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Silver(I) Perfluoroalcoholates: Synthesis, Structure, and their Use as Transfer Reagents

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Herein we report a general access to silver(I) perfluoroalcoholates, their structure in the solid state and in solution, and their use as transfer reagents. The silver(I) perfluoroalcoholates are prepared by the reaction of AgF with the corresponding perfluorinated carbonyl compounds in acetonitrile and are stable for a prolonged time at −18 °C. X-ray analysis of single crystals of perfluoroalcoholate species showed that two Ag(I) centers are bridged by the alcoholate ligands. In acetonitrile solution, Ag[OCF_3] forms different structures as indicated by IR spectroscopy. Furthermore, the silver(I) perfluoroalcoholates can be used as easy-to-handle transfer reagents for the synthesis of Cu[OCF_3], Cu[OC_2F_5], [PPh_4][Au$(CF_3)_3(OCF_3)$], and fluorinated alkyl ethers.

Introduction

In recent years, the trifluoromethoxy group (–OCF_3) gained importance as a unique functional group in medicinal research,[1,2] materials science,[3] and coordination chemistry.[4–7] Particularly, trifluoromethoxylation is a useful tool to tune the lipophilicity and metabolic stability, and to influence the conformation of bioactive compounds.[2] Unlike other fluorinated groups, the –OCF_3 group has the advantage of being degradable into non-persistent compounds, like CO_2 and HF.[8–10] Due to the high stability, mobility, and toxicity of some PFAS (per- and polyfluorinated alkyl substances), the EU demands a ban of these PFAS with some exceptions, especially for substances with –OCF_3 groups and for agrochemicals and pharmaceuticals.[11] This shifts the focus even more to the research towards valuable and economical methods to introduce the –OCF_3 group into organic molecules. Important examples for –OCF_3 containing drugs include Pretomanid[12] or the recently developed SARS-CoV-2 MPro inhibitor MI-09,[13] while Triflumuron[14] is a common insecticide (Figure 1).

In contrast to the well-established –OCF_3 group, higher perfluoroalkoxy groups remain underutilized despite their potential. For instance, the pentafluoroethoxy-substituted derivative of Riluzole shows a higher "antiglutamate" activity (ED_{50} = 2.5 mg/kg) compared to Riluzole (ED_{50} = 3.2 mg/kg), which is used for the treatment of amyotrophic lateral sclerosis (ALS).[15] Similarly, Flubendiamide, an insecticide for controlling lepidopterous insects, is functionalized with a perfluorinated *iso*-propyl group which highlights the potential of larger perfluorinated groups.[16] Therefore, it can be anticipated that higher perfluoroalkoxy groups such as –OC_2F_5, –O(*i*-C_3F_7), and –O(*n*-C_3F_7) could complement the toolbox of fluorinated moieties for the finetuning of pharmacological properties of drugs and for agrochemicals.

However, although several reagents have been developed that allow the convenient preparation of trifluoromethoxylated compounds, there are only a few suitable reagents for the introduction of higher perfluoroalkoxy groups.[17–19] While most

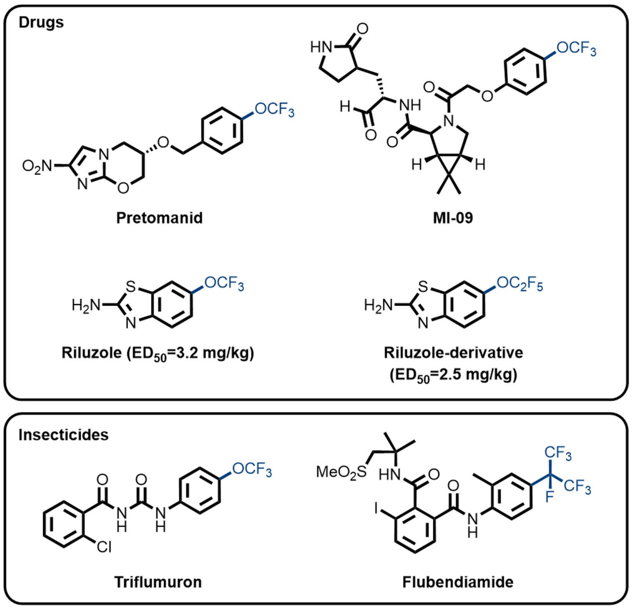

Figure 1. Examples of bioactive substances containing –OCF_3, –OC_2F_5, or –*i*-C_3F_7 groups under development or used as drugs or insecticides.

