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# Versatile Route to Arylated Fluoroalkyl Bromide Building Blocks

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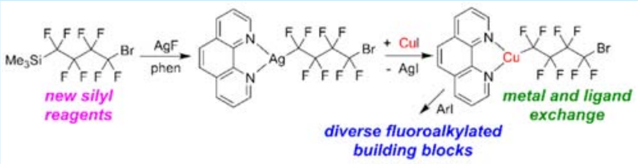
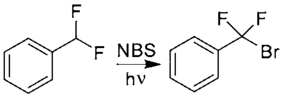
**S** *Supporting Information*

**ABSTRACT:** New difunctionalized and fluoroalkylated silyl reagents have been prepared that react with silver and copper salts to afford active catalysts that can be used to synthesize arylated fluoroalkyl bromide building blocks. It has been shown that the [(phen)Ag$(CF_2)_n$Br] intermediates are capable of transferring both the phenanthroline ligand and the fluoroalkyl bromide chain to copper iodide, eliminating the need for a preligated copper salt precursor. The methodology is compatible with various chain lengths of the fluoroalkyl halide functionality.



Arylated fluoroalkyl halides are important building blocks for discovery research[1−4] and in the preparation of electron acceptors for various applications in molecular electronics.[5] However, mild and versatile methods for their synthesis are lacking. Simple [Ar$CF_2$Br] complexes are typically made from reaction of [Ar$CF_2$H] with NBS under photochemical conditions (eq 1).[6] A synthesis for the longer chained [Ar$CF_2CF_2$X] building blocks was recently reported by Gouverneur and co-workers (eq 2).[7] In this example, Grignard reagents derived from aryl bromides were reacted with methyl chlorodifluoroacetate at −40 °C in THF to afford ketones, which upon treatment with diethylaminosulfur trifluoride (DAST) afforded the arylated fluoroalkyl chlorides (eq 2). Although elegant in design, this methodology is only useful for preparing [$C_2F_4$]-containing functionalities and uses a harsh fluorinating reagent that is incompatible with many organic functional groups. Methods for installing even longer fluoroalkyl halide chains are trickier and often involve high temperature radical reactions like that shown in eq 3.[3−5] Unless metal mediated, such radical processes can often lead to a mixture of regioisomers.[5]



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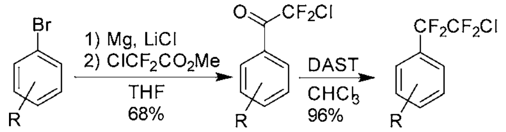

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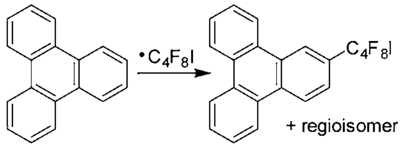

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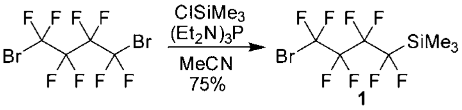

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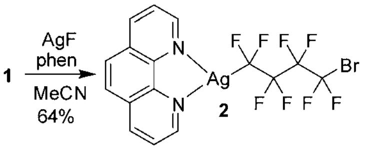

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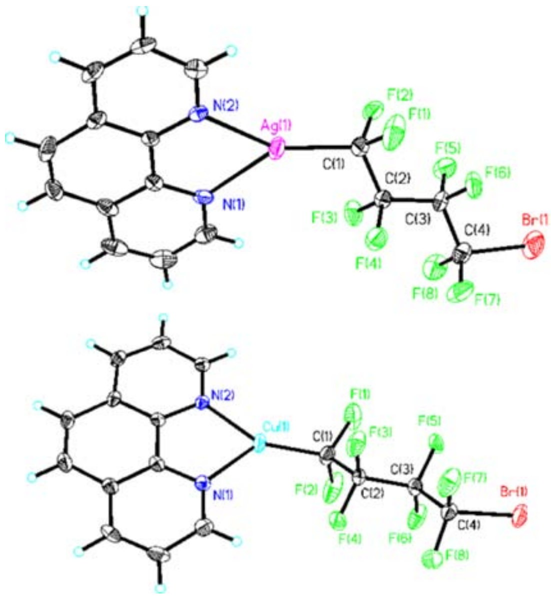

