solid was stored under an N₂ atmosphere in a flask equipped with a magnetic stirrer bar. Under a strong current of N₂, a separately prepared stock solution (1 mL) in DMF, containing I-Ar (0.061 mmol), the appropriate silane (0.12 mmol), and 5 (0.0012 mmol), was transferred by syringe. The flask was heated at 110°C until completion of the reaction or specified time. All reactions were monitored by ¹⁹F NMR spectroscopy of samples taken under an N₂ atmosphere. Termination of the reaction and yields were determined by GC-MS with Ph-Ph as an internal standard for the reaction mixture or integration of ¹⁹F NMR spectra, if possible, of samples taken under an N₂ atmosphere. Good correlation was found in all cases. The products could also be isolated after chromatography on silica gel with hexane as the eluent.

Isolation of the organic products

Determination of the isolated yields was carried out by running the reactions on twice the scale (0.122 mmol of aryl iodide). After termination of the reaction, a 2 m solution of KF (1 mL) was added and the crude reaction mixture was heated at 110 °C for 1 h. A saturated aqueous solution of NH₄Cl was added until neutralization (usually 2 mL). The aqueous phase was extracted with Et₂O (3 × 10 mL). All organic layers were combined and dried over MgSO₄. The solvent was removed under reduced pressure and the sample was dissolved in hexane and filtered through a short pad of silica gel. After evaporation of the solvent, the product obtained was usually pure. The products could also be isolated after chromatography on silica gel with hexane as the eluent.

Mechanistic studies

Reaction of copper salts and (aryl)triethoxysilanes: The corresponding Cu salt (10 mg) were added to an NMR tube. By using a Schlenk adaptor for NMR tubes, the sample was kept under an N₂ atmosphere. Under a strong current of N₂, DMF (0.5 mL), C₆F₅—Si(OEt)₃ (10 equiv), and CF₃—Ph (1 equiv) as an internal standard were added by means of a syringe. A capillary filled with $[D_6]$ acetone was added and the NMR tube was closed and wrapped with Teflon tape. The reaction was monitored by ¹⁹F NMR spectroscopy.

[(C_6F_5)Cu(DMF)] from CuF₂: CuF₂ did not react completely after 24 h at RT. Due to the presence of paramagnetic Cu^{II}, the signals in the ¹⁹F NMR spectra were broad. The *meta-* and *para-*fluorine atoms of [(C_6F_5)Cu(DMF)] overlapped with *para-* and *meta-*fluorine atoms of (C_6F_5)Si(OEt)₃ and C_6F_5 H. The *ortho* fluorine atoms were well resolved (see Figure S1 in the Supporting Information).

[(C_6F_5)Cu(bipy)] from [CuF₂(bipy)]·3H₂O: A quantitative yield, as determined by NMR spectroscopy, was obtained by integration of the *meta*-fluorine atoms with respect to the internal standard, Ph–CF₃. The signal corresponding to the *ortho*-fluorine atoms was broad due to fast relaxation (see Figure S2 in the Supporting Information). ¹⁹F NMR (470 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = -110.86$ (brs, 2F), -164.53 (t, *J*(F,F) = 19.2 Hz, 1F), -164.94 to -165.21 ppm (m, 2F).

Chem. Eur. J. 2016, 22, 4274 - 4284

[(C₆F₅)Cu(PPh₃)₃] from [CuF(PPh₃)₃·2 MeOH]: A quantitative yield, as determined by NMR spectroscopy, was obtained. ¹⁹F NMR (470 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = -110.73$ (m, 2F), -163.53 ppm (m, 3F); see Figure S3 in the Supporting Information.

Cu/Pd and Si/Cu/Pd transmetalation experiments

 $[(C_6F_5)Cu(bipy)] + trans-[Pd(C_6F_5)(Br)(PPh_3)_2]$: Following the reaction procedure described in the section on the reaction of copper salts and aryltris(ethoxy)silanes, a solution containing $[(C_6F_5)Cu(bipy)]$ was transferred by means of a syringe to a NMR tube charged with *trans*-[Pd(C_6F_5)(Br)(PPh_3)_2] (0.2 equiv) under an N₂ atmosphere. A capillary filled with $[D_6]$ acetone was added and the NMR tube was closed and wrapped with Teflon tape. The reaction was monitored by ¹⁹F NMR spectroscopy. Upon adding a solution of the copper organometallic compound to the NMR tube containing the palladium complex, *trans*-[Pd(C_6F_5)_2(PPh_3)(DMF)] formed in quantitative yield.

trans-[$Pd(C_6F_5)(Br)(PPh_3)_2$]: ¹⁹F NMR (470 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = -117.86$ (m, 2 F), -163.87 (m, 2 F), -164.38 ppm (t, J = 20.1 Hz); ³¹P NMR (202 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = 23.60$ ppm (m).

trans-[$Pd(C_6F_5)_2(PPh_3)(DMF)$]: ¹⁹F NMR (470 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = -112.61$ (m, 2F), -166.88 (m, 2F), -167.25 ppm (m, 1F); ³¹P NMR (202 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = 21.88$ ppm (q, J(P,F) = 12.1 Hz).