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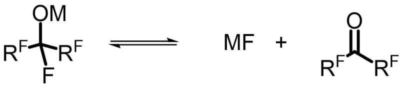
perfluoroalkoxylation reagents are bench-stable and easy-to-handle,[20,21] they also present some drawbacks. These include high cost, complex preparations, and poor atom economy. In addition, many reagents require stoichiometric amounts of silver(I) salts to promote the desired perfluoroalkoxylation reaction. Very recently, Schoenebeck and coworkers developed a valuable method for the simple preparation of a stable solution of Ag[OCF_3] in acetonitrile via the reaction of bis(trichloromethyl)carbonate (BTC) with AgF.[22] Additionally they could show that Ag[OCF_3] can be used for the effective synthesis of *N*-difluoromethyl amides.[23]

Stable salts of the trifluoromethoxide anion [OCF_3]$^-$ are reported and structurally analyzed for different cations like M^+ (M = K, Rb, and Cs),[24] Py^+ ((2,4-dinitrophenyl)(dimethylamino)pyridinium),[25] [NR_4]$^+$ (R = alkyl),[19] pip^+ (1,1,3,3,5,5-hexamethylpiperidinium),[26] and [$(Me_2N)_3S$]$^+$.[27] Cu[OCF_3] is also known in solution[28] and was crystalized as side product from the attempted synthesis of [(SIPr)Cu(OCF_3)].[6] For the pentafluoroethoxide anion [OC_2F_5]$^-$, salts with cations such as M^+ (M = Rb and Cs),[29,30] [NR_4]$^+$,[19] and pip^+[26] form stable compounds, while for other primary and secondary perfluorinated alkoxides only few examples are reported. Hexafluoroacetone reacts with CsF, KF, and AgF in acetonitrile under formation of the corresponding [*i*-OC_3F_7]$^-$ salts. By metathesis reaction of the potassium salt with [NEt_4]ClO_4 the [NEt_4][O(*i*-C_3F_7)] salt can be obtained.[31] Similarly, the pip^+[26] and [$(Me_2N)_3S$]$^+$[27] salts could be synthesized and structurally analyzed. Also oxalyl fluoride is known to react with one equivalent of [NMe_4]F forming the mono alkoxide [NMe_4][FC(O)CF_2O].[26]


(1)

Metal salts of perfluorinated tertiary alcoholates like the Ag[*t*-OC_4F_9] or Li[*t*-OC_4F_9] are relatively stable compounds,[32,33] while the metal alcoholates with an α-fluorine (M[OC(R^F)$_2$F]) are in an equilibrium with the carbonyl ((O)C(R^F)$_2$) and the corresponding metal fluoride (MF) (1). This equilibrium is shifted to M[OR^F] if the lattice energy of the MF is comparably low. In the row of the alkaline metal fluorides the lattice energy decreases from Li to Cs while the stability of the corresponding M[OR^F] species is increasing.[24] M[OC(R^F)$_2$F] species with the tendency to decompose can be stabilized by overcoming the lattice energy of MF by dissolution in a suitable solvent.[22] Alternatively, M[OCF_3] species like [(SIPr)M(OCF_3)] (M = Cu or Au),[6] [Ag(bpy)(PPh^tBu_2)(OCF_3)],[4] [Ag(PPh^tBu_2)(OCF_3)]$_2$,[7] or [Ag-(Aryl-BIAN)(THF)(OCF_3)][5] are stabilized by using, e.g., phosphines, NHC or bidentate nitrogen ligands. Therefore, we envisaged to prepare and investigate an array of silver(I) salts of perfluoroalkoxy groups that could be used as atom-economic reagents for the introduction of perfluoroalkoxy groups into organic and inorganic molecules.

Results and Discussion

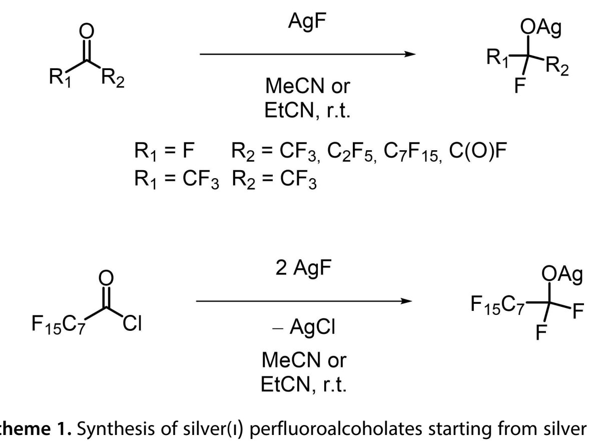
Silver(I) Trifluoromethoxide

At the outset, we envisioned the direct synthesis of Ag[OCF_3] from carbonyl fluoride and silver(I) fluoride as the simplest and most atom-economic starting materials. In a first experiment, we exposed a suspension of AgF in acetonitrile to an atmosphere of carbonyl fluoride providing Ag[OCF_3] in a quantitative yield according to ^{19}F NMR spectroscopy after only 15 minutes (Scheme 1). After filtration of the reaction mixture, a clear solution of Ag[OCF_3] in acetonitrile was obtained, which is in accordance with previous results.[22]

This solution decomposes slowly and showed a 15 % lower Ag[OCF_3] content after 6 days and had completely decomposed after one month at room temperature, while at −18 °C no significant decomposition was observed even after 15 months.

