Olefin Insertion Versus Cross-coupling in Trans-[Pd(Ar)X(AsPh$_3$)$_2$] Complexes (X = I, F, CF$_3$) Treated with a Phosphine-EWOlefin Ligand to Induce Ar-X Coupling

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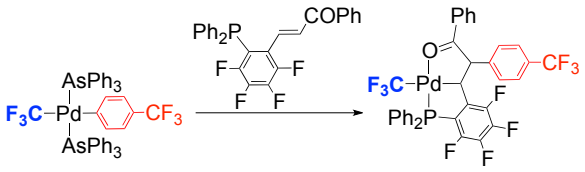
Supporting Information Placeholder

ABSTRACT: Addition of the coupling promoter PEWO ligand 1-(Ph$_2$P),2-(CH=CH-C(O)Ph)C$_6$F$_4$ (PhPEWO-F) to precursors with the displaceable AsPh$_3$ ligand *trans*-[PdXAr(AsPh$_3$)$_2$] (X = I, F, CF$_3$), fails to induce the pursued Ar-F or Ar-CF$_3$ coupling and results in formation of products of olefin insertion into the Pd-Ar bond for X = I, CF$_3$, and in Ar-Ar coupling for X = F. In the course of the processes, *trans*-[PdXAr(PhPEWO-F)(AsPh$_3$)] intermediates are observed for X = I, F, CF$_3$, with P-coordinated PhPEWO-F monodentate ligands and a dangling olefin group. For X = I, CF$_3$, subsequent insertion of the double bond into the Pd-Ar bond, and O-coordination, gives rise to complexes with a P,C,O-pincer system. The observed insertion rates suggest that the limiting step toward insertion is the trans to cis isomerization, while insertion itself is very fast. This is supported by the fast insertion observed when PhPEWO-F is added to *cis*-[Pd(CF$_3$)Ar(3-F-py)$_2$]. The insertion mechanism in PhPEWO-F resembles the initial phase of the dearomative rearrangement mechanism reported for PdArBrL (L = dialkyl biaryl phosphine).



KEYWORDS: Phosphine PEWO, Trifluoromethyl, Cross-coupling, Olefin-insertion, Pincer complex

INTRODUCTION

Ar-CF$_3$ reductive elimination from palladium(II) is the crucial event for the development of Pd-catalyzed reactions of trifluoromethylation of aryl halides.[1] It is an extremely challenging transformation that conventional tertiary phosphines that succeed in a broad variety of Pd-catalyzed coupling reactions of aryl halides cannot produce.[1] The first Ar-CF$_3$ reductive elimination from Pd, using Xantphos as ancillary ligand, was reported by Grushin more than a decade ago,[2] and subsequently studied in detail.[3] Since then only three more ligand types producing Ar-CF$_3$ reductive elimination from Pd^{II} have been reported: members of the family of PR$_2$(biaryl) phosphines developed by Buchwald (if we include vinyl-CF$_3$ coupling),[4,5] the diphosphine (F$_3$C)$_2$P(CH$_2$)$_2$P(CF$_3$)$_2$ designed by Schoenebeck,[6] and the alkyl phosphine PAd$_2$Bu (n-butyl-di-1-adamantylphosphine) used in a very recent paper by Beller.[7] In catalytic cross-coupling cycles, the reductive elimination step is typically irreversible, and is needed to pull forward the whole catalytic cycle.[8,9] Due to the high activation energy of the Ar-CF$_3$ reductive elimination step, the few reported catalytic methodologies require harsh conditions (110-140 °C) and unusually high palladium and ligand loadings (some examples require 10 mol% of Pd, and 10-20% of expensive ligands).[4a,5,7] Clearly, design of new ligands facilitating coupling of σ-aryls with CF$_3$ on Pd^{II} is highly desirable.

The use of electron-withdrawing olefin (EWO) ligands such as 1,4-benzoquinone or maleic anhydride can lower considerably the barrier to C-C reductive elimination from Pd^{II}. For instance, a combined experimental and computational study suggests that the barriers for Me-Me coupling can be up to 15-17 kcal.mol^{-1} lower for complexes containing one PMe$_3$ and one EWO group as ligands than for complexes with two conventional ligands (e.g. PMe$_3$).[10] However, there are two problems with the use of EWO ligands in palladium catalysis. First, EWOs provide extra stabilization to zerovalent [PdL$_2$(EWO)] complexes, which makes difficult the subsequent oxidative addition required for re-entrance of Pd^0 to the catalytic cycle. Second, unlike Pd^0, the less electron-rich Pd^{II} has only low affinity for EWOs. The first problem requires electronic tuning using somewhat less π-accepting olefin ligands; the second can be offset entropically, including the coordinating alkene moiety in a chelating system. Phosphine-EWO (PEWO) chelating ligands are a successful solution to combine reductive elimination and oxidative addition working in the same catalytic loop. For instance, the PEWO ligand shown in Chart 1 (PhPEWO-F), and its congeners, have been successfully used in Negishi-type Pd-catalyzed alkyl-aryl coupling reactions, using ArI as oxidant.[11,12] These couplings are problematic for conventional ligands due to the formation of Pd-alkyl intermediates that undergo fast β-hydride elimination leading to the arene plus alkene instead of the desired alkyl-aryl product. However, when the reductive elimination step is accelerated by the PEWO ligand on Pd, the β-hydride elimination side reaction is minimized or entirely suppressed.[12] The efficiency of PhPEWO-F as coupling promoter is demonstrated by its ability to carry out fast Et-Et reductive

elimination at -35 °C,[12b] while it is sluggish at room temperature with conventional ligands.[13]

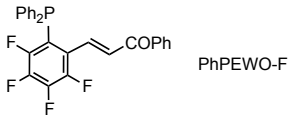


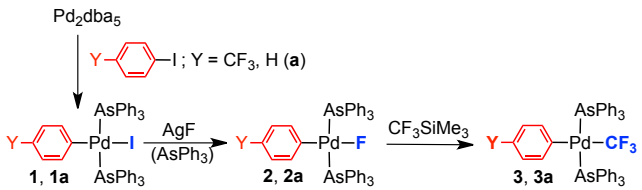
Chart 1. PhPEWO-F, the PEWO ligand used in this work

