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# Stoichiometric Studies on the Carbonylative Trifluoromethylation of Aryl Pd(II) Complexes using $TMSCF_3$ as the Trifluoromethyl Source

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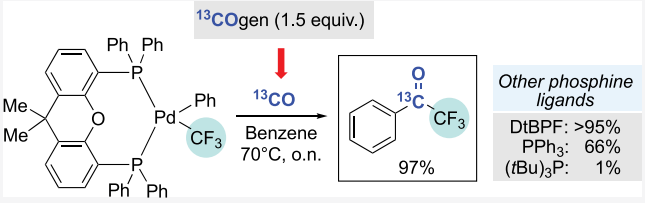
**ABSTRACT:** We have performed a series of stoichiometric studies in order to identify viable steps for a hypothetical catalytic cycle for the palladium-mediated carbonylative coupling of an aryl bromide with $TMSCF_3$. Our work revealed that benzoyl Pd(II) complexes bearing Xantphos or $t$Bu$_3$P as the phosphine ligands, which are generated from the corresponding $Pd^{II}$(Ph)Br complexes exposed to stoichiometric $^{13}CO$ from $^{13}COgen$, were unable to undergo transmetalation and reductive elimination to trifluoroacetophenone. Instead, in the presence of base and additional CO, these organometallic complexes readily underwent reductive elimination to the acid fluoride. Attempts to determine whether the acid fluoride could represent an intermediate for acetophenone production were unrewarding. Only in the presence of a boronic ester did we observe some formation of the desired product, although the efficiency of transformation was still low. Finally, we investigated the reactivity of four phosphine-ligated $Pd^{II}$(Ph)$CF_3$ complexes (Xantphos, D$t$BPF, $t$Bu$_3$P, and triphenylphosphine) with carbon monoxide. With the exception of the $t$Bu$_3$P-ligated complex, all other metal complexes led to the facile formation of trifluoroacetophenone. We also determined in the case of triphenylphosphine that CO insertion occurred into the Pd−Ar bond, as trapping of this complex with $n$-hexylamine led to the formation of $n$-hexylbenzamide.



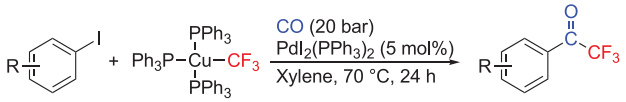



## INTRODUCTION

The development of mild and efficient methods for the introduction of fluorine has received widespread attention, as selective incorporation of fluorine-containing motifs into pharmaceutically relevant molecules can be used for the fine-tuning of chemical and biological activity.[1] Trifluoromethyl ketones represent one such motif exploited for preparing potent enzyme inhibitors but are also used as building blocks for the synthesis of fluorine-containing pharmaceuticals, trifluoromethylated heterocycles, and trifluoromethylated analogues of natural compounds.[2] Despite their high interest, the use of trifluoromethyl ketones is limited by the existing methods for their synthesis, which suffer from substrate-determined regioselectivity, low functional group tolerance, and side-product formation resulting from the reactive nucleophilic trifluoromethylating reagents applied.[3]

Over the past decade, palladium-catalyzed cross-coupling reactions of aryl halides with trifluoromethyl nucleophiles have been extensively studied as a viable approach for the introduction of a trifluoromethyl group onto (hetero)aryl ring systems. However, this transformation has proven to be highly challenging owing to the unique properties of the $CF_3$ group, which renders the reductive elimination step challenging.[4] Only a few ligands have been successfully employed in this transformation, including Xantphos,[5] BrettPhos,[4a] tri-*tert*-butylphosphine,[6] dfmpe,[7] and bis(di-*tert*-butylphosphino)-ferrocene,[8] promoting the reductive elimination by steric and/or electronic effects. To date, only one palladium-catalyzed carbonylative trifluoromethylation of aryl halides has been reported.[9] As depicted in Scheme 1, Wu and co-workers rely on the use of carbon monoxide at 20 bar pressure in combination with $(PPh_3)_3CuCF_3$ as the organometallic trifluoromethylating agent, effectively allowing for the construction of trifluoroacetophenones from aryl iodides.

**Scheme 1. Pd-Catalyzed Carbonylative Trifluoromethylation by Wu and Co-workers**




Since the palladium-catalyzed cross-coupling of aryl chlorides with $TESCF_3$ has been demonstrated by the Buchwald group,[4a] we questioned whether a related three-component carbonylative cross-coupling of aryl halides with carbon monoxide and a trifluoromethyl nucleophile could represent a convenient approach for accessing aryl trifluoromethyl ketones. Particularly, the electron-withdrawing effects

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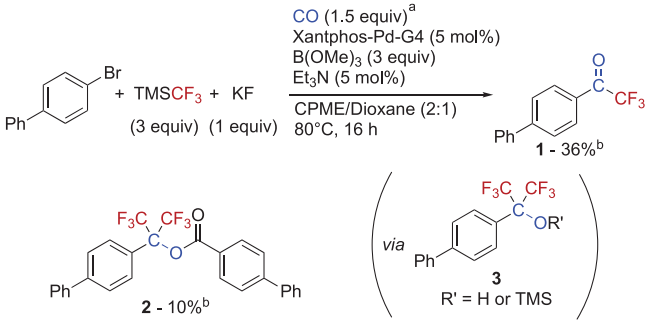
of the carbonyl intermediate on the metal center should facilitate the reductive elimination to the new C−C bond.[10] Furthermore, the coordination of carbon monoxide to palladium(II) acyl complexes has been previously reported to lower the activation barrier for a subsequent reductive elimination.[11]

We also questioned whether the more easily accessible Ruppert−Prakash reagent could be applied as the nucleophilic trifluoromethyl source in combination with aryl bromides and in the presence of only stoichiometric amounts of carbon monoxide, which would not only increase the applicability of this synthetic transformation but also allow for carbon isotope labeling of the target compounds.[12] Inspired by a copper-catalyzed cross coupling of aryl iodides with $TMSCF_3$, we used potassium fluoride for its activation in combination with trimethylborate. It is speculated that the reactive trifluoromethyl anions formed upon fluoride addition are stabilized by the presence of trimethylborate,[13] which also circumvents the formation of inactive Pd−$CF_3$ species.

After extensive attempts to optimize this transformation, the most efficient conditions obtained with this catalytic system are shown in Scheme 2. On application of Xantphos-Pd-G4[14]

**Scheme 2. Previous Attempts toward a Pd-Catalyzed Trifluoroacetophenone Synthesis**

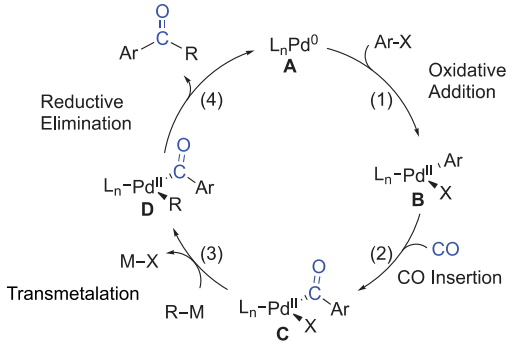



[a]Reactions were performed in a two-chamber setup. CO was released from a solid precursor (see the Supporting Information for details). [b]Yields were determined by $^{19}F$ NMR spectroscopy using (trifluoromethoxy)benzene as an internal standard.

along with 1.5 equiv of carbon monoxide released from COgen in the two-chamber system COware, the carbonylative cross coupling delivered up to 36% of the desired trifluoroacetophenone with 10% of the side product **2** present. Without trimethylborate, no fluorine-containing products were observed. When $Cs_2CO_3$ was employed for the activation of $TMSCF_3$ instead of KF, the selectivity changed completely, leading only to the bis(trifluoromethyl)carbinol **3** and its *O*-trimethylsilylated derivative. Generally, the yields and product distribution fluctuated between 10 and 20% in attempts under identical conditions. Using strong bases, the formation of the carboxylic acid fluoride was observed in some cases. In other attempts, optimizing reagent ratios, temperature, solvents, activating reagents, phosphine ligands, and Pd sources did not provide increased yields or a more consistent performance of the catalytic system. Furthermore, the reaction often delivered mixtures of trifluoroacetophenone **1** accompanied by the side products **2** and **3**, thought to arise from the addition of the trifluoromethyl anion to the desired product **1** to form the bis(trifluoromethyl)carbinol **3**,[15] followed by an ensuing alkoxycarbonylation to generate ester **2**.