Structure

Single crystals of Ag[OCF_3] were obtained by cooling an acetonitrile solution to −40 °C. X-ray analysis of these crystals reveals the formation of polymeric chains of [Ag(MeCN)$_2$(OCF_3)]$_n$ (Figure 2). In this structure, the silver cation is distorted trigonally pyramidal (τ_4 = 0.80) coordinated by two acetonitrile molecules and two [OCF_3]$^-$ anions, while the [OCF_3]$^-$ anion coordinates as a bridging ligand via the oxygen atom to two silver centers. Due to the disorder of the –CF_3 group we do not discuss the C–F bond lengths. However, this does not affect so much the C–O bond, which shows a bond length of 123.28(19) pm and is similarly short as in [$(Me_2N)_3S$][OCF_3] (122.7(4) pm)[27] due to its high double bond character, despite the coordination of the [OCF_3]$^-$ anion to the silver atom. In the similar ligand-stabilized compounds [Ag(bpy)(PPh^tBu_2)(OCF_3)] (128.1(3) pm)[4] and [Ag(Aryl-BIAN)(THF)(OCF_3)] (131.5(6) pm)[5] the C–O bonds are significantly longer. When warming up these crystals to room temperature, decomposition under evolution of a gas was observed, indicating the formation of COF_2, AgF, and MeCN.



Scheme 1. Synthesis of silver(I) perfluoroalcoholates starting from silver fluoride and fluorinated carbonyl compounds.

By adding 2 equivalents of 2,2′-bipyridine (bpy) to a solution of $Ag[OCF_3]$ the room-temperature-stable compound $[Ag(bpy)_2][OCF_3]$ can be isolated (2). X-ray analysis of single crystals obtained similarly to the ones of $Ag[OCF_3]$ revealed an ion separation in the solid state (Figure 2). The exchange of the acetonitrile ligands by the stronger bpy ligands leads to the formation of the $[Ag(bpy)_2]^+$ cation, in which the coordination sphere of Ag is saturated by bpy ligands. The $[OCF_3]^-$ anion is slightly distorted ($\tau_4 = 0.90$) like in $Ag[OCF_3]$ and the bond lengths are similar to the corresponding ones in $Ag[OCF_3]$ and $[(Me_2N)_3S][OCF_3]$.[27]

$$[Ag(MeCN)_2(OCF_3)]_n \xrightarrow[\text{MeCN, r.t.}]{\text{2 eq. bpy}} n\,[Ag(bpy)_2][OCF_3] \quad (2)$$

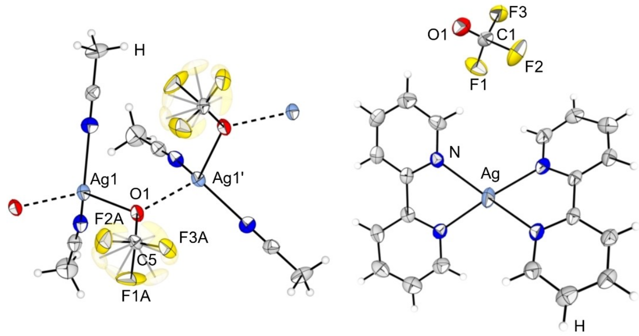


Figure 2. Polymeric chain structure of $[Ag(MeCN)_2(OCF_3)]_n$ (left) and molecular structure of $[Ag(bpy)_2][OCF_3]$ (right) in the solid state. Thermal ellipsoids are set at 50% probability. Disorder of the CF_3 group (left) and solvent and second molecule (right) are omitted for clarity. Selected bond lengths [pm] and angles [°] of $[Ag(MeCN)_2(OCF_3)]_n$: 133.9(8) (C5−F1 A), 138.3(8) (C5−F2 A), 136.6(9) (C5−F3 A), 123.28(19) (C5−O1), 234.17(12) (O1−Ag1), 239.98(12) (O1−Ag1′), 116.5(6) (O1−C5−F1 A), 102.2(7) (F1 A−C5−F2 A). Selected bond lengths [pm] and angles [°] of $[Ag(bpy)_2][OCF_3]$: 122.5(5) (C1−O1), 137.9(5) (C1−F1), 137.5(5) (C1−F2), 137.9(5) (C1−F3), 116.2(4) (O1−C1−F1), 102.5(3) (F1−C1−F2).