Recently we ranked the ability of a number of ligands to promote difficult couplings at Pd^{II} by measuring their activation energy $\Delta G^{\ddagger}$(Pf-Pf) to produce decafluorobiphenyl (Pf-Pf) and $Pd^{0}L$ from *cis*-[$Pd(C_6F_5)_2(THF)_2$] at room or lower temperature.[14] Among the phosphines able to couple Ar-CF_3 (or vinyl-CF_3 in the case of *t*BuXPhos),[5] the biaryl phosphine *t*BuXPhos showed a very high Pf-Pf coupling efficiency at 0 °C ($\Delta G^{\ddagger}$(Pf-Pf) = 21.8 kcal.mol^{-1}. XantPhos was much less efficient even at 25 °C ($\Delta G^{\ddagger}$(Pf-Pf) = 24.2 kcal.mol^{-1}), although it produces quantitative Ar-CF_3 coupling from [$Pd(CF_3)$Ar(Xantphos)] at 80 °C.[15] Compared to them, PhPEWO-F, showing $\Delta G^{\ddagger}$(Pf-Pf) = 22.3 kcal.mol^{-1} at 25 °C, looked promising to induce Ar-CF_3 bond formation, and we decided to check it. Herein we report the synthesis and characterization of some $Pd(CF_3)$(Ar) complexes stabilized by $AsPh_3$, and their reactivity when attempting to promote Ar-CF_3 reductive elimination upon addition of PhPEWO-F.

RESULTS AND DISCUSSION

Synthesis and characterization of [PdFAr($AsPh_3$)$_2$] and [Pd(CF_3)Ar($AsPh_3$)$_2$]. The chosen synthetic strategy was to prepare the $AsPh_3$ analogues of [PdXAr(PPh_3)$_2$] complexes previously reported by Grushin,[1-3,16] where X = F[1,16] and CF_3.[2,3] Since $AsPh_3$ is a weaker ligand for Pd^{II} than PPh_3,[17] these precursors were hoped to facilitate chelating coordination of the hemilabile PhPEWO-F ligand, via $AsPh_3$ displacement.

The iodo complexes *trans*-[PdIAr($AsPh_3$)$_2$] (Ar = 4-$CF_3C_6H_4$ (**1**), Ph (**1a**)), were prepared by oxidative addition of ArI to a solution of $Pd_2(dba)_5$ and $AsPh_3$.[18] Using the methods reported for PPh_3 complexes, the trans iodides **1** and **1a** were converted to the corresponding trans fluorides **2** and **2a** in >90% isolated yield by reaction with AgF in the presence of $AsPh_3$ under sonication. In another series of experiments, complexes **2** and **2a** were generated in solution and treated in situ with Ruppert's reagent (CF_3SiMe_3) to produce *trans*-[$Pd(CF_3)$Ar($AsPh_3$)$_2$] **3** (Ar = 4-$CF_3C_6H_4$) and **3a** (Ar = Ph), respectively. These transformations are summarized in Scheme 1.



Scheme 1. Syntheses of the aryl complexes.

The structures of **1**, **2**, **2a, 3**, and **3a**, established by single-crystal X-ray diffraction, are shown in Figure 1. Tables of bond distances and angles are given in the SI section. All five structurally characterized complexes are trans, displaying square-planar geometries typical of Pd^{II} compounds. The σ-aryl planes are roughly orthogonal to the coordination plane. Within the series [PdX(4-$CF_3C_6H_4$)($AsPh_3$)$_2$], the Pd-C_{aryl} bond lengths 2.050(4) Å (X = CF_3), 2.012(4) Å (X = I), and 1.983(2) Å (X = F) show that the structural trans influence decreases in the order CF_3 > I >> F. The strikingly strong trans influence of CF_3,[19] an electron acceptor in organic chemistry,[20] has been reviewed[21] and studied in further detail.[22]

As a general rule the trans isomers are thermodynamically preferred for Pd complexes with a carbyl group and a halide.[23] Complexes **1**, **2**, and **2a** follow this tendency. On the contrary, the cis isomer is often preferred for complexes with two high trans influence alkyl or aryl ligands, as found crystallographically in *cis*-[$Pd(CF_3)$Ar(3-Fpy)$_2$] for the pair CF_3/Ph,[6] and for many stable *cis*-[$Pd(C_6F_5)_2L_2$][24] or *cis*-[$Pd(C_6F_3Cl_2)_2L_2$][25] complexes, or unambiguously assigned spectroscopically (IR or NMR) for many more.[26] Somewhat unexpectedly considering the high trans influences of Ar and CF_3, [$Pd(CF_3)$(Ar)($AsPh_3$)$_2$] (**3, 3a**) retain the trans structure of their precursors **1, 1a**.[27]