Palladium-catalyzed carbonylative versions of Negishi, Suzuki, Sonogashira, Stille, and Hiyama couplings have already been established for the synthesis of nonsymmetrical ketones.[16] These transformations are generally considered to proceed via a four-step catalytic cycle (Scheme 3): (1)

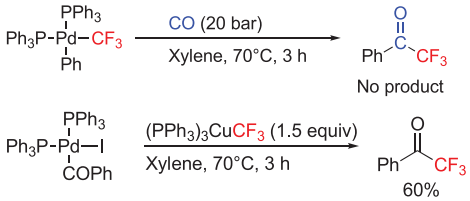
**Scheme 3. General Catalytic Cycle for Carbonylative Cross-Coupling Reactions**




oxidative addition of the $Pd^0$ center into the Ar−X bond to generate $L_nPd^{II}(Ar)X$ (**B**), (2) insertion of carbon monoxide resulting in the palladium(II) acyl complex **C**, (3) transmetalation of $L_nPd^{II}(COAr)X$ (**C**) with an organometallic reagent to form $L_nPd^{II}(COPh)R$ (**D**), and finally (4) reductive elimination to the unsymmetrical ketone and regeneration of $L_nPd^0$ (**A**).

This mechanism was proposed for the carbonylative trifluoromethylation reported by Wu (Scheme 1), involving aryl iodides, CO, and the organometallic reagent $(PPh_3)_3CuCF_3$. They demonstrated that exposure of the isolated complex $(PPh_3)_2Pd(Ph)CF_3$ formed by transmetalation of the oxidative addition complex $(PPh_3)_2Pd^{II}(Ph)I$ does not insert CO with subsequent trifluoroacetophenone formation (Scheme 4, top). In contrast, when the $Pd^{II}$ acyl complex $(PPh_3)_2Pd(COPh)I$ is treated with $(PPh_3)_3CuCF_3$, trifluoroacetophenone is successfully generated in a 60% yield (Scheme 4, bottom).[9]

**Scheme 4. Stoichiometric Experiments by Wu and Co-workers[9]**




To gain insight into the reactivity of carbonylative cross-coupling reactions with fluorinated organometallic reagents or nucleophiles, we set out to perform a stoichiometric study of the plausible intermediates in a hypothetical catalytic cycle. In this paper, we report on our investigations on the feasibility of each of the possible elementary steps employing the Ruppert−Prakash reagent in combination with a fluoride source for its activation. Since the ligands Xantphos, DtBPF, and tri-*tert*-butylphosphine have previously been reported to support the reductive elimination to aryl-$CF_3$ from the corresponding $LPd^{II}(Ph)CF_3$ complexes, and Xantphos is the only ligand viable in the catalytic system, these ligands were chosen for our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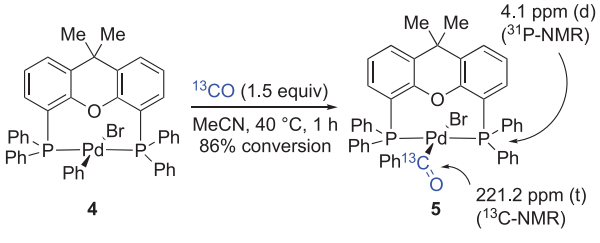
stoichiometric studies. In this work, we demonstrate new reactivity of bidentate phosphine-ligated complexes of the type $LPd^{II}(Ph)CF_3$ with the ligands Xantphos and D*t*BPF on treatment with stoichiometric amounts of carbon monoxide. With these complexes, CO insertion and reductive elimination are sufficiently efficient under mild reaction conditions to generate trifluoroacetophenone in high yields. On the other hand, we uncover that the use of the monodentate ligand P*t*Bu$_3$ only results in trace amounts of the desired ketone. Furthermore, our investigations reveal that transmetalation of a Pd(II) acyl complex with $TMSCF_3$ activated by a fluoride source is not a viable process.

## RESULTS AND DISCUSSION

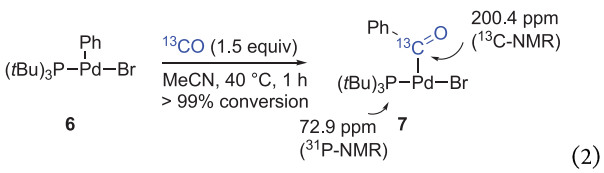
**Steps 1 and 2: Oxidative Addition of Bromobenzene and Carbon Monoxide Insertion.** The oxidative addition complex of bromobenzene with Xantphos as the ligand was prepared by treatment of $Pd(dba)_2$ with 1 equiv of the diphosphine ligand and excess bromobenzene in benzene at 80 °C for 4 h.[17] Upon workup, the desired complex (Xantphos)-Pd(Ph)Br (**4**) was obtained in a 61% yield. When complex **4** was subjected to 1.5 equiv of $^{13}C$-carbon monoxide in acetonitrile at 40 °C for 1 h in the two-chamber system COware, carbon monoxide insertion successfully resulted in the formation of the palladium(II) acyl complex **5** with an 86% conversion, as determined by the shift in the phosphine signal from a singlet at 8.7 ppm to a doublet at 4.1 ppm in the $^{31}P$ NMR spectrum of the crude reaction mixture (eq 1).



(1)

Furthermore, formation of the $Pd^{II}$ acyl complex was confirmed by the appearance of a distinct triplet at 221.2 ppm in the $^{13}C$ NMR spectrum arising from the metal-bound $^{13}C$-carbonyl group.

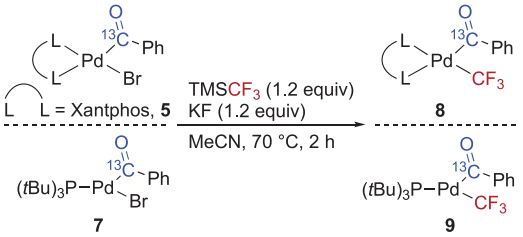
The oxidative addition complex containing P(*t*Bu)$_3$ as a ligand was synthesized by stirring $Pd(P(tBu)_3)_2$ in excess bromobenzene for 2 h at 70 °C, affording (*t*Bu$_3$P)Pd(Ph)Br (**6**) in 75% yield after workup.[18] Complex **6** behaved similarly to the Xantphos-ligated complex **4**, and full conversion to the $Pd^{II}$ acyl complex **7** was observed according to $^{31}P$ NMR spectroscopy accompanied by a doublet at 200.4 ppm in the $^{13}C$ NMR spectrum when **6** was subjected to 1.5 equiv of $^{13}C$-carbon monoxide at 40 °C for 1 h (eq 2).



