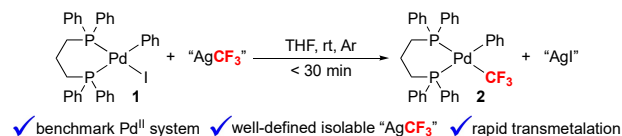


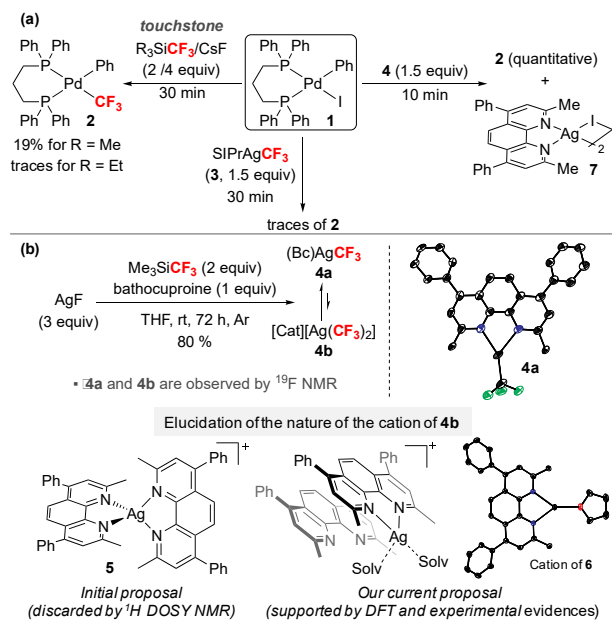


prevents the formation of inactive poly(trifluoromethyl)palladium compounds and the resulting product (**2**) does not undergo Ph–CF<sub>3</sub> coupling.<sup>8</sup> Secondly, only well-defined isolable trifluoromethylsilver(I) complexes were targeted to avoid potential reproducibility issues associated with in situ generated species. Finally, we pursued fast I-for-CF<sub>3</sub> exchanges (< 30 minutes), to minimize possible undesired by-products related to long reaction times.



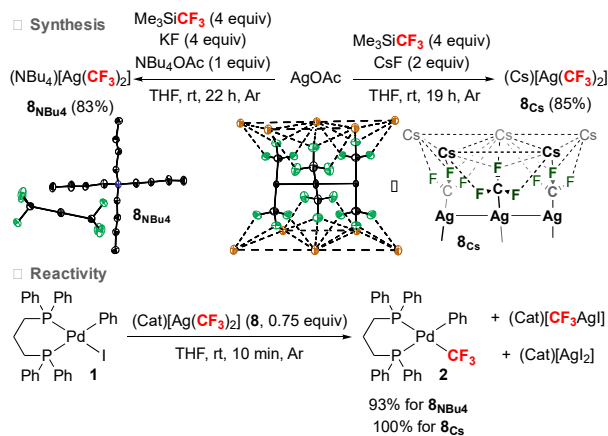
**Scheme 1.** Requirements for the initial study