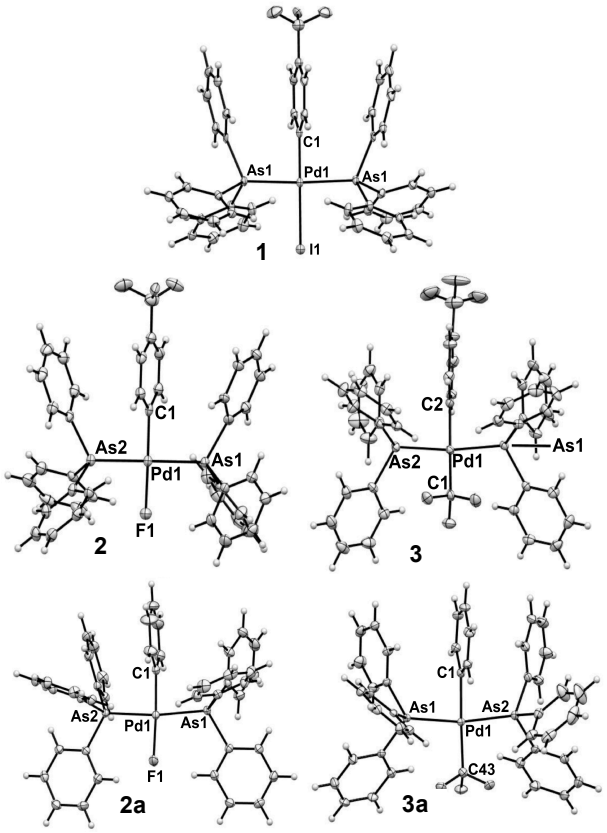


Figure 1. ORTEP drawings of [PdI(4-$CF_3C_6H_4$)($AsPh_3$)$_2$] (1), [PdF(4-$CF_3C_6H_4$)($AsPh_3$)$_2$] (2), [Pd(CF_3)(4-$CF_3C_6H_4$)($AsPh_3$)$_2$] (3), [PdFPh($AsPh_3$)$_2$] (2a) and [Pd(CF_3)Ph($AsPh_3$)$_2$] (3a), with thermal ellipsoids drawn at the 50% probability level.

The ^{19}F NMR spectra of **2** and **2a** in toluene-d_8 display broadened singlets for the F ligand at -317 and -312 ppm, respectively. These resonances are considerably upfield from those reported for [PdFPh(PPh_3)$_2$] (-274 ppm) and [PdF(4-$CF_3C_6H_4$)(PPh_3)$_2$] (-280 ppm),[16a,b] suggesting tighter bonding of the F ligand to Pd in the $AsPh_3$ complexes as compared to their phosphine congeners.[28] The single-crystal structures of **2** and **2a** corroborate this assumption: the Pd-F bond distances in **2** (2.052(1) Å) and **2a** (2.056(2) Å) are noticeably shorter

than in [PdFPh(PPh$_3$)$_2$] (2.085(3) Å).[16a] The ^{19}F NMR spectra of **3** and **3a** display sharp singlets for the CF$_3$ group at -10.65 and -11.09 ppm, respectively, somewhat upfield from that reported for [Pd(CF$_3$)Ph(PPh$_3$)$_2$] (-16.1 ppm). Furthermore, the Pd-CF$_3$ bond in **3a** (2.093(3) Å) is also shorter than in [Pd(CF$_3$)Ph(PPh$_3$)$_2$] (2.129(2) Å).[2] These results are consistent with AsPh$_3$ being a weaker donor to Pd^{II} than PPh$_3$.[29]

The protecting presence of AsPh$_3$ in the I/F exchange reaction of **1** with AgF (Scheme 1) is necessary for a clean reaction. When this reaction was carried out in the absence of extra AsPh$_3$, the work up and crystallization gave rise not only to **2**, but also to a small amount of a new complex (**4**). The remarkable structure of **4**, established by X-ray analysis (Figure 2), features a tetrahedral O-bridging connection of four cis-PdAr(AsPh$_3$) units that, in turn, are pairwise bridged by two fluorine atoms. While μ^4-O bridges are well known for harder metals,[30] they are rarely observed in complexes of softer late transition metals. Just a few Pd^{II} complexes featuring (μ^4-O) bridges have been reported.[31] The formation of **4** from **1a** and AgF was obviously due to: *(i)* facile dissociation of AsPh$_3$;[32] and *(ii)* adventitious water in the system. It is noteworthy that AgF manufactured under aqueous conditions always contains residual water that cannot be removed completely.[33]

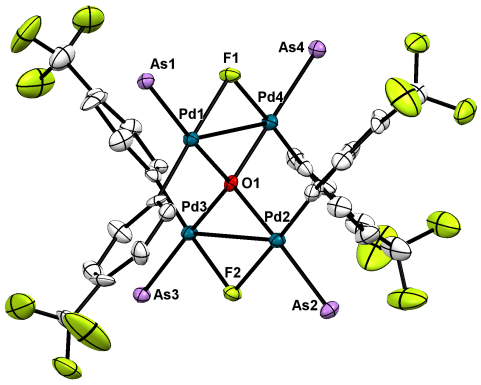
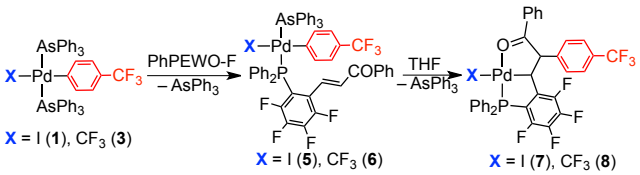


Figure 2. ORTEP drawing of (μ^4-O)[{(μ-F)Pd$_2$(4-CF$_3$C$_6$H$_4$)$_2$(AsPh$_3$)$_2$}$_2$] (4). Thermal ellipsoids drawn at the 50% probability level. Co-crystallized solvents (C$_6$H$_6$ and hexanes) and the Ph groups of AsPh$_3$ are omitted for clarity.

Thermal evolution of 2 and 3. From this point the study was carried out with Ar = *p*-CF$_3$C$_6$H$_4$, more informative in NMR. It is well established that reductive elimination reactions are favored in 3-coordinated intermediates when these can be formed by dissociation of weak ligands.[10,14] For this reason the possibility that couplings that fail on PPh$_3$ complexes might occur on AsPh$_3$ complexes cannot be discarded *a priori*. However, the thermal decompositions of **3**, after heating for several hours in toluene at 85 °C, produced complex mixtures of decomposition products that contained 4-PhC$_6$H$_4$CF$_3$, Ph$_2$, (4-CF$_3$C$_6$H$_4$)$_2$, and CF$_3$Ph (^{19}F NMR and GC-MS), indicating Pd-Ar/As-Ph exchange,[34,35,36] but did not furnish any detectable 1,4-(CF$_3$)$_2$C$_6$H$_4$. Similarly, the decomposition of the fluoro complex **2** gave rise to AsF$_2$Ar$_3$ (^{19}F NMR: -88.2 ppm; As-F), but no traces of 4-CF$_3$C$_6$H$_4$F. The products identified reveal that the thermal decomposition reactions of **2** and **3** are mechanistically similar to those of their PPh$_3$ analogues,[34,2] supporting that the As-F bond formation is probably mediated by a metalloarsorane.[37] The latter evidently emerges from nucleophilic attack of the coordinated fluoride on the As atom of an adjacent AsPh$_3$ ligand. This is probably the first time that this reactivity, well known for phosphines, is observed for arsines.