(2)

**Step 3: Transmetalation Studies.** Previous reports have established the feasibility of oxidative addition of palladium(II) complexes to undergo transmetalation with nucleophilic $TMSCF_3$/fluoride systems.[4a,b,19] The success of this step in such systems relies on the coordination strength of the phosphine ligands. Palladium complexes with strongly bound ligands successfully undergo transmetalation with $CF_3$ anions, while more weakly bonded ligands result in nonselective exchange with halides and/or phosphine ligands.[4a,5,19,20] To investigate this event with the palladium(II) acyl complexes **5** and **7**, a series of experiments was set up, the results of which are revealed in Table 1. As can be seen in entry 1, when the

**Table 1. Transmetalation Studies with LPd(COPh)Br**[a]




| entry | complex | variation | result[b] |
|---|---|---|---|
| 1 | **5** | | **8** not obsd |
| 2 | **5** | $^{13}CO$ (1.5 equiv) | **8** not obsd |
| 3 | **5** | $B(OMe)_3$ (1.2 equiv) | **8** not obsd |
| 4 | **5** | without KF | **8** not obsd |
| 5 | **7** | | **9** not obsd |
| 6 | **7** | $^{13}CO$ (1.5 equiv) | **9** not obsd |

[a]A representative procedure is provided in the Supporting Information. [b]The results were analyzed by $^{13}C$ NMR, $^{31}P$ NMR, and $^{19}F$ NMR spectroscopy.

(Xantphos)$Pd^{II}$ acyl complex **5** was heated to 70 °C in acetonitrile in the presence of 1.2 equiv of $TMSCF_3$ and equimolar amounts of potassium fluoride, the Pd−$CF_3$ complex **8** was not observed. The signals in both the $^{31}P$ NMR and $^{13}C$ NMR spectra indicated partial decomposition of the $Pd^{II}$ acyl complex, while by $^{19}F$ NMR spectroscopy, 13% of the recovered $TMSCF_3$ provided the major signal. Similar treatment of the (*t*Bu$_3$P)$Pd^{II}$ acyl complex **7** (entry 5) did not result in the generation of the corresponding Pd−$CF_3$ complex, which should have presented itself by a signal at approximately −27 ppm in the $^{19}F$ NMR spectrum.[6] When the reaction was carried out in the presence of 1.5 equiv of $^{13}C$-labeled carbon monoxide using compound **5**, the formation of **8** was not detected. The disappearance of the signals in the $^{31}P$ NMR and $^{13}C$ NMR spectra and the formation of a complex mixture according to the $^{19}F$ NMR spectrum suggest decomposition of the starting material. Treatment of the palladium(II) acyl complex **7** under similar conditions did not provide any improvement according to the NMR spectra in comparison to the reaction without $^{13}CO$ (entry 6).

Addition of 1.2 equiv of trimethylborate to the reaction mixture of complex **5** with $TMSCF_3$ did not aid the transmetalation either, as only decomposition of the starting material was observed by $^{13}C$ NMR and $^{31}P$ NMR spectroscopy. There is literature precedence for a transmetalation event between $TMSCF_3$ with (Xantphos)Pd(Ph)F without activation of the silicon.[5] Whether a similar event could occur with the acyl complex **5** was tested by treating this organometallic complex with 1.2 equiv of $TMSCF_3$ and omitting the addition of KF (entry 4). However, according to the $^{19}F$ NMR spectrum of the crude reaction mixture, the Pd−$CF_3$ complex **8** was not formed. Only partial decomposition of the starting material was observed.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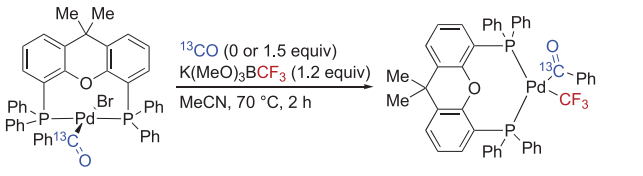
All in all, these results indicate that the Pd−$CF_3$ complexes were not easily formed from the corresponding palladium(II) acyl complexes. The results indicate that the Xantphos-ligated complex is unstable when it is treated with $TMSCF_3$ and potassium fluoride, which is consistent with the previously reported results by Grushin and Marshall, who observed the facile displacement of Xantphos in attempting to transmetalate [(Xantphos)Pd(Ph)I] with a similar mixture of $TMSCF_3$ and CsF.[5]

Since the addition of trimethylborate was previously found to be necessary for the catalytic system to function, it was hypothesized that potassium (trifluoromethyl)-trimethoxyborate, $K(MeO)_3BCF_3$, could initially be formed in the reaction mixture and subsequently act as the trifluoromethylating agent. Use of $K(MeO)_3BCF_3$ as a $CF_3$ source has previously been exploited by Goo*β*en and co-workers in a Cu-catalyzed trifluoromethylation of aryl iodides.[21] However, when (Xantphos)$Pd^{II}$ acyl complex **5** was treated with this reagent at 70 °C for 2 h (eq 3), no

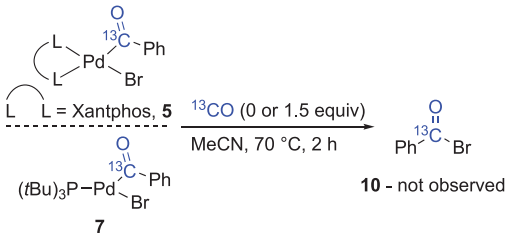


(3)

transmetalated species was detected. Similarly, when the experiment was repeated in the presence of $^{13}C$-carbon monoxide, the $Pd^{II}$−$CF_3$ complex **8** was not observed either. On the other hand, a small amount of the corresponding methyl benzoate was noted by $^{13}C$ NMR spectroscopy (167.6 ppm)[22] and GC-MS analysis, indicating the transfer of methoxide instead of a trifluoromethyl group followed by reductive elimination of the ester.[23]

Because the formation of Pd−$CF_3$ complexes could not be observed from the corresponding palladium(II) complexes **5** and **7** under the applied reaction conditions, we questioned whether the role of the Pd-catalyzed carbonylation was to form an activated intermediate, which upon subsequent reaction with the Ruppert−Prakash reagent could generate the desired aryl trifluoromethylketone. Inspired by the work of Arndtsen and co-workers on the Pd-catalyzed synthesis of aroyl chlorides,[11] we initially tested if reductive elimination to benzoyl bromide **10** could be a viable process.

As illustrated in eq 4, heating palladium(II) acyl complexes **5** and **7** to 70 °C for 2 h in acetonitrile did not result in the

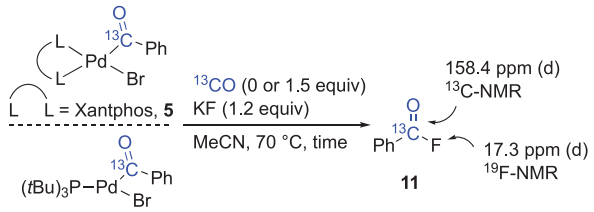


(4)

formation of benzoyl bromide, as determined by the absence of a carbonyl signal at approximately 166 ppm in the $^{13}C$ NMR spectrum.[24] Instead, considerable decomposition of complex **5** was observed. Performing the reaction in the presence of $^{13}C$-carbon monoxide did not result in the formation of benzoyl bromide either; however, complexes **5** and **7** were both stable under the reaction conditions. This lack of decomposition could be explained by an equilibrium between either (Xantphos)Pd(Ph)Br or ($tBu_3P$)Pd(Ph)Br with ($^{13}CO$)Pd($^{13}COPh$)Br in the presence of $^{13}CO$. However, analysis by $^{13}C$ and $^{31}P$ NMR spectroscopy of the reaction mixture in the presence of $^{13}CO$ did not reveal any new signals corresponding to the latter complex.