**Figure 1.** ORTEP diagram of **2** (top). Selected bond lengths (Å): Ag1−C1 2.096(10); Ag1−N2 2.281(7); Ag1−N1 2.353(8). Selected bond angles (deg): C1−Ag1−N2 150.5(3); C1−Ag1−N1 137.6(3); N2−Ag1−N1 71.9(3). ORTEP diagram of **6** (bottom). Selected bond lengths (Å): Cu1−C1 1.928(7); Cu1−N2 2.022(4); Cu1−N1 2.091(5). Selected bond angles (deg): C1−Cu1−N2 145.5(3); C1−Cu1−N1 133.1(2); N2−Cu1−N1 80.78(19).

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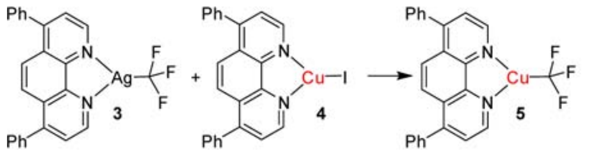

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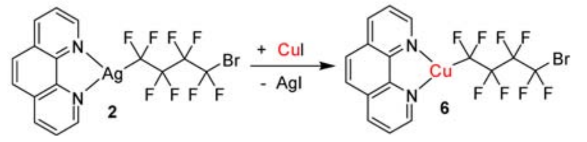

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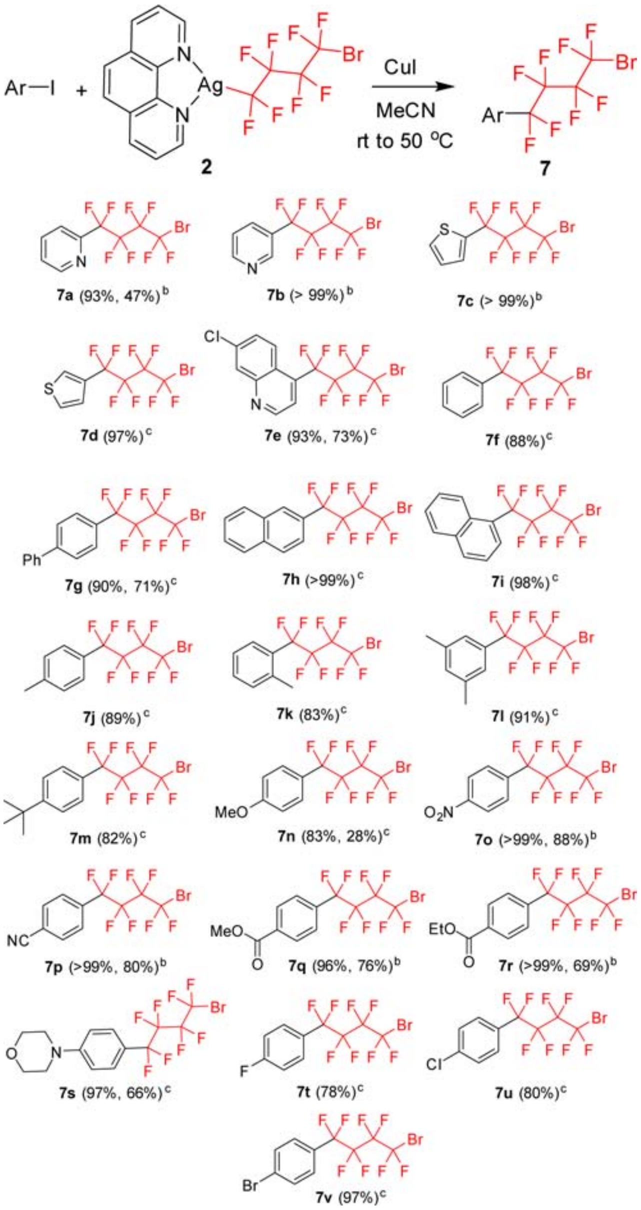
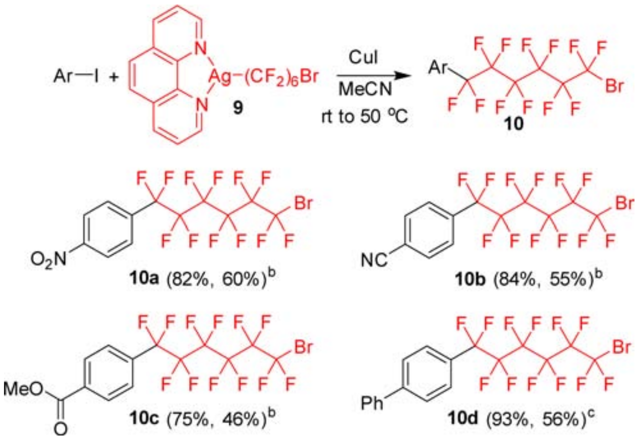
## Scheme 1. Preparation of Arylated Octafluoropentyl Bromide Building Blocks from Aryl Iodides[a]