Reactions of [PdXAr(AsPh$_3$)$_2$] (X = I, CF$_3$) with PhPEWO-F. We confirmed first that some previously reported complexes with strong chelating ligands [Pd(CF$_3$)ArL$_2$] (L$_2$ = Xantphos, dppe) could be formed from **3** via AsPh$_3$ displacement, as expected. Then, the more critical coordination and reactivity of the hemilabile chelate PhPEWO-F was investigated on **1**-**3**

The reactivity of **1** or **3** with 1 equiv. of PhPEWO-F at 80 °C was studied, trying to induce Ar-CF$_3$ reductive elimination in the case of **3**. Both AsPh$_3$ molecules were eventually displaced but, to our disappointment, neither the possible complexes [PdXAr(PhPEWO-F)] (X = I, CF$_3$) with a chelating PhPEWO-F ligand, nor the coupling product 1,4-(CF$_3$)$_2$C$_6$H$_4$ (from **3**) were observed. Interestingly the reactions produced **7** and **8** (Scheme 2), from **1** and **3** respectively, via intramolecular migratory insertion of the σ-aryl into the C=C bond of PhPEWO-F. In reactions of **1** or **3** carried out at lower temperatures, intermediates **5** and **6** were observed. The reactions can be discussed using the common Scheme 2.



Scheme 2. Reactivity of 1 (X = I) or 3 (X = CF$_3$) with PhPEWO-F in THF at 80 °C. The insertion step takes place at 10 °C for 1 and at 50 °C for 3.

The final insertion products **7** (X = I) and **8** (X = CF$_3$) were isolated and fully characterized. The single-crystal X-ray diffraction structure of **7** (Figure 3) shows a P,C,O-pincer Pd^{II} complex with iodo in the fourth coordination site. The conformations of C8 and C35 show that the double bond was coordinated as the E isomer at the moment it underwent the migratory insertion (1,2-cis addition). The coordination square plane is noticeably distorted, which is particularly evident in the O-Pd-P angle (162.99(14)°). A similar structure is assigned to **8** (with CF$_3$ in place of I) based on the high similarity of the ^{1}H, ^{19}F and ^{31}P NMR spectral patterns of **7** and **8**.

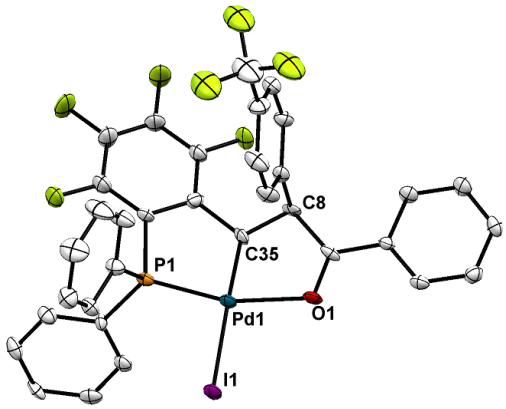


Figure 3. [PdI{Ph$_2$P(C$_6$F$_4$CHCH(C$_6$H$_4$CF$_3$)COPh)}] (7). Thermal ellipsoids drawn at the 50% probability level. The hexane molecule and H atoms are omitted for clarity.

For the iodo derivative **1** intermediate **5** (Scheme 2) was observed during its evolution to **7** monitored at -20 °C. When the reaction under monitoring was allowed to warm at room temperature, the insertion reaction on **5** took place, with formation of **7** and simultaneous release of the second arsine. The ^{1}H, ^{31}P, and ^{19}F NMR spectral information of **5** suggested a structure [PdIAr(PhPEWO-F)($AsPh_3$)], with the PhPEWO-F ligand acting as P-monodentate (uncoordinated olefine bond),[38] and the two neutral ligands arranged mutually trans. Intermediate **5**, was formed quantitatively in a 1:1 reaction at -20°C, and could be independently isolated and crystallized at low temperature. Its solid-state structure (Figure 4) confirmed the proposal made by NMR in solution. The Pd atom shows slightly distorted square planar coordination by the four coordinated ligands, and the olefin bond is not coordinated to Pd. The shortest Pd···C_{olefin} non-bonding distance is 3.321(5) Å, to the C atom C7 that ends up binding to the Pd atom after migratory insertion at the higher temperature.

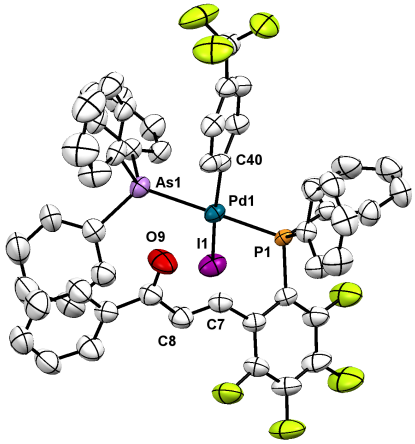
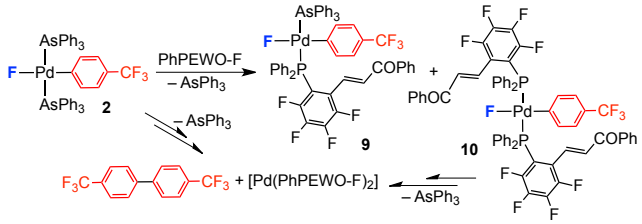


Figure 4. ORTEP drawing of [PdIAr(PhPEWO-F)($AsPh_3$)] (5). Thermal ellipsoids are drawn at the 50% probability level. $CHCl_3$ molecules and H atoms were omitted for clarity.