In contrast, when the palladium(II) acyl complexes **5** and **7** were subjected to potassium fluoride under similar conditions, formation of carboxylic acid fluoride **11** was obtained, as revealed by a doublet at 17.3 ppm in the $^{19}F$ NMR spectrum and a doublet at 158.4 ppm in $^{13}C$ NMR spectrum. Treatment of the Xantphos complex **5** with potassium fluoride at 70 °C in acetonitrile for 2 h provided a 10% conversion to **11**, whereas the conversion was increased to 22% by leaving the reaction mixture for 18 h (Table 2, entries 1 and 2). When the reactions

**Table 2. Reductive Elimination Studies to Benzoyl Fluorides**[a]




| complex | $^{13}CO$ (equiv) | time (h) | conversn to **11** (%)[b] |
|---|---|---|---|
| **5** | 0 | 2 | 10 |
| **5** | 0 | 18 | 22 |
| **5** | 1.5 | 2 | 68 |
| **5** | 1.5 | 18 | >95 |
| **7** | 0 | 2 | 0 |
| **7** | 0 | 18 | <5 |
| **7** | 1.5 | 2 | 15 |
| **7** | 1.5 | 18 | 61 |

[a]A representative procedure is provided in the Supporting Information. [b]The results were analyzed by $^{13}C$ NMR, $^{31}P$ NMR, and $^{19}F$ NMR spectroscopy. Conversion was determined by $^{13}C$ NMR spectroscopy.

were performed in the presence of 1.5 equiv of $^{13}C$-carbon monoxide, the yields were significantly improved, providing a 68% conversion in 2 h and full conversion when the reaction mixture was heated for 18 h. In contrast, when the $Pd^{II}$ acyl complex **7** was subjected to potassium fluoride, no conversion was noted after 2 h, and after an overnight experiment, only trace amounts of benzoyl fluoride **11** could be detected. Nevertheless, when the reaction mixture was exposed to 1.5 equiv of carbon monoxide, complex **7** provided a 15% conversion to **11**, and a significant increase to a 61% conversion was obtained by prolonged heating of the reaction mixture.

Reductive elimination of benzoyl fluoride from the corresponding $(PPh_3)_2$Pd(COPh)F complex has previously been reported by Grushin to occur at a temperature below 10 °C,[25] and Pd-catalyzed carbonylative protocols for the synthesis of aryl carboxylic acid fluorides have been similarly developed.[26] Furthermore, the necessity for carbon monoxide to promote the reductive elimination has previously been demonstrated by the Arndtsen group in their experimental and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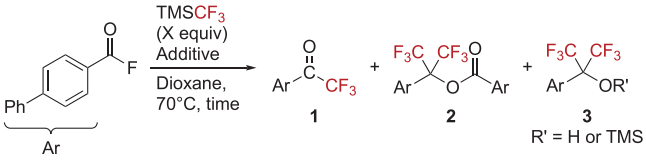
computational investigations of the mechanism for the Pd-catalyzed synthesis of aroyl chlorides. In this work, it was discovered that the reductive elimination did not take place without the presence of carbon monoxide. Computational calculations using P*t*Bu$_3$ as the ligand revealed that CO binding to a free coordination site on the palladium complex prior to reductive elimination could lower the activation energy for reductive elimination of benzoyl chloride from 23.6 to 14.2 kcal/mol.[11] Thus, the carboxylic acid fluoride could be a plausible intermediate in a catalytic system (Scheme 2).

In 2018, Schoenebeck reported a decarbonylative trifluoromethylation of aroyl fluorides utilizing a Pd/Xantphos catalyst system and TESCF$_3$ as the trifluoromethyl source.[29] By computational methods, they proposed that the Pd(II) acyl complex (Xantphos)Pd(COPh)F is an intermediate efficiently undergoing transmetalation with TESCF$_3$ without external activation to form (Xantphos)Pd(COPh)CF$_3$. Moreover, they found the activation energy for the reductive elimination step from this Pd(II)−CF$_3$ acyl complex to be lower than that for a decarbonylation. With this, we speculated whether a similar complex could be formed from an intermediate aryl acid fluoride in our system. This suggestion was examined by treating [1,1′-biphenyl]-4-carbonyl fluoride with TMSCF$_3$ in dioxane at 70 °C (Table 3). Without additives trace amounts

**Table 3. Reactivity Studies of a Carboxylic Acid Fluoride with TMSCF$_3$[a]**

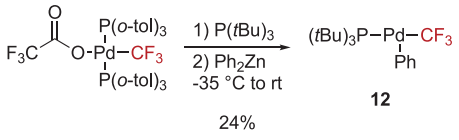



| entry | time (h) | X | additive (equiv) | yield **1**/**2**/**3** (%)[b] |
|---|---|---|---|---|
| 1 | 2 | 1.2 | | <5/0/0 |
| 2 | 16 | 1.2 | | <5/0/0 |
| 3 | 2 | 1.2 | Pd(dba)$_2$ (1) + Xantphos (1) | <5/0/0 |
| 4 | 16 | 1.2 | Pd(dba)$_2$ (1) + Xantphos (1) | <5/0/0 |
| 5 | 16 | 3.0 | Pd(dba)$_2$ (1) + Xantphos (1) | 7/0/0 |
| 6[c] | 2 | 3.0 | KF (1) + B(OMe)$_3$ (3) | 13/9/< 5 |
| 7[c] | 16 | 3.0 | KF (1) + B(OMe)$_3$ (3) | <5/38/31 |

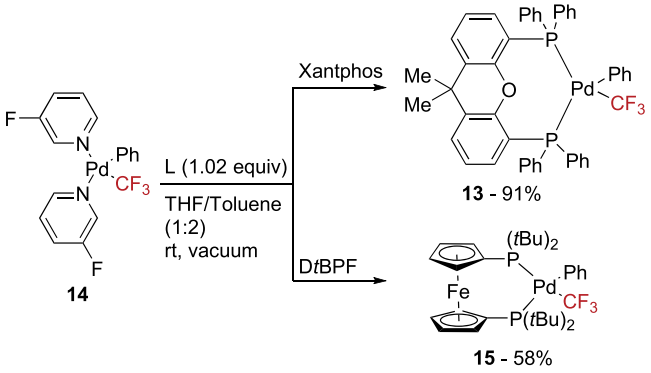
[a]A representative procedure is provided in the Supporting Information. [b]Yields were determined by $^{19}$F NMR spectroscopy using (trifluoromethoxy)benzene as an internal standard. [c]Reaction performed at 80 °C in CPME/dioxane (2/1).

of trifluoroacetophenone **1** were formed (entries 1 and 2). Similarly, in the presence of Pd(dba)$_2$ and Xantphos in stoichiometric amounts, only trace amounts of the trifluoromethylated ketone could be generated (entries 3 and 4). When the amount of TMSCF$_3$ was increased, 7% of **1** was observed (entry 5). These results indicate that the Pd-mediated trifluoromethylation of the carboxylic acid fluoride is not a viable pathway at these temperatures. To further elucidate the reactivity of the carboxylic acid fluoride in relation to the catalytic system, it was treated with TMSCF$_3$, KF, and B(OMe)$_3$ at 80 °C in the CPME/dioxane solvent mixture for 2 h, resulting in formation of a mixture of compounds **1**−**3**. Furthermore, with a prolonged reaction time of 16 h, 79% of the carboxylic acid fluoride was converted into the side products **2** and **3**, and only traces of the desired trifluoroacetophenone **1** was observed (entry 7). As such, formation of an intermediate aroyl fluoride species can be the source of the product mixtures observed for this catalytic system.