[a] The yields of $Ar(CF_2)_4Br$ were determined by $^{19}F$ NMR spectroscopy using α,α,α-trifluorotoluene as internal standard. Isolated yields of nonvolatile products are the second number in parentheses. [b] Reactions run at room temperature for 24 h. [c] Reactions run at room temperature for 20 h followed by an additional 24 h at 50 °C.

## Scheme 2. Preparation of Arylated Dodecafluoroheptyl Bromide Building Blocks from Aryl Iodides[a]



[a] Yields reported as ($^{19}F$ NMR, isolated). [b] Reactions run at room temperature for 24 h. [c] Reactions run at room temperature for 20 h followed by 24 h at 50 °C.

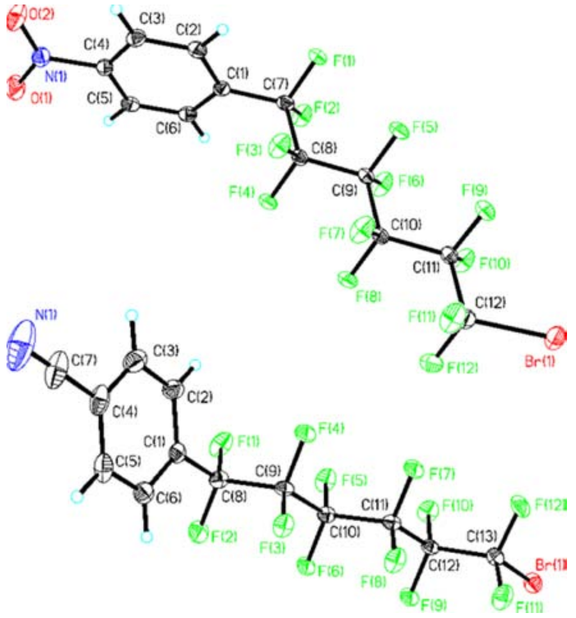


**Figure 2.** ORTEP diagrams of **10a** (top) and **10b** (bottom). See the Supporting Information for bond lengths and angles.

We sought to develop a user-friendly method that would satisfy two important conditions. First, the aryl groups would originate from the large number of commercially available aryl iodides. Second, the method would be compatible with various chain lengths of the fluoroalkyl halide functionality. We thought the best approach to satisfy these conditions would be to create a difunctionalized fluoroalkyl reagent that is capped on one side of the fluoroalkyl chain with a bromine atom and on the other side with a trimethylsilyl group. This way, transferring the fluoroalkyl chain to a transition-metal catalyst can be initiated at the silicon atom while leaving the carbon−bromine bond intact (see below). We first explored whether such a reagent could be prepared from commercially available 1,4-dibromooctafluorobutane. Gratifyingly, we found that reacting a stoichiometric amount of $[ClSiMe_3]$ with 1,4-dibromooctafluorobutane under conditions known to generate perfluoroalkylated silanes[8] led to the formation of the difunctionalized product **1** in 75% isolated yield (eq 4). The formation of the disilylated product, [$Me_3Si(CF_2)_4SiMe_3$],[9] occurred in less than 5% yield.