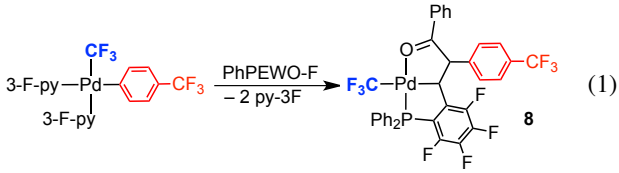
For the CF_3 derivative **3**, the overall insertion process is similar, including the formation of an intermediate **6** with monodentate PhPEWO-F, identified as [Pd(CF_3)Ar(PhPEWO-F)($AsPh_3$)] by ^{1}H and ^{19}F NMR. In this case, however, the substitution reaction in 1:1 ratio to form complex **6** in THF at room temperature was not complete and produced an equilibrium with approx. 1:0.12:0.12:1 ratio of **6**:**3**:free-PhPEWO-F:free-$AsPh_3$. The subsequent insertion from this mixture was much slower than for **5** and only occurred upon heating at 50 °C, with complete conversion to **8**.

Finally, the evolution of complex **2** (X = F) when adding PhPEWO-F was monitored in toluene at 0 ºC. The NMR spectra allowed us to observe the formation of a mixture of intermediates *trans*-[PdArF(PhPEWO-F)($AsPh_3$)] (**9**) and *trans*-[PdArF(PhPEWO-F)$_2$] (**10**), and unreacted **2** (Scheme 3). From there or from **2** an evolution occurs, faster at room temperature, with extremely complicated spectra that precluded obtaining meaningful information. Eventually, the spectra of the final mixture confirmed the absence of Ar-F, and the presence of the biaryl *p*-F_3C-C_6H_4-C_6H_4-CF_3-*p* and the Pd^0 complex [Pd(PhPEWO-F)$_2$] as the very major products. The formation of biaryl from the related [PdFPh(py)$_2$] has been reported and thoroughly studied by Grushin and Marshall.[28] It involves ligand predissociation, followed by transmetalation and Ar-Ar reductive elimination. Hence, the details of this known reactivity were not further investigated in our system.

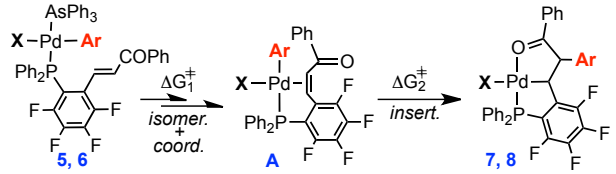


Scheme 3. Reactivity of 2 with PhPEWO-F in toluene at 0 °C.

In our previous works with PhPEWO-F insertion products were not detected, suggesting that the insertions of the PhPEWO-F double bond into Pd-C_6F_5, Pd-C_6H_4COOEt-*o* or Pd-Et bonds have higher energy barriers than the corresponding C_6F_5-C_6F_5, *o*-COOEt(C_6H_4)-Et, or Et-Et couplings.[12,14] In contrast, the results here suggest that the insertion into a Pd-Ar bond has lower activation energy than the Ar-CF_3 coupling. In fact, in the reaction of PhPEWO-F on the alternative coupling precursor *cis*-[Pd(CF_3)Ar(3-F-py)$_2$],[6] the very weak 3-F-py ligands are quickly substituted by a chelating PhPEWO-F ligand, producing instantaneous insertion at room temperature (Equation 1).



This result confirms that the double bond insertion into the Pd-Ar bond is certainly fast and has a lower barrier than the Ar-CF_3 coupling. Moreover, it also supports that the comparatively high energetic barriers found for the slow evolution from **5** to **7** or from **6** to **8** (Scheme 4) must be assigned to the trans/cis isomerization + olefin coordination process being slower than the insertion step, that is $\Delta G_1^{\ddagger} > \Delta G_2^{\ddagger}$.



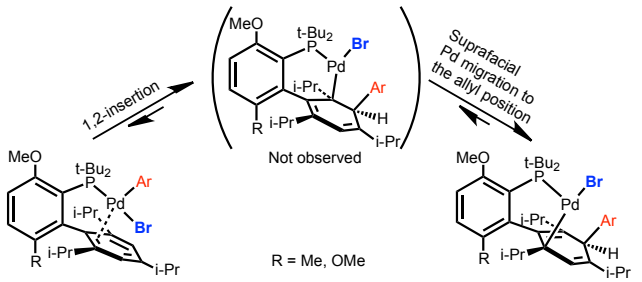
Scheme 4. Proposed pathway to insertion.

In a less complex related system, *cis*-[Pd($C_6F_3Cl_2$)I(PPh_3)$_2$] we found the concurrence of four cis/trans isomerization mechanisms, two ligand dependent and two ligand independent.[23] The most contributing one (mechanism A) involved PPh_3 associative substitution by a second [Pd($C_6F_3Cl_2$)I(PPh_3)$_2$] molecule, leading to I-bridged binuclear intermediates on which cis/trans isomerization occurred by bridge formation and splitting. With less contribution and also ligand dependent, there was a contribution with solvent (THF) acting as entering ligand (mechanism B).[39] Finally, there were ligand independent Berry pseudo-rotation or turnstile[40] isomerizations on a pentacoordinated intermediate.

The higher complexity of the molecular system in Scheme 4 ($AsPh_3$ is released as the insertion reaction proceeds, changing its concentration throughout the reaction) makes the study of the mechanisms for the slow isomerization + olefin coordination process unaffordable. Yet, it is easy to understand from our previous study that the main reason for the slowness of the reaction on **6** is that, compared to I, CF_3 is not efficient to form bridges. Hence the most effective isomerization mechanism discussed above, mechanism A, can operate for **5** but not for **6**. Complex **6** might follow the less efficient solvent assisted associative mechanism (mechanism B).

We monitored the effect of addition of $AsPh_3$ on the rate of formation of the inserted product from **5** and from **6** (Figures S1 and S2). The addition of arsine slows down the reaction more efficiently for X = CF_3 (**6**) than for X = I (**5**). This is consistent with the fact that $AsPh_3$ is more strongly coordinated in **6** than in **5**, in agreement with the expected higher stabilization for **6** of the d orbitals involved in the Pd-$AsPh_3$ bond,[41,42] and with the shorter Pd-$AsPh_3$ distance observed in **3** than in **1**. In other words, the rate dependence observed is not in contradiction with the proposal of mechanisms A and B providing, respectively, the main isomerization contribution to **5** and **6**.