Before exploring the CF<sub>3</sub> group transfer from Ag to (dppp)Pd(Ph)I, we established as touchstone the trifluoromethylation of **1** with the widely used nucleophilic trifluoromethyl sources R<sub>3</sub>SiCF<sub>3</sub> (R = Me,<sup>9</sup> Et<sup>4b,h,i</sup>) in combination with CsF. After 30 minutes, we only observed **2** in 19% and traces using Me<sub>3</sub>SiCF<sub>3</sub> and Et<sub>3</sub>SiCF<sub>3</sub>, respectively (Figure 2a).<sup>10</sup> With these results as a reference, we then focused on the activity of the scarce examples of isolated trifluoromethylsilver(I) compounds reported in the literature to date: SIPrAgCF<sub>3</sub><sup>11</sup> (SIPr = bis(1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene) and (bathophenanthroline)Ag(CF<sub>3</sub>).<sup>12</sup> The treatment of (dppp)Pd(Ph)I with 1.5 equiv of SIPrAgCF<sub>3</sub> (**3**)<sup>13</sup> resulted in <5% yield of (dppp)Pd(Ph)(CF<sub>3</sub>) after 30 minutes (Figure 2a). We discarded the exploration of the other known LAgCF<sub>3</sub>, bearing the bathophenanthroline ligand,<sup>12</sup> due to stability issues under our reaction conditions.<sup>14</sup> Notably, after some experimentation, using bathocuproine, we were able to prepare **4** in THF, as a mixture of (Bc)Ag(CF<sub>3</sub>) (**4a**; Bc = bathocuproine) in equilibrium with an ionic [Ag(CF<sub>3</sub>)<sub>2</sub>]<sup>-</sup> species (**4b**) (Figure 2b). Initially, we hypothesized that the structure of **4b** was [(Bc)<sub>2</sub>Ag][Ag(CF<sub>3</sub>)<sub>2</sub>], by analogy to related copper compounds.<sup>15</sup> However, a detailed NMR spectroscopic analysis, including DOSY experiments, confirmed the absence of [(Bc)<sub>2</sub>Ag]<sup>+</sup> as the cation of **4b**, on the basis of the higher hydrodynamic radius measured for [(Bc)<sub>2</sub>Ag](SbF<sub>6</sub>) (**5**) (6.86 Å), compared to **4** (4.33 Å). Challenged by this unexpected outcome, we performed computational studies which suggested,<sup>16</sup> as the most stable cation for **4b**, a structure that contains the silver center coordinated to a bathocuproine ligand along with two molecules of THF, and a second Bc bound to the system through stabilizing π–π interactions.<sup>17</sup> In line with the DFT calculations, we observed the formation of [(Bc)Ag(THF)](SbF<sub>6</sub>) (**6**), characterized by X-ray diffraction, upon exposure of **5** to THF. With the structural information of **4a/4b** in hand, we assessed the reactivity of this equilibrium mixture. Gratifyingly, the trifluoromethylation of (dppp)Pd(Ph)I with 1.5 equiv of **4** proceeded cleanly and quantitatively in 10 minutes to afford **2** and an iodo-bridged dimeric compound with Ag–Ag interactions (**7**) (Figure 2a).



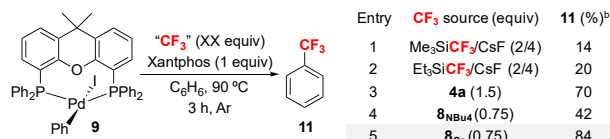
**Figure 2.** (a) Reactivity of Me<sub>3</sub>SiCF<sub>3</sub>, Et<sub>3</sub>SiCF<sub>3</sub>, **3** and **4** towards **1**. (b) Synthesis and characterization of **4**.

Inspired by the extraordinary transmetalating ability of **4**, and prompted by its different behavior from **3**, we wondered whether [Ag(CF<sub>3</sub>)<sub>2</sub>]<sup>-</sup> could be a non-innocent spectator and participate as CF<sub>3</sub> shuttle.<sup>7</sup> To unravel this key question, we targeted the synthesis of two well-defined (Cat)[Ag(CF<sub>3</sub>)<sub>2</sub>] salts, Cat = NBu<sub>4</sub> (**8NBu4**) or Cs (**8Cs**) to evaluate their relative stability and reactivity. As shown in Figure 3, the reaction of AgOAc with 4 equiv of Me<sub>3</sub>SiCF<sub>3</sub>, in THF at room temperature, in the presence of 4 equiv of KF and 1 equiv of NBu<sub>4</sub>OAc afforded a white crystalline solid, **8NBu4**, in 83% isolated yield. Following a similar synthetic route but using 2 equiv of CsF instead of the combination KF/NBu<sub>4</sub>OAc, we synthesized (Cs)[Ag(CF<sub>3</sub>)<sub>2</sub>] in 85% yield as a yellow solid. The structures of both salts, that can be stored for months at –30 °C under inert atmosphere in the dark,<sup>18</sup> were unambiguously confirmed by NMR spectroscopy, ESI-MS and single crystal X-ray diffraction. It is worth mentioning the different bonding situation between these ionic species. The X-ray structure of **8NBu4** shows a linear bis(trifluoromethyl)argentate paired together with the NBu<sub>4</sub> cation. In sharp contrast, **8Cs** presents a rather unique structure, with the silver atoms forming linear chains, and the cesium cations interacting with twelve different fluorine atoms.<sup>19</sup> Having synthesized and fully-characterized these singular ionic species, we next investigated their efficiency as nucleophilic trifluoromethyl sources. To our delight, the reaction of (dppp)Pd(Ph)I with 0.75 equiv of either of the two silver salts resulted in the quantitative formation of **2** in 10 minutes, when using **8Cs**, and in 93% yield for **8NBu4**.<sup>20</sup>