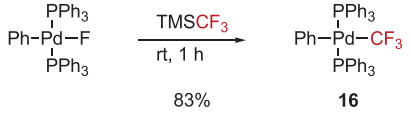
**Synthesis of Phosphine-Ligated Pd$^{II}$(Ph)CF$_3$ Complexes.** As we were not able to observe an efficient transformation to trifluoroacetophenone from the attempted transmetalation of the Pd(II) acyl complex with TMSCF$_3$, we speculated whether the reductive elimination to the target compound could be achieved by an initial transmetalation event with the oxidative addition complexes followed by CO insertion. The trifluoromethyl tri-*tert*-butylphosphine complex **12** was prepared by treating ((*o*-tol)$_3$P)Pd(OCOCF$_3$)CF$_3$ with P(*t*Bu)$_3$, followed by the addition of diphenylzinc as reported by Sanford et al. (eq 5),[6] providing a 24% yield of the desired




complex **12**. To synthesize the corresponding Xantphos complex **13**, we initially attempted to use a literature procedure starting from (Xantphos)Pd(Ph)F.[5] Unfortunately, the synthesis of this fluoride complex resulted in decomposition of the starting material or low conversion to the desired complex in our hands. The (Xantphos)Pd(Ph)CF$_3$ complex **13** is known to reductively eliminate to produce trifluorotoluene when it is heated to 50−80 °C, and therefore, it was important to develop an alternative pathway under mild conditions for its synthesis. Inspiration for this was drawn from the synthesis of (D*t*BPF)Pd(Ph)CF$_3$ reported earlier this year, in which Pd$^{II}$(Ph)CF$_3$ bearing labile 3-fluoropyridine ligands (complex **14**) was used as an intermediate to allow ligand exchange at room temperature.[8] The Xantphos complex **13** was thus prepared in a 91% yield by adapting this approach (eq 6). Similarly, the 1,1′-bis(di-*tert*-butylphosphino)ferrocene complex **15** could be generated in a 58% yield.




Finally, (PPh$_3$)$_2$Pd$^{II}$(Ph)CF$_3$ was prepared from (PPh$_3$)$_2$Pd(Ph)F by treatment with TMSCF$_3$ at rt for 1 h, following a procedure reported by Grushin et al.[5] As such, the triphenylphosphine complex **16** was synthesized in an 83% yield (eq 7).





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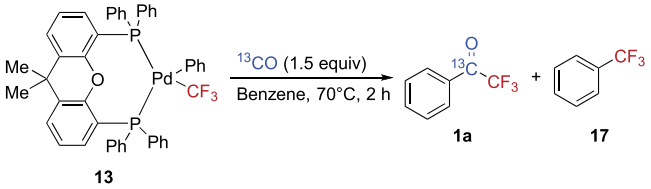
**Step 4: CO Insertion and Reductive Elimination from Phosphine-Ligated $Pd^{II}(Ph)CF_3$ Complexes.** Complexes **12**, **13**, and **15** are all known to reductively eliminate Ph−$CF_3$ upon heating to 80 °C in benzene in the presence of additional ligand.[5,6,8] Interestingly, heating the Xantphos complex **13** in benzene at 70 °C for 2 h in the presence of 1.5 equiv of $^{13}C$-carbon monoxide resulted in the formation of 1,1,1-trifluoroacetophenone (**1a**) in an 84% yield (Table 4, entry 1). The structure was confirmed by a distinct doublet at −71.4 ppm in the $^{19}F$ NMR spectrum and a quartet at 179.8 ppm in the $^{13}C$ NMR spectrum along with only trace amounts of α,α,α-trifluorotoluene (**17**). As summarized in Table 4, and as expected, omission of $^{13}CO$ did not lead to the formation of trifluoroacetophenone **1a** but instead led to a 35% yield of trifluorotoluene **17**. Generally, in reactions investigating reductive eliminations, extra ligand is added to the reaction mixture to stabilize the $Pd^0$ complex and thus limit unwanted side reactions.[8] However, when Xantphos was added, a decrease in the yield of **1a** was observed (entry 3). Addition of reagents such as potassium fluoride alone or in combination with $TMSCF_3$ did not change the reaction outcome (entries 4 and 5). When the temperature was lowered to 40 °C, a yield of 67% of **1a** could be obtained in 2 h, whereas heating the mixture to 40 °C for 18 h resulted in full conversion to the trifluoroacetophenone **1a**. Hence, the obtained results demonstrate that (Xantphos)$Pd^{II}(Ph)CF_3$ (**13**) effectively undergoes CO insertion and reductive elimination when it is subjected to carbon monoxide.

**Table 4. Competition Experiments between Reductive Elimination and CO Insertion/Reductive Elimination from (Xantphos)$Pd^{II}(Ph)CF_3$[a]**

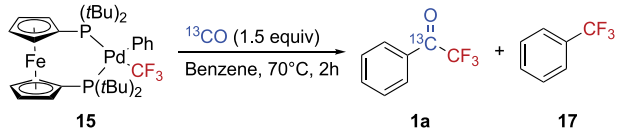



| entry | variation | yield **1a**/**17** (%)[b] |
|---|---|---|
| 1 | | 84/<5 |
| 2 | without $^{13}CO$ | 0/35 |
| 3 | Xantphos (1.2 equiv) added | 71/<5 |
| 4 | KF (1.2 equiv) added | 77/<5 |
| 5 | $TMSCF_3$ (1.2 equiv) and KF (1.2 equiv) added | 81/<5 |
| 6 | 40 °C | 67/<5 |
| 7 | 40 °C, 18 h | 97/0 |

[a]A representative procedure is provided in the Supporting Information. [b]Yields were determined by $^{19}F$ NMR spectroscopy using (trimethoxy)benzene as internal standard.

Further investigations revealed that the complex (D*t*BPF)-$Pd^{II}(Ph)CF_3$ (**15**) operated in a similar manner. As depicted in Table 5, heating **15** to 70 °C in the presence of $^{13}CO$ for 2 h produced trifluoroacetophenone **1a** in a 28% yield along with an 11% yield of **17** as a side product. Increasing the reaction time to 18 h improved the yield of **1a** to 54%, while the amount of α,α,α-trifluorotoluene remained unchanged (entry 2). When carbon monoxide was omitted, trifluorotoluene was the sole product in the reaction, forming in a 38% yield (entry 3). Addition of potassium fluoride to the reaction mixture did not have any influence on the yields (entries 4 and 5).

**Table 5. Competition Experiments between Reductive Elimination and CO Insertion/Reductive Elimination from (D*t*BPF)$Pd^{II}(Ph)CF_3$[a]**



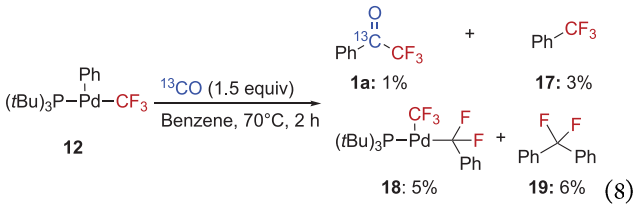

| entry | variation | yield **1a**/**17** (%)[b] |
|---|---|---|
| 1 | | 28/11 |
| 2 | 18 h | 54/11 |
| 3 | without $^{13}CO$ | 0/38 |
| 4 | KF (1.2 equiv) added | 31/13 |
| 5 | KF (1.2 equiv) added, 18 h | 68/15 |
| 6 | 40 °C | 28/<5 |
| 7 | 40 °C, 18 h | >95/<5 |

[a]A representative procedure is provided in the Supporting Information. [b]Yields were determined by $^{19}F$ NMR spectroscopy using (trimethoxy)benzene as an internal standard.