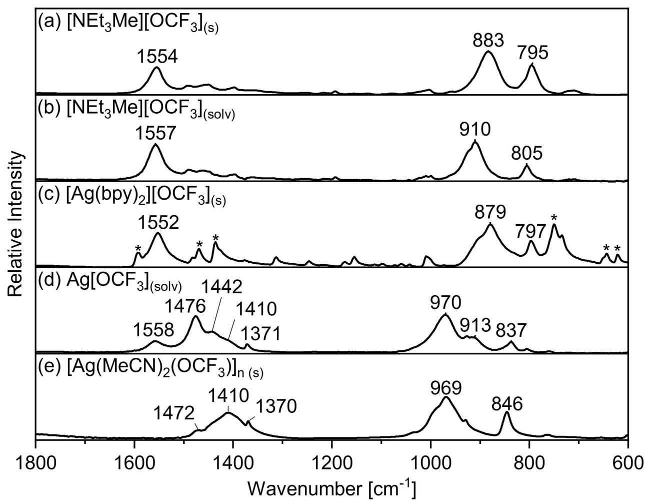


Figure 3. ATR infrared spectra between 600 and 1800 cm^{-1} of solid (s) or dissolved in acetonitrile (solv) $[OCF_3]^-$ compounds. (a): solid $[NEt_3Me][OCF_3]$ at r.t., (b): $[NEt_3Me][OCF_3]$ 0.65 M solution in acetonitrile at r.t., (c): $[Ag(bpy)_2][OCF_3]$ solid at r.t. (* = $[Ag(bpy)_2]^+$), (d): $[Ag][OCF_3]$ 0.65 M solution in acetonitrile at r.t., (e) crystals of $[Ag(MeCN)_2(OCF_3)]_n$ at $T = -40$ °C.

IR Spectroscopic Investigations

To get more insights into the nature and especially the stability of $Ag[OCF_3]$ in solution and their effects on the reactivity we compared the ATR infrared spectra of different $[OCF_3]^-$ containing compounds in the solid state or in acetonitrile solution (Figure 3). Quaternary ammonium cations like $[NEt_3Me]^+$ are known for their weak interactions with anions.[34] Therefore, we anticipated that the ion interactions in $[NEt_3Me][OCF_3]$ should be weak as well. The ATR IR spectrum of solid $[NEt_3Me][OCF_3]$ (a) obtained by reacting $[NEt_3Me]Cl$ with $Ag[OCF_3]$, shows a strong band for the C–O stretching (ν(C–O)) at 1554 cm^{-1} and at 883 and 795 cm^{-1} for the antisymmetric (ν_{as}(C–F)) and symmetric (ν_s(C–F)) C–F stretching mode, respectively. In solution (MeCN) the C–F stretching bands are slightly blue shifted (b). The ATR IR spectrum of solid $[Ag(bpy)_2][OCF_3]$ (c) shows bands of the $[OCF_3]^-$ anion similar to the corresponding ones in $[NEt_3Me][OCF_3]$. Since the ion separation in $[Ag(bpy)_2][OCF_3]$ crystals is known from the X-ray analysis the weak ion interactions in $[NEt_3Me][OCF_3]$ can be confirmed from the IR spectra. However, the ATR IR spectrum of $Ag[OCF_3]$ in solution (d) show bands for different $[OCF_3]^-$ anion species. Besides smaller bands for the isolated $[OCF_3]^-$ anion, bands for different oligo and polymeric structures are observed. In the case of the solid $[Ag(MeCN)_2(OCF_3)]_n$ the ν(C–O) appear as a broad band with a red shifted maximum at 1472 cm^{-1} and minor bands at 1410 and 1370 cm^{-1}. Contrary to the similar C–O bond lengths in $[Ag(MeCN)_2(OCF_3)]_n$ and $[Ag(bpy)_2][OCF_3]$, the ν(C–O) is significantly shifted in solid $[Ag(MeCN)_2(OCF_3)]_n$ to lower wavenumbers indicating a lower bond strength. This mismatch is most likely due to effects regarding the polymeric structure. The comparison of IR spectra of different $[OCF_3]^-$ species cannot fully clarify the structure of $Ag[OCF_3]$ in MeCN solution. The observation of different species indicates an equilibrium between isolated $[OCF_3]^-$ anions and those bound to silver cations. The occurrence of many species can also be an explanation for the very broad ^{19}F NMR signal of $Ag[OCF_3]$. Nevertheless, the partially isolated $[OCF_3]^-$ anions should have a higher nucleophilicity than those bound to silver centers, while the coordination to silver can facilitate reactivities over the coordination sphere of the metal.