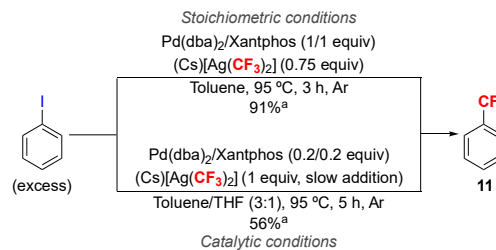
**Figure 3.** Synthesis, Characterization and Reactivity of  $(\text{Cat})[\text{Ag}(\text{CF}_3)_2]$  (Cat =  $\text{NBu}_4$ , Cs)

Next, we aimed at evaluating the real potential of our silver nucleophiles, focusing our attention on one of the few  $\text{Pd}^{\text{II}}$  systems which affords relatively facile  $\text{PhCF}_3$  coupling. In 2006, Grushin et al. reported the first example of C– $\text{CF}_3$  bond-forming reductive elimination from an isolated Xantphos-based  $\text{Pd}^{\text{II}}$  derivative, synthesized by treatment of  $(\text{Xantphos})\text{Pd}(\text{Ph})\text{F}$  with  $\text{Me}_3\text{SiCF}_3$ .<sup>4a</sup> In this work and subsequent elegant mechanistic studies,<sup>4d</sup> the authors explained in detail, not only the challenges associated to the reductive elimination from this system, but also the appealing difficulties related to unfruitful attempts to achieve the nucleophilic trifluoromethylation of  $(\text{Xantphos})\text{Pd}(\text{Ph})\text{I}$  (**9**) using  $\text{Me}_3\text{SiCF}_3/\text{CsF}$ , such as: i) ligand displacement by  $\text{CF}_3^-$ ; and/or ii) the formation of unproductive  $\text{Ph}-\text{Ph}$  homocoupling. Encouraged by our previous results, we envisioned that our silver nucleophiles could overcome these shortcomings and provide the unprecedented formation of  $\text{PhCF}_3$  using **9** as starting material (Scheme 2). Following the same strategy used for **1**, we first defined as touchstone the reactivity of **9** with  $\text{R}_3\text{SiCF}_3/\text{F}^-$  ( $\text{R} = \text{Me}$ , Et), under comparable reaction conditions to those reported previously for the high-yielding formation of  $\text{PhCF}_3$  from  $(\text{Xantphos})\text{Pd}(\text{Ph})(\text{CF}_3)$  (**10**).<sup>4a,d</sup> As expected, we observed the formation of the coupling product in low yields in the presence of  $\text{CsF}$  (14% and 20%, for  $\text{Me}_3\text{SiCF}_3$  and  $\text{Et}_3\text{SiCF}_3$  respectively). Then, we examined the reactivity of **9** with our most efficient  $\text{Ag}-\text{CF}_3$  sources, **4a**,<sup>21</sup>  $\mathbf{8}_{\text{NBu}_4}$  and  $\mathbf{8}_{\text{Cs}}$ . We were pleased to observe that all these transformations led to the targeted product in moderate to excellent yields (**4**: 70%,<sup>22</sup>  $\mathbf{8}_{\text{NBu}_4}$ : 42%, and  $\mathbf{8}_{\text{Cs}}$ : 84%). The lower reactivity of  $(\text{Bc})\text{Ag}(\text{CF}_3)$  and  $(\text{NBu}_4)[\text{Ag}(\text{CF}_3)_2]$  can be ascribed to unproductive pathways:<sup>23</sup> ligand scrambling between both metals which affords  $(\text{Bc})\text{Pd}(\text{Ph})(\text{CF}_3)$  for **4**, and the formation of poly(trifluoromethyl)complexes and decomposition to  $\text{Ag}^{\text{III}}$  for  $\mathbf{8}_{\text{NBu}_4}$ .<sup>18,23</sup> For  $\mathbf{8}_{\text{Cs}}$ , we corroborated the rapid and selective  $\text{CF}_3$  transfer by observing full conversion of **9** into **11** in less than 10 minutes in  $\text{C}_6\text{H}_6$  at room temperature.