Compound **1** is a colorless oil that displays four signals with near-equivalent coupling constants in the $^{19}F$ NMR spectrum ($CDCl_3$) at $\delta$ −64.0 (br t, $J$ = 13.7 Hz), −118.1 (br t, $J$ = 14.4 Hz), −119.1 (br t, $J$ = 13.6 Hz), −129.3 (br t, $J$ = 13.9 Hz). With the reagent **1** in hand, we then explored its reactivity with transition metals. We found that **1** reacted cleanly with [AgF] in the presence of 1,10-penanthroline to afford **2** in 64% isolated yield (eq 5). The X-ray structure of **2** is provided in Figure 1 and confirmed that upon fluoroalkylation of silver the carbon−bromine bond remained intact.

Transfer of the fluoroalkyl moiety of **2** from the silver atom to a copper complex was explored because copper is known to mediate the fluoroalkylation of aryl iodides.[10] Weng and coworkers showed that [(bathophen)$AgCF_3$] (**3**) reacts with [(bathophen)CuI] (**4**) to afford complex **5** in high yields (eq 6).[11] The fate of the silver complex in that report was not disclosed. Here, we show that preligation to a copper halide precursor is not needed to achieve such a transmetalation and that simple [CuI] will react with **2** to afford the fluoroalkyl copper reagent **6** where *both* the fluoroalkyl group and the diimine ligand are transferred to copper from silver. The reaction is quantitative by $^{19}F$ NMR spectroscopy, and **6** can be obtained in 67% isolated yield (see the Supporting Information). X-ray data support the dual transmetalations to copper (Figure 1). Complex **6** is difficult to isolate in the solid state as evidence of shock sensitivity upon drying was observed. The reaction described in eq 7 can also be monitored colorimetrically, as the formation of **6** is concurrent with a change from a colorless to an orange solution.

Complex **6**, either used directly or generated in situ, is a highly active catalyst for the construction of (hetero)arylated octafluoropentyl bromide building blocks from aryl iodides. Heteroaryl iodides afforded diverse products in yields up to 99% (Scheme 1, **7a−e**). Electron-deficient arenes all reacted similarly to give products (**7g−i,o−r**) in excellent yields. Electron-rich arenes were also amenable to the reaction conditions, and alkylated arenes gave products (**7j−m**) in yields up to 91%. Even 4-iodoanisole afforded fluoroalkylated product **7n** in 83% NMR yield. Finally, dihaloarenes provided difunctionalized products **7t−v** in good to excellent yields. The sensitivity of the perfluoroalkyl bromide functional group, the volatility of the products, and the similarity of the retention factors between starting materials and products are believed to contribute to the differences between NMR and isolated yields. X-ray structures of **7o** and **7p** have been obtained and are included in the Supporting Information.

Having shown that the perfluoroalkyl copper reagents can fluoroalkylate aryl iodides, we set out to satisfy our second condition for the methodology by showing that it works for other fluoroalkyl bromide chain lengths. Indeed, the dodecylfluorohexyl derivative [$Me_3Si(CF_2)_6Br$] (**8**) can be prepared by a method similar to that described in eq 4. Moreover, the silver complex [(phen)$Ag(CF_2)_6Br$] (**9**) can be readily isolated (see the Supporting Information) and used to generate a reactive copper complex in situ for use in cross-coupling reactions (see below).

Proof-in-principle that the longer chained dodecylfluorohexyl bromide building blocks can be prepared with this methodology is provided in Scheme 2. 4-Iodonitrobenzene reacted with **9** in the presence of [CuI] to afford **10a** in 82% yield. This product has been structurally characterized, and the ORTEP diagram is shown in Figure 2. Other functional groups on the aryl iodide substrate like cyano, ester, and phenyl groups were also tolerated to provide fluoroalkylated **10b−d**.

In summary, we have developed a convenient method to prepare arylated fluoroalkyl bromide building blocks. The methodology involves the use of the large pool of commercially available aryl iodides as substrates and is compatible with various chain lengths of the fluoroalkyl halide functionality. The observation that preligated copper salt precursors are not needed when preparing activate copper fluoroalkyl complexes from well-defined silver analogues may be useful to other fluoroalkylation methodologies.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00032.

X-ray crystallographic data (CIF)
Experimental procedures and full spectroscopic data for all new compounds (PDF)

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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