Reaction Energy of Ag[OCF3] Synthesis

During the synthesis of $Ag[OCF_3]$ we noticed an exothermic reaction when adding carbonyl fluoride to AgF. To quantify the released energy, we investigated the thermodynamic properties of the reaction by heat flow calorimetry. The reaction enthalpy was determined to be $\Delta_R H = -66.7$ kJ mol^{-1}. This is in good agreement with the solvation corrected (MeCN) fluoride ion affinity FIA_{solv}(MeCN) = 71 kJ mol^{-1} of COF_2 obtained from the experimental FIA (208.8 kJ mol^{-1})[35] and the calculated solvation energy at PW6B95-D3(BJ)/def2-QZVPP level of theory. However, the value for the FIA disregards the interaction of the $[OCF_3]^-$ anion with the silver cations or the energy contribution of the solvation of AgF in acetonitrile.

Higher Silver(I) Alkoxides

Intrigued by the easy and clean formation of Ag[OCF_3] we anticipated that this reactivity could be extended to further carboxylic acid fluorides. The calculated solvation (MeCN) corrected FIA values at PW6B95-D3(BJ)/def2-QZVPP level of theory of trifluoroacetyl fluoride ($CF_3C(O)F$, 69 kJ mol^{-1}), pentafluoropropionyl fluoride ($C_2F_5C(O)F$, 68 kJ mol^{-1}), hexafluoroacetone ($CF_3C(O)CF_3$, 74 kJ mol^{-1}), oxalyl fluoride (F(O)CC(O)F, 60 kJ mol^{-1}), and perfluorooctanic acid fluoride ($C_7F_{15}C(O)F$, 49 kJ mol^{-1}) show only a small difference to the value of COF_2 (See Experimental Section for Details). Indeed, the reaction of AgF with these fluorinated carbonyls gave the corresponding $AgOR^F$ compounds in quantitative yields within 15 minutes (Scheme 1). F(O)CC(O)F was found to react with only one equivalent of AgF forming the monoanion. Instead of $C_7F_{15}C(O)F$ the corresponding acid chloride was used together with 2 equiv. of AgF (Scheme 1).

The ^{19}F NMR spectra of the silver(I) perfluoroalcoholates show a broad signal for the α-fluorine atom with shifts of δ(ppm) = −0.3 ppm (Ag[$OCF_2C(O)F$]), −25.9 ppm (Ag[OCF_3]), −33.2 ppm (Ag[OC_8F_{17}]), −34.5 ppm (Ag[O(n-C_3F_7)]), −41.0 ppm (Ag[OC_2F_5]), and −80.8 ppm (Ag[O(i-C_3F_7)]). The other $-CF_2-$ and $-CF_3$ groups have relatively sharp signals in the normal region for these groups. Notably, Ag[$OCF_2C(O)F$] shows only one signal for all three fluorine atoms indicating a fast exchange of the fluoride between the two sides.

X-ray Analysis

Ag[OC_2F_5] and Ag[O(i-C_3F_7)] were crystallized by cooling propionitrile solution to −77 °C. In contrast to the polymeric chain structure of Ag[OCF_3], the X-ray diffraction analysis of both colorless crystals reveals the formation of dimeric species [Ag(EtCN)$_2$(OC_2F_5)]$_2$ and [Ag(EtCN)$_2${O(i-C_3F_7)}]$_2$ (Figure 4). Even though these structures differ from the polymeric structure of Ag[OCF_3] there are several similarities. In [Ag(EtCN)$_2$(OC_2F_5)]$_2$ and [Ag(EtCN)$_2${O(i-C_3F_7)}]$_2$ the silver atoms are coordinated by two propionitrile molecules and two bridging alcoholate ligands in a trigonal pyramidal (τ_4 = 0.82) and distorted seesaw geometry (τ_4 = 0.73), respectively.

The C–F bond lengths at the α carbon atom are in good agreement with those in the corresponding pip salts.[26] The C–O bond lengths are in the typical range[26] and increase from Ag[OCF_3] (123.28(19) pm) to [Ag(EtCN)$_2$(OC_2F_5)]$_2$ (124.8(2) pm) and to [Ag(EtCN)$_2${O(i-C_3F_7)}]$_2$ (129.07(14) pm), possibly due to the exchange of fluorine atoms by the slightly less electronegative CF_3 groups, resulting in a higher electron density at the central carbon atom.