Lowering the temperature to only 40 °C delivered a outcome similar to that of the reaction at 70 °C, however with increased selectivity toward trifluoroacetophenone **1a**, while only traces of **17** could be observed.

Finally, when the reaction mixture was heated to 40 °C overnight, full conversion to trifluoacetophenone **1a** was observed, thereby indicating that complex **15** is less stable at 70 °C than at 40 °C (entry 7). Nonetheless, it performs the carbon monoxide insertion and reductive elimination effectively, but with a lower rate than for the corresponding Xantphos complex **13** (Table 4, entry 7).

Finally, the complex ($tBu_3P$)$Pd^{II}(Ph)CF_3$ (**12**) was tested under similar reaction conditions. As shown in eq 8, when



(8)

complex **12** was subjected to $^{13}C$-carbon monoxide at 70 °C for 2 h, only trace conversion to the desired trifluoroacetophenone **1a** was noted. Traces of α,α,α-trifluorotoluene **17** were similarly observed along with complex **18** and side product **19**. These side products have been reported to arise from complex **12** in the original thermolysis experiments by Sanford and co-workers.[6] They suggest that the side products arise due to the empty site on palladium, which enables α-fluoride elimination. The side products are released upon transmetalation with Pd−$CF_3$ or Pd−Ph and reductive elimination. Since only trace amounts of trifluoroacetophenone **1a** were observed, we conclude that complex **12** is inefficient for CO insertion and reductive elimination of trifluoroacetophenone **1a** in comparison to complexes **13** and **15**. As such, this complex was not investigated further.

To conclude this study, we attempted to determine into which of the two bonds (Pd−Ph vs Pd−$CF_3$) CO was inserting. As Wu reported that treatment of $(PPh_3)_2Pd^{II}(Ph)$-$CF_3$ did not result in formation of trifluoroacetophenone (Scheme 4, top),[9] we hypothesized that a slow reductive elimination could be the cause of the low reactivity, and as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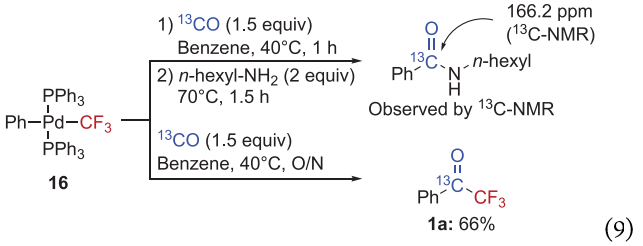
such, this complex could represent an opportunity to examine the Pd(II) acyl complex upon treatment with carbon monoxide.

Initially, the $Pd^{II}-CF_3$ complex **16** was treated with 1.5 equiv of *13*CO in benzene for 1 h. $^{13}C$ NMR analysis revealed the presence of a new quartet at 250.7 ppm indicating CO insertion, whereas $^{19}F$ NMR and $^{31}P$ NMR spectroscopic analysis revealed that full conversion of complex **16** was not achieved. Upon treatment of the reaction mixture with *N*-hexylamine, the $^{13}C$-carbonyl signal at 250.7 ppm disappeared and new a singlet at 166.2 ppm appeared in the $^{13}C$ NMR spectrum of the reaction mixture, which is consistent with the formation of the corresponding *N*-hexylbenzamide (eq 9).[27] This preliminary result indicates that CO insertion takes place into the Pd−Ph bond. In an attempt to obtain full CO insertion, complex **16** was treated with $^{13}C$-labeled CO at 40 °C for 18 h. Surprisingly, instead of formation of a Pd(II) acyl complex, a 66% yield of the trifluoroacetophenone **1a** was observed (eq 9). The formation of trifluoroacetophenone **1a** by subjecting complex **16** to carbon monoxide is in contrast to the results reported by Wu and co-workers, who did not observe formation of trifluoroacetophenone by treatment of this complex with 20 bar of CO at 70 °C for 3 h. This discrepancy in observations from the same initial complex may be related to the pressure of CO used in the two experiments, whereby higher pressures of CO may effectively surpress the reductive elimination step.



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## CONCLUSION

In summary, we have performed a series of stoichiometric studies in order to identify viable steps for a hypothetical catalytic cycle for the palladium-mediated carbonylative coupling of an aryl bromide with $TMSCF_3$. Our work revealed that benzoyl Pd(II) complexes bearing Xantphos or $t$Bu$_3$P as the phosphine ligands, being generated with stoichiometric $^{13}CO$ from $^{13}CO$gen from the corresponding aryl Pd(II) bromide complexes were incapable of undergoing transmetalation and reductive elimination to trifluoroacetophenone. Instead, in the presence of base and additional CO, these organometallic complexes could undergo facile reductive elimination to the acid fluoride. Attempts to determine whether the acid fluoride could represent an intermediate for acetophenone production were unrewarding. Only in the presence of a boronic ester did we observe some formation of the desired product, although the efficiency was still low. Finally, we investigated the reactivity of four $L_nPd(Ph)CF_3$ complexes bearing phosphine ligands with carbon monoxide. In all but one case, we observed the facile formation of trifluoroacetophenone and also determined for one of the complexes that CO insertion occurred into the Pd−Ar bond.

## EXPERIMENTAL SECTION

**Preparation of (Xantphos)Pd(Ph)Br (4).** In an argon-filled glovebox, a flame-dried 50 mL round-bottom flask was charged with $Pd(dba)_2$ (517.5 mg, 0.90 mmol), Xantphos (520.8 mg, 0.90 mmol, 1 equiv), benzene (25 mL), and bromobenzene (1.8 mL, 17.0 mmol, 19 equiv). The flask was sealed and brought out of the glovebox, and the mixture was stirred at 80 °C for 4 h. The reaction mixture was filtered through a pad of Celite with toluene and concentrated before $Et_2O$ (10 mL) was added to force precipitation. The yellow solid was isolated by filtration, washed with $Et_2O$ (3 × 10 mL), and dried under vacuum to provide (Xantphos)Pd(Ph)Br (**4**; 459.2 mg, 61%) as a yellow solid. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.61 (dd, $J$ = 6.7, 2.6 Hz, 2H), 7.37−7.32 (m, 8H), 7.26−7.22 (m, 4H), 7.15−7.10 (m, 12H), 6.54 (bs, 2H), 6.28 (t, $J$ = 7.2 Hz, 1H), 6.11 (t, $J$ = 7.5 Hz, 2H), 1.79 (s, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$): $\delta$ (ppm) 157.2, 155.7 (t, $J$ = 5.7 Hz), 134.9 (t, $J$ = 6.2 Hz), 134.6−134.5 (m), 132.1, 131.7 (t, $J$ = 22.3 Hz), 129.6, 129.2, 128.0 (t, $J$ = 5.0 Hz), 127.2, 126.6, 124.4 (t, $J$ = 3.4 Hz), 122.2 (t, $J$ = 21.1 Hz), 121.0, 36.3, 28.7. $^{31}P$ NMR (162 MHz, $CDCl_3$): $\delta$ (ppm) 8.7 (s, 2P). $^1H$, $^{13}C$, and $^{31}P$ NMR spectra are consistent with literature data.[17]