**Scheme 2.** Thermolysis of **9** with different “ $\text{CF}_3^-$ ” sources. <sup>a</sup>Reaction conditions: **9** (0.006 mmol), Xantphos (0.006 mmol),  $\text{C}_6\text{H}_6$  (0.01 M) under Ar. <sup>b</sup><sup>19</sup>F NMR analysis using fluorobenzene or 4,4'-difluorobiphenyl as internal standards.

Based on these promising data, we next examined the compatibility of  $\mathbf{8}_{\text{Cs}}$  with all elementary steps involved in the catalytic cycle, under stoichiometric conditions in the presence of excess of PhI. As previously described, the accumulation of the oxidative addition product,  $(\text{Xantphos})\text{Pd}(\text{Ph})\text{I}$ , could favor the mismatched transmetalation shown in Figure 1. Delightfully, using  $\text{Pd}(\text{dba})_2$  as  $\text{Pd}^0$  source and 30 equiv of PhI, we observed the desired product (**11**) in slightly higher yield (91%) when compared to the entry 5 of Scheme 2 (Scheme 3), along with the regeneration of the oxidative addition product.<sup>24</sup> This result points out the capability of  $\mathbf{8}_{\text{Cs}}$  for precluding the side-product formation that could potentially lead to dead-end routes under catalytic conditions using Xantphos as ligand. Indeed, as a proof-of-concept, preliminary results show the formation of **11** in 56% yield by slow addition of  $\mathbf{8}_{\text{Cs}}$  under catalytic conditions in the presence of 60 equiv of PhI (Scheme 3).<sup>25</sup>



**Scheme 3.** Stoichiometric and catalytic reactions. <sup>a</sup><sup>19</sup>F NMR analysis using fluorobenzene as internal standard.

In summary, this work presents the potential of discrete “ $\text{AgCF}_3$ ”, including a unique  $(\text{Cs})[\text{Ag}(\text{CF}_3)_2]$  salt, as  $\text{CF}_3$  shuttle to  $\text{Pd}^{\text{II}}$  systems. Our results, not only provide the first reported example of stoichiometric and catalytic one-pot formation of  $\text{Ph}-\text{CF}_3$  starting from PhI, but also confirm the crucial role of the nucleophile in the transmetalation step, which can be decisive, enabling or preventing the product formation. Further work towards unravelling the potential of silver nucleophiles as transmetalating agents is currently ongoing in our laboratory.

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## Conflict of interest

The authors declare no conflict of interest.

**Keywords:** organometallic synthesis • silver • structural elucidation • transmetalation • trifluorometalation

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- [21] In benzene, the equilibrium is totally shifted towards **4a**, see p. S17.
- [22] This experimental result, along with those obtained in THF for the benchmark system, suggest the participation of **4a** and **4b** in the CF<sub>3</sub> group exchange.
- [23] See supporting information for further details on the thermolysis of **9** with the different CF<sub>3</sub>.
- [24] Grushin observed the formation of the mismatched product  $(Xantphos)Pd(CF_3)I$  during the thermolysis of  $(XantPhos)Pd(Ph)(CF_3)$  and PhI during 8 h at 70 °C. See SI p 5-7 from reference 4a.
- [25] The formation of **11** in moderate yield (56% yield or catalyst turnover number of 5.6) is not due to the well-precedented unproductive reactions discussed along the text, but for practical challenges related to the use of **8cs** as transmetalating agent under catalytic conditions. The product yield was calculated taking as limiting reagent **8cs** and considering the transmetalation of both CF<sub>3</sub> groups. See SI pS84 for further details.