Transmetallation Reactions and Coordination

Besides the perfluoroalcoholates of silver(I), the transfer to other metal centers is of interest with respect to new pathways for the incorporation of these groups into organic molecules. Therefore, we re-evaluated the less described Cu[OCF_3] by the transmetalation reaction of Ag[OCF_3] with CuCl (Scheme 2a). The ^{19}F NMR spectrum shows a very broad signal at δ = −24.2 ppm (fwhm = 1500 Hz) for the [OCF_3]$^-$ anion. In the same manner Cu[OC_2F_5] can be obtained starting from Ag[OC_2F_5] and CuCl (Scheme 2a). The ^{19}F NMR spectrum shows a very broad signal at δ = −39.4 ppm (fwhm = 1600 Hz) for the fluorine atoms at the α carbon and a singlet at δ = −83.9 ppm for the CF_3 group. Both substances are stable for a short time in MeCN solution but decompose upon removal of the solvent. Crystals of [Cu(MeCN)$_4$][OCF_3] and [Cu(MeCN)$_4$][OC_2F_5] suitable for X-ray diffraction could be obtained by slowly cooling the corresponding acetonitrile solutions to −40 °C. In contrast to the silver(I) derivatives, [Cu(MeCN)$_4$][OCF_3] and [Cu(MeCN)$_4$][OC_2F_5] show a different connectivity (Figure 5). The Cu atoms are coordinated by four MeCN molecules, while the [OR^F]$^-$ anions are isolated. In [Cu(MeCN)$_4$][OCF_3] one of the three crystallographically independent [OCF_3]$^-$ anions in the unit cell is disordered. The C–F and C–O bond lengths are similar to the ones in the corresponding silver(I) perfluoroalcoholates.

In contrast, attempts to crystallize Cu[O(n-C_3F_7)] and Cu[O(i-C_3F_7)], obtained by transmetalation reactions, failed, although

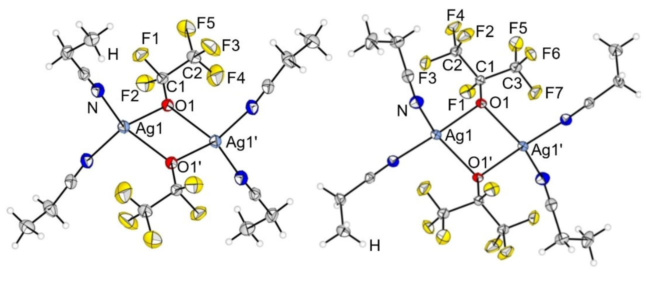
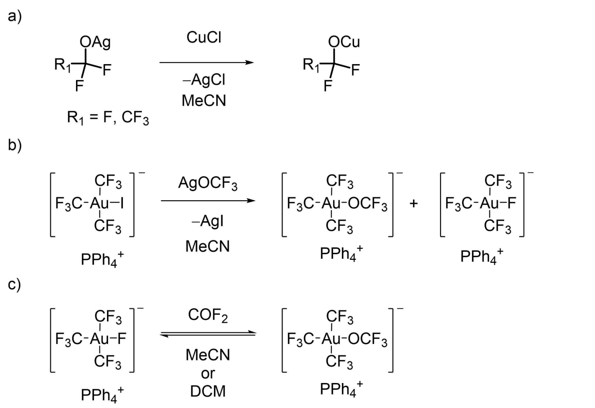


Figure 4. Molecular structure of [Ag(EtCN)$_2$(OC_2F_5)]$_2$ (left) and [Ag(EtCN)$_2${O{i-C_3F_7)}]$_2$ (right) in the solid state. Thermal ellipsoids are set at 50% probability. Co-crystallized solvent molecules are omitted for clarity. Selected bond lengths [pm] and angles [°] of [Ag(EtCN)$_2$(OC_2F_5)]$_2$: 140.1(2) (C1−F1), 141.4(2) (C1−F2), 124.8(2) (C1−O1), 235.45(13) (O1−Ag1), 238.73(13) (O1−Ag1′), 114.90(15) (O1−C1−F1), 100.82(14) (F1−C1−F2). Selected bond lengths [pm] and angles [°] of [Ag(EtCN)$_2${O{i-C_3F_7)}]$_2$: 143.19(13) (C1−F1), 129.07(14) (C1−O1), 231.21(9) (O1−Ag1), 242.05(9) (O1−Ag1′), 114.16(9) (O1−C1−F1).



Scheme 2. a) Transmetalation reaction of Ag[OCF_3] with CuCl under formation of Cu[OCF_3], b) reaction of [PPh_4][Au(CF_3)$_3$I] with Ag[OCF_3] and c) reaction of [PPh_4][Au(CF_3)$_3$F] with COF_2.

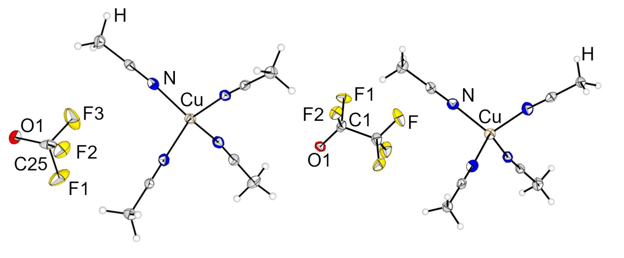


Figure 5. Molecular structure of $[Cu(MeCN)_4][OCF_3]$ (left) and $[Cu(MeCN)_4][OC_2F_5]$ (right) in the solid state. Thermal ellipsoids are set at 50% probability. Co-crystallized solvent molecules are omitted for clarity. Selected bond lengths [pm] and angles [°] of $[Cu(MeCN)_4][OCF_3]$: 124.0(6) (C25–O1), 138.8(7) (C25–F1), 139.4(7) (C25–F2), 137.2(7) (C25–F3), 115.8(6) (O1–C25–F1), 102.6(4) (F1–C25–F2). Selected bond lengths [pm] and angles [°] of $[Cu(MeCN)_4][OC_2F_5]$: 126.2(5) (C1–O1), 143.3(3) (C1–F1), 140.1(5) (C1–F2), 111.8(3) (O1–C1–F1), 104.0(3) (F1–C1–F2).