**General Procedure 1: Preparation of L−Pd$^{II}$(COPh)Br Complexes (5 and 7).** In an argon-filled glovebox, in one chamber of a two-chamber system was placed oxidative addition complex **4** or **6** (0.05 mmol) and solvent (0.5 mL). The second chamber was charged with 9-methyl-9*H*-fluorene-9-carbonyl-$^{13}C$ chloride (18.3 mg, 0.08 mmol), $HBF_4P(t\text{Bu})_3$ (1.3 mg, 0.005 mmol, 6 mol %), $Pd(cod)Cl_2$ (1.3 mg, 0.005 mmol, 6 mol %), DMF (0.5 mL), and $Cy_2NMe$ (32 $\mu$L, 0.15 mmol, 2 equiv). The chambers were immediately sealed tightly with screw caps fitted with Teflon seals. The two-chamber system was brought out of the glovebox, and the contents were stirred in a preheated heating block at 40 °C for 1 h. The two-chamber system was brought back into the glovebox, where the reaction mixture was transferred directly to an NMR tube. The NMR tube was sealed and brought out of the glovebox. A $^{31}P$ NMR spectrum was obtained to determine the conversion of starting material to LPd$^{II}$(COPh)Br complexes **5** and **7**. $^{13}C$ and $^{31}P$ NMR spectra for complexes **5** and **7** are available in the Supporting Information. This mixture was used directly in the subsequent reactions.

**Preparation of ($t$Bu$_3$P)Pd(Ph)Br (6).** In an argon-filled glovebox, a flame-dried 8 mL vial was charged with $Pd(Pt\text{Bu}_3)_2$ (102.2 mg, 0.2 mmol) and bromobenzene (942 $\mu$L, 9.0 mmol, 45 equiv). The reaction mixture was stirred at 70 °C for 2 h before the mixture was transferred to a flame-dried 50 mL flask containing $Et_2O$ (8 mL) and concentrated to a yellow oil under vacuum. The oily residue was treated with pentane (12 mL) and placed in the glovebox freezer (−35 °C) to force precipitation of a yellow solid that was collected by filtration, washed with pentane, and dried under vacuum to provide ($t$Bu$_3$P)Pd(Ph)Br (**6**; 69.5 mg, 75%) as a yellow solid. $^1H$ NMR (400 MHz, THF-$d_8$): $\delta$ (ppm) 7.22 (d, $J$ = 7.7 Hz, 2H), 6.81−6.72 (m, 3H), 1.47 (d, $J$ = 12.5 Hz, 27H). $^{31}P$ NMR (162 MHz, THF-$d_8$): $\delta$ (ppm) 62.2 (s, 1P). $^1H$ and $^{31}P$ NMR spectra are consistent with literature data.[18]

**Preparation of Potassium (Trifluoromethyl)-trimethoxyborate.** In a flame-dried 50 mL flask were placed KF (383.5 mg, 6.6 mmol), THF (15 mL), $B(OMe)_3$ (0.90 mL, 8.1 mmol, 1.2 equiv), and $TMSCF_3$ (1.04 mL, 7.1 mmol, 1.1 equiv) under an argon atmosphere. The suspension was stirred at rt O/N. The reaction mixture was concentrated to half volume under reduced pressure, and dry pentane (11 mL) was added. The resulting colorless precipitate was isolated by filtration, washed with pentane, and dried under vacuum to provide potassium (trifluoromethyl)-trimethoxyborate (903.9 mg, 60%) as a colorless solid. $^1H$ NMR (400 MHz, $D_2O$): $\delta$ (ppm) 3.31 (s, 9H). $^{13}C$ NMR (101 MHz, $D_2O$): $\delta$ (ppm) 48.9. $CF_3$ was not resolved. $^{19}F$ NMR (376 MHz, $D_2O$): $\delta$ (ppm) −74.7 to −74.9 (m, 3F). $^1H$, $^{19}F$, and $^{13}C$ NMR spectra are consistent with literature data.[21,28]

**Preparation of ($t$Bu$_3$P)Pd(Ph)CF$_3$ (12).** In an argon-filled glovebox, a flame-dried 20 mL vial was charged with $[(o\text{-tol})_3P]_2Pd(OC(O)CF_3)(CF_3)$ **SI3** (150.0 mg, 0.15 mmol), $Pt\text{Bu}_3$ (182.2 mg,


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0.90 mmol, 6 equiv), and THF (8.8 mL). The solution was cooled to −35 °C in the glovebox freezer for 14 min. During this time, a flame-dried 4 mL vial was charged with $Ph_2Zn$ (18.1 mg, 0.08 mmol, 0.55 equiv). After it was cooled, the reaction mixture was removed from the freezer and $Ph_2Zn$ was immediately added. The vial containing $Ph_2Zn$ was washed with the reaction solution and the wash was recombined with the reaction mixture. The reaction was left at rt for 7 min and then moved to the glovebox freezer for 15 min. The solution was concentrated under vacuum to give a yellow oil. The oily residue was treated with pentane (2 mL), and the vial was shaken to force precipitation of a yellow precipitate. The mixture was left in the glovebox freezer for 5 min. The pentane layer was removed by decantation, and the solid was washed with pentane (3 × 2 mL) and $Et_2O$ (0.5 mL) and dried under vacuum to provide ($t$Bu$_3$P)Pd(Ph)-($CF_3$) (**12**; 16.2 mg, 24%) as a yellow solid. $^1$H NMR (400 MHz, $C_6D_6$): $\delta$ (ppm) 7.66 (d, $J$ = 7.7 Hz, 2H), 6.98 (t, $J$ = 7.5 Hz, 2H), 6.88 (t, $J$ = 7.2 Hz, 1H), 0.95 (d, $J$ = 12.1 Hz, 27H). $^{31}$P NMR (162 MHz, $C_6D_6$): $\delta$ (ppm) 54.5 (q, $J$ = 39.6 Hz, 1P). $^{19}$F NMR (376 MHz, $C_6D_6$): $\delta$ (ppm) −28.3 (d, $J$ = 40.0 Hz, 3F). $^1$H, $^{31}$P, and $^{19}$F NMR spectra are consistent with literature data.[6]

**Preparation of (Xantphos)Pd(Ph)CF$_3$ (13).** In an argon-filled glovebox, a flame-dried 25 mL round-bottom flask was charged with (3-F-Py)$_2$Pd(Ph)$CF_3$ (**14**; 77.0 mg, 0.17 mmol), Xantphos (101.8 mg, 0.18 mmol, 1.02 equiv), THF (1.5 mL), and toluene (3.0 mL). The yellow solution was cooled to −35 °C in the glovebox freezer for 15 min before the volatiles were removed under vacuum. The solid was dissolved in a THF/toluene mixture (1/2) and concentrated under vacuum again. This process was repeated three times in total to remove the 3-fluoropyridine. The remaining solids were collected by filtration, washed with pentane and $Et_2O$, and dried under vacuum to provide (Xantphos)Pd(Ph)$CF_3$ (**13**; 130.1 mg, 91%) as a pale yellow solid. $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ (ppm) 7.68 (bs, 2H), 7.31−6.91 (m, 26H), 6.69−6.68 (m, 3H), 1.79 (s, 6H). $^{31}$P NMR (162 MHz, $CD_2Cl_2$): $\delta$ (ppm) 18.0 (app q, $J$ = 14.0 Hz, 2P, trace *trans*-**13**), 12.6 (bs, 1P, *cis*-**13**), 9.1−7.7 (m, 1P, *cis*-**13**). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): $\delta$ (ppm) −14.3 (t, $J$ = 15.8 Hz, trace *trans*-**13**), −15.8 to −16.0 (m, 3F, *cis*-**13**). $^{31}$P NMR (162 MHz, $C_6D_6$): $\delta$ (ppm) 17.6 (app q, $J$ = 15.6 Hz, 2P, *trans*-**13**), 9.6 (br m, 1P, *cis*-**13**), 5.1−3.9 (br m, 1P, *cis*-**13**). $^{19}$F NMR (376 MHz, $C_6D_6$): $\delta$ (ppm) −13.1 (t, $J$ = 16.2 Hz, 3F, *trans*-**13**), −14.6 to −14.8 (br m, 3F, *cis*-**13**). $^{31}$P and $^{19}$F NMR spectra in $C_6D_6$ are consistent with literature data.[5]