Related systems. With respect to the insertion observed here, it is worth commenting that this behavior is closely related to the dearomative rearrangement reported by Buchwald for biaryl phosphine-ligated Pd^{II} complexes.[43,44,45] The final result of this rearrangement is formally a 1,4-addition of the Pd-aryl bond components to the biaryl part ligated to Pd, which starts with a 1,2-addition followed by Pd-migration (Scheme 5).



Scheme 5. Dearomative rearrangement mechanism proposed by Buchwald on PdArBrL (L = dialkyl biaryl phosphine).

In parallel to Scheme 5, the olefin insertion reported here is a 1,2-addition of the Pd-aryl bond components to the olefin, and compound **7** corresponds to the non-observed intermediate in Scheme 5. In the case of the biaryl phosphines the aromatization can be recovered by treatment with DBU, affording a new phosphine ligand that has been arylated in the lower aryl ring of the initial biaryl. In our case, all attempts to complete a Heck-type process by treating **7** with base to regenerate a double bond from the metallated ligand were unsuccessful. For instance, treatment of **7** with DBU only displaces the coordinated ketone group by N coordinated DBU.

CONCLUSIONS

The frustrated Ar-F and Ar-CF_3 couplings using PhPEWO-F as ligand, and the analysis of the insertion reaction observed for the iodo and CF_3 complexes, gives us a less simple view of the coupling *vs*. insertion problem than it looked at first sight. In fact the opportunity for coupling or insertion from the trans starting complex is not controlled only by the corresponding activation energies of these two processes, but additionally by an often neglected step, isomerization. Certainly a too high coupling barrier will preclude coupling in any circumstance, and a low insertion barrier will facilitate easy insertion, but the isomerization rate will be decisive for the persistence of other intermediates. Thus, in the cases studied here the trans to cis isomerization barrier is rate determining for insertion.

The combination of a CF_3 group (which contributes to produce high coupling barriers), with an Ar group (which undergoes easy olefin insertion) is unfortunate and certainly discards PhPEWO-F for this specific kind of coupling. Considering the demonstrated coupling potential of RPEWO-F ligands, designing other RPEWO-F ligands that could hinder insertion can be interesting. But the scope of utilization of RPEWO-F ligands in catalysis should not be confined to promote couplings as challenging as attempted here. Many other fairly difficult couplings take place without traces of insertion,[12,14] and any coupling will occur at much lower temperatures with RPEWO-F than with common ligands. Therefore, the most general, useful, and already available application of this kind of ligands can be carrying out less selective coupling processes at lower temperatures, in order to improve their selectivity. Research in this direction is in progress.

SUPPORTING INFORMATION

The Supporting Information (general methods, synthesis of new compounds, determination of rate constants, additional experiments, X-ray crystallographic data, references; 39 pages; PDF) is available free of charge on the ACS Publications website.

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REFERENCES

1 (a) Grushin, V. V. *Acc. Chem. Res.* **2010**, *43*, 160. (b) Grushin, V. V. *Chem. Eur. J.* **2002**, *8*, 1006.

2 Grushin, V. V.; Marshall, W. J. *J. Am. Chem. Soc.* **2006**, *128*, 12644.

3 Bakhmutov, V. I.; Bozoglian, F.; Gómez, K.; González, G.; Grushin, V. V.; Macgregor, S. A.; Martin, E.; Miloserdov, F. M.; Novikov, M. A.; Panetier, J. A.; Romashov, L. V. *Organometallics* **2012**, *31*, 1315.

4 (a) Cho, E.; Senecal, T.; Kinzel, T.; Zhang, Y.; Watson, D.; Buchwald S. L. *Science* **2010**, *328*, 1679. (b) See also: Maleckis A.; Sanford. M. S. *Organometallics*, **2014**, *33*, 2653.

5 Cho, E. J.; Buchwald, S. L. *Org. Lett.* **2011**, *13*, 6552.

6 Nielsen, M. C.; Bonney, K. J.; Schoenebeck, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 5903.

7 Natte, K.; Jagadeesh, R. V.; He, L.; Rabeah, J.; Chen, J.; Taeschler, C.; Ellinger, S; Zaragoza, F.; Neumann, H.; Brückner, A.; Beller, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 2782.

8 Steric and electronic effects of ligands on this fundamental step have been extensively studied. See, for example: (a) Ozawa, F. Reductive Elimination. In *Fundamentals of Molecular Catalysis*; Kurosawa, H.; Yamamoto, A. Eds.; Elsevier: New York, **2003**; Vol. *3*, p. 479. (b) Birkholz, M.; Freixa, Z.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2009**, *38*, 1099. (c) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852. (d) Hartwig, J. F. *Inorg. Chem.* **2007**, *46*, 1936.

9 Pérez-Temprano, M. H.; Nova, A.; Casares, J. A.; Espinet, P. *J. Am. Chem. Soc.* **2008**, *130*, 10518.

10 Pérez-Rodríguez, M.; Braga, A. A. C.; García-Melchor, M.; Pérez-Temprano, M. H.; Casares, J. A.; Ujaque, G.; de Lera, A. R.; Álvarez, R.; Maseras, F.; Espinet, P. *J. Am. Chem. Soc.* **2009**, *131*, 3650.

11 (a) Luo, X.; Zhang, H.; Duan, H.; Liu, Q.; Zhu, L.; Zhang, T.; Lei, A. *Org. Lett.* **2007**, *9*, 4571. (b) Shi, W.; Luo, Y.; Luo X.; Chao, L.; Zhang, H.; Wang, J.; Lei, A. *J. Am. Chem. Soc.* **2008**, *130*, 14713. (c) Zhang, H.; Luo, X.; Wongkhan, K.; Duan, H.; Li, Q.; Zhu, L.; Wang, J.; Batsanov, A. S.; Howard, J. A. K.; Marder, T. B.; Lei, A. *Chem. Eur. J.* **2009**, *15*, 3823.