the ^{19}F NMR spectra showed signals for perfluoroalcoholate species. Instead of the desired Cu(I) compounds, crystals of mixed valent Cu(I/II) species were obtained. From an experiment to synthesize $Cu[O(i\text{-}C_3F_7)]$ in propionitrile solution, crystals could be obtained showing a species with a Cu(II) center coordinated by the chelating ligand $[OC(CF_3)_2–O–C(CF_3)_2O]^{2-}$and $[Cu(MeCN)_4]^+$ cations (SI, Figure S1).

Very recently our group synthesized the first Au(III) complex with $[OCF_3]^-$ as a ligand, $[AuF_2(OCF_3)(SIMes)]$, by the reaction of $[AuF_3(SIMes)]$ and COF_2.[36] Herein we report the formation of the anionic Au(III) complex $[Au(CF_3)_3(OCF_3)]^-$. The well understood system $[PPh_4][Au(CF_3)_3X]$ were X is an anionic ligand, mostly a halogen or similar behaving system is easily accessible from the iodide complex $[PPh_4][Au(CF_3)_3I]$ and a silver salt (AgX).[37,38] Transferring this reactivity to our $Ag[OCF_3]$ system led to the formation of $[PPh_4][Au(CF_3)_3(OCF_3)]$ in solution (Scheme 2b). ^{19}F NMR spectroscopy of the reaction mixture revealed the formation of the species $[PPh_4][Au(CF_3)_3(OCF_3)]$, with ^{19}F NMR shifts of $\delta = -28.0$ ppm (sept) for *trans*-CF_3, $\delta = -36.8$ ppm (br, s) for the $[OCF_3]^-$ ligand and $\delta = -39.4$ ppm (q) for the *cis*-CF_3 groups. The signals for the $–CF_3$ groups show no resolved coupling to the broad signal for the OCF_3. Additionally the fluoride complex $[PPh_4][Au(CF_3)_3F]$ (δ(ppm) $= -28.5$ (dsept, CF_3-Au–X), -40.8 (dq, CF_3-Au-CF_3), and -250.0 (qsept, Au–F)) is formed.[38] During the NMR experiments we noticed the decomposition of $[PPh_4][Au(CF_3)_3(OCF_3)]$, even when storing the solution at lower temperatures. ESI mass spectrometry of a freshly prepared sample of $[PPh_4][Au(CF_3)_3(OCF_3)]$ confirmed the formation of the $[Au(CF_3)_3(OCF_3)]^-$ anion with a molecule peak at 488.9429 m z^{-1} (calc. 488.94286). The species $[Au(CF_3)_3F]^-$ with a molecule peak at 422.9569 m z^{-1} (calc. 422.95113) is not only formed during the synthesis reaction, but also during the mass spectrometry experiments. This could be confirmed by a MSMS experiment isolating the $[Au(CF_3)_3(OCF_3)]^-$ anion. Attempts to crystallize $[PPh_4][Au(CF_3)_3(OCF_3)]$ failed due to decomposition. To further investigate the desired product, we reacted the fluoride complex $[PPh_4][Au(CF_3)_3F]$ in MeCN or DCM with an atmosphere of carbonyl fluoride (Scheme 2c), as it was already described for the similar $[AuF_2(OCF_3)(SIMes)]$.[36] In both solvents the ^{19}F NMR spectra showed a mixture of the $[OCF_3]^-$ and the F^- complex and carbonyl fluoride. In the case where MeCN was the solvent, decomposition of $[Au(CF_3)_3(OCF_3)]^-$ was observed. In DCM solution it was stable for a few days, but the conversion of $[PPh_4][Au(CF_3)_3F]$ into the product was lower. The ^{19}F NMR spectrum revealed the formation of a 1:1.2:2.4 mixture of $[PPh_4][Au(CF_3)_3(OCF_3)]$, $[PPh_4][Au(CF_3)_3F]$ and COF_2 in DCM-d_2, while giving sufficiently resolved signals to determine the coupling constant $^5J(^{19}F, ^{19}F) = 2.3$ Hz between the fluorine atoms of the $–OCF_3$ and the $–CF_3$ groups. This is in good agreement with the known complex $[AuF_2(OCF_3)(SIMes)]$, which shows a quartet signal at -40.2 ppm ($^4J(^{19}F,^{19}F) = 1.9$ Hz) for the $[OCF_3]^-$ ligand.[36] Crystallization attempts failed from the DCM mixture.