[(Mes)Cu(bipy)] + trans-[Pd(C₆H₄CF₃)(I)(PPh₃)₂]: [CuF₂(bipy)]·3 H₂O (7.9 mg) was added to a Schlenk flask. The sample was kept under an N₂ atmosphere. Under a strong current of N₂, DMF (0.5 mL), and Mes–Si(OEt)₃ (73 µL, 10 equiv with respect to the Cu complex) were added by means of a syringe. When the Cu salt dissolved after stirring at RT, the solution containing [(Mes)Cu(bipy)] was transferred by means of a syringe to a NMR tube charged with *trans*-[Pd(C₆H₄CF₃)(I)(PPh₃)₂] (0.2 equiv) under an N₂ atmosphere. A capillary filled with [D₆]acetone was added and the NMR tube was closed and wrapped with Teflon tape. The NMR tube was heated at 110 °C for 1 h. After this time, the reaction was monitored by '¹⁹F NMR spectroscopy, and Mes–C₆H₄–CF₃ formed in quantitative yield.

$[CuF(PPh_3)_3 \cdot 2 MeOH] + trans - [Pd(C_6F_5)(Br)(PPh_3)_2] + C_6F_5 - Si(OEt)_3:$

An NMR tube was charged with *trans*-[Pd(C₆F₅)(Br)(PPh₃)₂] (5 mg, 0.0057 mmol) and [CuF(PPh₃)₃·2 MeOH] (24 mg, 0.028 mmol) in air. By using a Schlenk adaptor for NMR tubes, the sample was kept under N₂. DMF (0.5 mL), C₆F₅–Si(OEt)₃ (15 µL, 0.057 mmol), and CF₃–Ph (1 equiv; internal standard) were added by means of syringe under a strong current of N₂. A capillary filled with [D₆]acetone was added and the NMR tube was closed and wrapped with Teflon tape. The reaction was monitored by ¹⁹F NMR spectroscopy. The reaction was completed in 20 h, yielding the quantitative formation of *trans*-[Pd(C₆F₅)₂(PPh₃)₂]. The NMR chemical shifts matched those reported in the literature.^[58] ¹⁹F NMR (470 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = -115.25$ (m, 2F), -164.05 ppm (m, 3F); ³¹P NMR (202 MHz, protic DMF, lock signal referenced to an [D₆]acetone capillary): $\delta = 18.01$ ppm (m).

 $[CuF(PPh_3)_3 \cdot 2MeOH] + trans - [Pd(C_6H_4CF_3)(I)(PPh_3)_2] + Mes$ Si(OEt),: An NMR tube was charged with trans- $[Pd(C_6H_4CF_3)(I)(PPh_3)_2]$ (5 mg, 0.0057 mmol) and [CuF(PPh₃)₃·2 MeOH] (24 mg, 0.028 m mol) in air. By using a Schlenk adaptor for NMR tubes, the sample was kept under N₂. DMF (0.5 mL), Mes–Si(OEt)₃ (16.5 μ L, 0.057 mmol) and C₆F₆ (1 equiv; internal standard) were added by means of a syringe under a strong current of N₂. A capillary filled with [D₆]acetone was added and the NMR tube was closed and wrapped with Teflon tape. The reaction was monitored by ¹⁹F NMR spectroscopy. The reaction was completed upon mixing, yielding the quantitative formation of the organic product, CF₃-Ph-Mes, and [Pd(PPh₃)₂]. The results were confirmed by GC-MS analysis of the crude reaction mixture. The ³¹P NMR spectrum shows a broad signal at $\delta = 0$ ppm, as a result of a fast exchange between [Pd(PPh₃)_n] and [XCu(PPh₃)₃]. Addition of an excess of I-Ph-CF₃ regenerated [Pd(C₆H₄CF₃)(I)(PPh₃)₂] as a sharp signal, which showed no exchange with XCu(PPh₃)₃ on the NMR spectroscopy timescale, and shifted the signal corresponding to the copper complex to $\delta = -5$ ppm.

Direct Si/Pd transmetalation of bulky groups: An NMR tube was charged with *trans*-[Pd($C_6H_4CF_3$)(F)(PPh_3)_2] (7.5 mg, 0.0094 mmol) under N₂. DMF (0.5 mL), Mes–Si(OEt)₃ (14 µL, 0.047 mmol), and C_6F_6 (1 equiv; internal standard) were added by means of a syringe under a strong current of N₂. A capillary filled with [D₆]acetone was added and the NMR tube was closed and wrapped with Teflon tape. The reaction was monitored by ¹⁹F NMR spectroscopy. After 24 h, the reaction reached equilibrium. 10% CF₃–Ph–Mes and 70% CF₃–Ph–H were quantified by integration of the ¹⁹F NMR spectrum, in comparison with the internal standard. Both products were identified by spiking the tube with authentic samples. Some unidentified signals were present in the ¹⁹F NMR spectrum, which accounted for the remaining 20% of the ¹⁹F signal.

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