12 (a) Gioria, E.; Martínez-Ilarduya, J. M.; García-Cuadrado, D.; Miguel, J. A.; Genov, M.; Espinet, P. *Organometallics* **2013**, *32*, 4255. (b) Gioria, E.; Martínez-Ilarduya, J. M.; Espinet, P. *Organometallics* **2014**, *33*, 4394.

13 It is well known that coupling barriers follow the trend Csp^3-Csp^3 > C_{Ar}-C_{Ar} > Csp^2-Csp^2 with aryl-aryl > aryl-alkyl > alkyl-alkyl: Ananikov, V. P.; Musaev, D. G.; Morokuma, K. *Organometallics* **2005**, *24*, 715.

14 Gioria, E.; del Pozo, J.; Martínez-Ilarduya, J. M.; Espinet, P. *Angew. Chem. Int. Ed.* **2016**, *55*, 13276.

15 These are measurements at room temperature. However, for Ar-CF_3 coupling these ligands are tremendously efficient when used at higher temperatures (80-110 °C). For the ligand tBuBrettPhos, very inefficient in this classification, it was shown that it probably requires previous isomerization (see reference 14), which happens at higher temperatures and makes its equivalent CyBrettPhos very efficient for Ar-CF_3 coupling (see ref. 4a).

16 (a) Fraser, S. L.; Antipin, M. Yu.; Khroustalyov, V. N.; Grushin, V. V. *J. Am. Chem. Soc.* **1997**, *119*, 4769. (b) Pilon, M. C.; Grushin, V. V. *Organometallics* **1998**, *17*, 1774. (c) Marshall, W. J.; Thorn, D. L.; Grushin, V. V. *Organometallics* **1998**, *17*, 5427. (d) Roe, D. C.; Marshall, W. J.; Davidson, F.; Soper, P. D.; Grushin, V. V. *Organometallics* **2000**, *19*, 4575.

17 The large difference between PPh_3 and $AsPh_3$ in processes requiring ligand substitution from $PdArXL_2$ complexes has been quantitatively studied in the context of an analysis of the "copper effect" in the Stille reaction: Casado, A. L.; Espinet, P. *Organometallics* **2003**, *22*, 1305.

18 The composition $Pd_2(dba)_5$ was established on the basis of analytical data. The reaction works equally well with $Pd_2(dba)_3$. See: Ushkov, A. V.; Grushin, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 10999.

19 (a) Appleton, T. G.; Chisholm, M. H.; Clark, H. C.; Manzer, L. E. *Inorg. Chem.* **1972**, *11*, 1786. (b) Bennett, M. A.; Chee, H.-K.; Robertson, G. B. *Inorg. Chem.* **1979**, *18*, 1061. (d) Bennett, M. A.; Chee, H.-K.; Jeffery, J. C.; Robertson, G. B. *Inorg. Chem.* **1979**, *18*, 1071. (e) Hughes, R. P.; Overby, J. S.; Williamson, A.; Lam, K.-C.; Concolino, T. E.; Rheingold, A. L. *Organometallics* **2000**, *19*, 5190. (f) Hughes, R. P.; Meyer, M. A.; Tawa, M. D.; Ward, A. J.; Williamson, A.; Rheingold, A. L.; Zakharov, L. N. *Inorg. Chem.* **2004**, *43*, 747. (g) Grushin, V. V.; Marshall, W. J. *J. Am. Chem. Soc.* **2006**, *128*, 4632. (h) Goodman, J.; Grushin, V. V.; Larichev, R. B.; Macgregor, S. A.; Marshall, W. J.; Roe, D. C. *J. Am. Chem. Soc.* **2009**, *131*, 4236. (i) Goodman, J.; Grushin, V. V.; Larichev, R. B.; Macgregor, S. A.; Marshall, W. J.; Roe, D. C. *J. Am. Chem. Soc.* **2010**, *132*, 12013.

20 Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

21 Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475.

22 Algarra, A. G.; Grushin, V. V.; Macgregor, S. A. *Organometallics* **2012**, *31*, 1467.

23 The *cis* to *trans* isomerization mechanisms have been studied: Casado, A. L.; Espinet, P. *Organometallics* **1998**, *17*, 954.

24 (a) Ara, I.; Forniés, J.; Martín, A.; Martín, L.F.; Menjón, B.; Miedes, H. *Dalton Trans.* **2010**, *39*, 7301. (b) Miki, K.; Kasai, N.; Kurosawa, H. Acta Crystallogr., Sect. C: Cryst. Struct. Commun. **1988**, 44, 1132 (c) Ruiz, J.; Cutillas, N.; Rodríguez, V.; Sampedro, J.; López, G.; Chaloner, P. A.; Hitchcock P. B. *J. Chem. Soc., Dalton Trans.* **1999**, 2939. (d) Ruiz, J.; Rodríguez, V.; Cutillas, N.; López, G.; Pérez, J.; *Organometallics* **2002**, *21*, 4912. (e) Falvello, L. R.; Forniés, J.; Navarro, R.; Sicilia, V.; Tomás, M. *J. Chem.Soc., Dalton Trans.* **1994**, 3143. (f) Ruiz, J.; Cutillas, N.; Vicente, C.; Villa, M. D.; López, G.; Lorenzo, J.; Avilés, F. X.; Moreno, V.; Bautista, D. *Inorg. Chem.* **2005**, *44*, 7365. (g) Ruiz, J.; Santana, M. D.; Lozano, A.; Vicente, C.; Garcia, G.; López, G.; Pérez, J.; Garcia L. *Eur. J. Inorg. Chem* **2005**, 3049. (h) Ohashi, M.; Doi, R.; Ogoshi S. *Chem.-Eur. J.* **2014**, 2040.