**Preparation of (3-F-Py)$_2$Pd(Ph)(CF$_3$) (14).** In an argon-filled glovebox, a flame-dried 20 mL vial containing a stir bar was charged with [($o$-tol)$_3$P]$_2$Pd(OC(O)$CF_3$)($CF_3$) (**SI3**; 620.0 mg, 0.62 mmol), 3-fluoropyridine (853 μL, 9.93 mmol, 16 equiv), and THF (8.2 mL). The mixture was cooled to −35 °C in the glovebox freezer for 15 min. During this time, $Ph_2Zn$ (74.9 mg, 0.34 mmol, 0.55 equiv) was weighed out into a flame-dried 4 mL vial. The reaction mixture was removed from the freezer, upon which the preweighed $Ph_2Zn$ was immediately added, resulting in a homogeneous solution. The vial containing $Ph_2Zn$ was washed with the reaction mixture, and the wash was recombined with the reaction mixture. The vial was sealed, brought out of the glovebox, and stirred at rt for 20 min. The vial was opened in air, $H_2O$ (1 mL) was added, and the mixture was stirred for an additional 20 min. The solution was filtered through a pad of Celite with dichloromethane, concentrated under reduced pressure, and transferred to a separatory funnel with dichloromethane (20 mL). The organic layer was washed with $H_2O$ (2 × 20 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The remaining oil was treated with hexane (30 mL), resulting in formation of a yellow precipitate. The solids were isolated by filtration, washed with hexane (30 mL) and $Et_2O$ (2 mL), and dried under vacuum to provide (3-F-Py)$_2$Pd(Ph)($CF_3$) (**14**; 155.6 mg, 56%) as a colorless solid. $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ (ppm) 8.63−8.62 (m, 1H), 8.56 (app d, $J$ = 5.2 Hz, 1H), 8.25−8.24 (m, 1H), 8.21 (app d, $J$ = 5.4 Hz, 1H), 7.60−7.56 (m, 1H), 7.46−7.41 (m, 4H), 7.26 (app dt, $J$ = 8.5, 5.3 Hz, 1H), 6.94 (t, $J$ = 7.3 Hz, 2H), 6.87 (d, $J$ = 7.2 Hz, 1H). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): $\delta$ (ppm) −21.2 (s, 3F), −122.2 (s, 1F), −122.72 (bs, 1F). $^{13}$C NMR (101 MHz, $CD_2Cl_2$): $\delta$ (ppm) 161.4 (d, $J$ = 22.2 Hz), 158.9 (d, $J$ = 22.3 Hz), 153.5 (q, $J$ = 9.8 Hz), 147.6, 147.3 (d, $J$ = 4.3 Hz), 140.3, 140.0, 139.8, 136.4, 127.1, 126.6 (d, $J$ = 5.5 Hz), 125.9, 125.7, 123.5. The remaining quartet from Pd−$CF_3$ was not resolved by $^{13}$C NMR spectroscopy. $^1$H NMR and $^{19}$F NMR spectra are consistent with literature data.[8]

**Preparation of (D$t$BPF)Pd(Ph)(CF$_3$) (15).** In an argon-filled glovebox, a flame-dried 25 mL round-bottom flask was charged with (3-F-Py)$_2$Pd(Ph)($CF_3$) (**14**; 150.0 mg, 0.34 mmol), 1,1′-bis(di-*tert*-butylphosphino)ferrocene (162.5 mg, 0.34 mmol, 1.02 equiv), THF (3.0 mL), and toluene (6.0 mL). The yellow solution was cooled to −35 °C in the glovebox freezer for 15 min before the volatiles were removed under vacuum. The remaining solids were redissolved in the THF/toluene mixture and concentrated again under vacuum. This process was repeated three times in total to remove 3-fluoropyridine. The solids were collected by filtration, washed with pentane and $Et_2O$, and dried under vacuum to provide (D$t$BPF)Pd(Ph)$CF_3$ (**15**; 142.4 mg, 58%) as a yellow solid. $^1$H NMR (400 MHz $C_6D_6$): $\delta$ (ppm) 8.10 (d, $J$ = 7.8 Hz, 2H), 7.22−7.19 (m, 2H), 7.05 t, $J$ = 7.2 Hz, 1H), 4.13 (s, 4H), 3.95 (s, 4H), 1.37−1.19 (m, 36H). $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ (ppm) 7.67 (d, $J$ = 7.5 Hz, 2H), 6.69 (t, $J$ = 7.5 Hz, 2H), 6.87 (t, $J$ = 7.3 Hz, 1H), 4.41 (s, 8H), 1.41−1.15 (m, 36H). $^{31}$P NMR (162 MHz, $C_6D_6$): $\delta$ (ppm) 38.0 (broad resonance, 1P), 32.5 (broad resonance, 1P). $^{19}$F NMR (376 MHz, $C_6D_6$): $\delta$ (ppm) −13.3 (t, $J$ = 31.5 Hz, 3F). $^1$H, $^{31}$P, and $^{19}$F NMR spectra are consistent with literature data.[8]

**Preparation of (Ph$_3$P)$_2$Pd(Ph)CF$_3$ (16).** In an argon-filled glovebox, a flame-dried 8 mL vial was charged with (Ph$_3$P)$_2$Pd(Ph)F (**SI5**; 190.0 mg, 0.26 mmol), benzene (3 mL), and $TMSCF_3$ (384 μL, 2.6 mmol, 10 equiv). The reaction mixture was stirred at rt for 1 h. The solution was concentrated, and pentane (3 mL) was added to force precipitation. The solids were collected by filtration, washed with pentane, and dried under vacuum to provide (Ph$_3$P)$_2$Pd(Ph)$CF_3$ (**16**; 167.3 mg, 83%) as a colorless solid containing trace amounts of benzene, which could not be removed by prolonged drying under vacuum. $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ (ppm) 7.45−7.41 (m, 12H), 7.38−7.34 (m, 6H), 7.29−7.25 (m, 12H), 6.52 (d, $J$ = 7.4 Hz, 2H), 6.28 (t, $J$ = 7.3 Hz, 1H), 6.15 (t, $J$ = 7.3 Hz, 2H). $^{31}$P NMR (162 MHz, $CD_2Cl_2$): $\delta$ (ppm) 26.6 (q, $J$ = 13.3 Hz, 2P). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): $\delta$ (ppm) −17.0 (t, $J$ = 13.6 Hz, 3F). $^{31}$P and $^{19}$F NMR spectra are consistent with literature data.[5,29]

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.9b00849.

Experimental procedures, compound characterization, and NMR spectra (PDF)

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### Notes

The authors declare the following competing financial interest(s): T.S. is co-owner of SyTracks A/S, which commercializes the two-chamber system (COware) and *13*C-COgen.

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