25 Salas, G.; Casares, J. A.; Espinet, P. *Dalton Trans.* **2009**, 8413.

26 (a) Usón, R.; Forniés, J.; Espinet, P.; Navarro, R.; Martínez, F.; Tomás, M. *J. Chem. Soc., Dalton Trans.* **1981**, 463. (b) Espinet, P.; Martínez-Ilarduya, J. M.; Pérez-Briso, C. *J. Organomet. Chem.* **1993**, *447*, 145. (c) Albéniz, A. C.; Casado, A. L.; Espinet, P. *Inorg. Chem.* **1999**, *38*, 2510. (d) Espinet, P.; Albéniz, A. C.; Casares, J. A.; Martínez-Ilarduya, J. M.; *Coord. Chem. Rev.*, **2008**, 252, 2180.

27 These trans complexes are probably the kinetic products of the syntheses, which do not find low energy pathways for easy isomerization. There are several X-ray structures of Pt complexes with two cis $AsPh_3$ ligands, for instance, the structure of *cis*-$[PtCl_2(AsPh_3)_2]$: Otto, S.; Johansson, M. H. *Inorg. Chim. Acta* **2002**, *329*, 135. This discards that cis bis(arsine) complexes are necessarily disfavored versus their trans isomers for steric hindrance reasons. In contrast, the iodo ligand is large enough to be decisive in favor of *trans*-$[PtI_2(AsPh_3)_2]$: Otto, S.; Roodt, A. *Acta Cryst.* **1997**, *C53*, 280. These examples suggest that the covalent radius of As (r = 1.19 Å) does not impose trans arrangement by itself as much as the covalent radius of I (r = 1.39 Å) does. Covalent radii taken from: Cordero, B.; Gómez, V.; Platero-Prats, A. E.; Revés, M.; Echeverría, J.; Cremades, E.; Barragán, F.; Álvarez, S. *Dalton Trans.* **2008**, 2832.

28 Grushin, V. V.; Marshall, W. J. *J. Am. Chem. Soc.* **2009**, *131*, 918.

29 See, for example: Grant, G. J. *Dalton Trans.* **2012**, *41*, 8745 and references cited therein.

30 (a) Cotton, F. A., Wilkinson, G. *Advanced Inorganic Chemistry. A Comprehensive Text*, 4th edition, John Wiley & Sons: New

York, 1980, p. 278. (b) Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon Press: Oxford, 1985, p. 136.

31 (a) Zhang, Y; Puddephatt, R. J.; Manojlovic-Muir, L.; Muir, K. W. *Chem. Comm.* **1996**, 2599. (b) Izarova, N. V.; Dickman, M. H.; Biboum, R. N.; Keita, B.; Nadjo, L.; Ramachandran, V.; Dalal, N. S.; Kortz, U. *Inorg. Chem.* **2009**, *48*, 7504. (c) Allscher, T.; Klüfers, P. *Chem. Eur. J.* **2012**, 18, 10571. (d) Bedford, R. B.; Bowen, J. G.; Davidson, R. B.; Haddow, M. F.; Seymour-Julen, A. E.; Sparkes, H. A.; Webster, R. L. *Angew. Chem. Int. Ed.* **2015**, *54*, 6591. (e) Frey, G. D.; Schoeller, W. W.; Herdtweck, E.; Herrmann W. A. *J. Organomet. Chem.* **2016**, *810*, 46. (f) Scullion, A.; Surman, A. J.; Xu, F.; Mathieson, J. S.; Long, D-L.; Haso, F.; Liu, T.; Cronin L. *Angew. Chem., Int. Ed.* **2014**, *53*, 10032.

32 This complication suggests that the choice of weak ligands bearing this chemistry is limited and ligands weaker than $AsPh_3$ would probably afford more extensive participation of side reactions.

33 Horn, E.; Snow, M. R. *Aust. J. Chem.* **1980**, *33*, 2369.

34 (a) Grushin, V. V. *Organometallics* **2000**, *19*, 1888; (b) Grushin, V. V.; Marshall, W. J. *Organometallics* **2007**, *26*, 4997.

35 Kwong, F. Y.; Lai, C. W.; Chan K. S. *J. Am. Chem. Soc.* **2001**, *123*, 8864.

36 Kwong, F. Y.; Lai, C. W.; Yu, M.; Tan, D.-M.; Lam, F. L.; Chan, A. S. C.; Chan K. S. *Organometallics* **2005**, *24*, 4170.

37 Goodman, J.; Macgregor, S. A. *Coord. Chem. Rev.* **2010**, *254*, 1295.

38 The chemical shifts for the olefinic protons are very informative and one of them appears at 8.36 ppm (dd, J = 16.1, 4.8 Hz) for free PhPEWO-F. Complex **5** shows a ^{1}H signal at 8.54 (dd, J = 15.6, 2.3 Hz) confirming that the double bond is uncoordinated. (See. ref. 12a and Supporting Information for full characterization of products).

39 Minniti, D. *Inorg. Chem.* **1994**, *33*, 2631.

40 Turnstile isomerization mechanism was found to operate in Pd complexes wearing a chelating ligand: Casares, J. A.; Espinet, P. *Inorg. Chem.*, **1997**, *36*, 5428.

41 This d-orbital stabilization as a function of changing a ligand (I *vs*. CF_3) is usually discussed on the basis of their electronegativity, a rather complex concept in the case of group electronegativity. In this case the electronegativity is CF_3 > I. See: Bernhardt, E.; Henkel, G.; Willner, H.; Pawelke, G.; Bürger, H. *Chem. Eur. J.* **2001**, *7*, 4696.

42 However, the electronegativity order deduced in the paper above may look in contradiction with the high trans influences observed, CF_3 > I. For an excellent study of this contradiction and the stabilization of d-orbitals by CF_3, see ref. 22.

43 Maimone, T. J.; Milner, P. J.; Kinzel, T.; Zhang, Y.; Takase, M. K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2011**, *133*, 18106.

44 Milner, P. J.; Maimone, T. J.; Su, M.; Chen, J.; Müller, P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 19922.

45 Milner, P. J.; Kinzel, T.; Zhang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2014**, *136*, 15757.