Transfer Reactions to Organic Halides

As the introduction of fluorinated groups is one of the key techniques in contemporary medicinal chemistry to tune properties such as lipophilicity and stability of potential drugs, we investigated the application of the prepared silver(I) perfluoroalcoholates as transfer reagents (Figure 6). Assuming that silver(I) perfluoroalcoholates would behave as relatively weak nucleophiles, our experiments concentrated on highly reactive benzyl bromides and alkyl iodides. During the reaction,

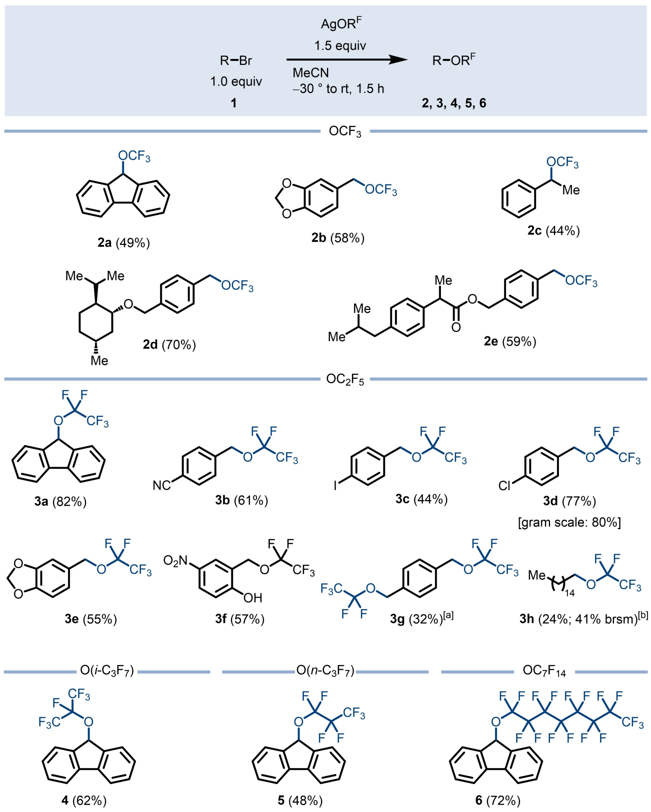


Figure 6. Scope of organic compounds for the introduction of perfluoroalkyl ether groups to alkyl bromides. Conditions: alkyl bromide (1.0 equiv), silver(I) perfluoroalcoholate (2.5 equiv), MeCN, –30 °C to r.t., 1 h.[a] 2.5 equiv. of $Ag[OC_2F_5]$.[b] The corresponding alkyl iodide was used. Brsm = based on recovered starting material.

these substrates would precipitate silver(I) bromide or silver(I) iodide, respectively, thereby further activating the substrates. By treating various alkyl bromides **1** with silver(I) perfluoroalcoholates at −30 °C, the corresponding fluorinated ethers **2**–**6** were obtained in up to 82 % yield. Following this procedure, trifluoromethoxylation of the corresponding benzyl bromides afforded the products **2 a**–**2 e** in 44 % to 70 % yield. Interestingly, this reaction was also successful for the (−)-menthol derivative **2 d** (70 % yield) and the trifluoromethoxylated ibuprofen ester **2 e** (59 % yield) (See the Supporting Information for limitations of this protocol).

As there are only few protocols for the introduction of $-OC_2F_5$ groups by substitution,[19] we explored the usage of the silver salt $Ag[OC_2F_5]$ to realize this desirable transformation. Following the same procedure, the fluorenyl ether **3 a** was obtained in a yield of 82 %. This method accommodates various functional groups, including nitriles (**3 b**, 61 % yield), aryl halides (**3 c**, 44 %; **3 d**, 77 %), acetals (**3 e**, 55 % yield), and nitrophenols (**3 f**, 57 % yield). To demonstrate the scalability of this reaction, we performed the synthesis of fluorinated alkyl ether **3 d** on a gram scale in a slightly better yield of 80 %. Notably, by using 2.5 equiv. of $Ag[OC_2F_5]$ also a twofold substitution could be realized providing product **3 g** (38 % yield). In addition, this method is also applicable for alkyl compounds as shown for the fluorinated alkyl ether **3 h**, although the reaction proceeded slower in this case (24 % yield).

Finally, we tested the higher silver(I) alcoholates for the substitution reaction with fluorenyl bromide providing the corresponding $-i\text{-}OC_3F_7$ ether **4** in 62 % yield, the $-n\text{-}C_3F_7$ ether **5** in 48 % yield, and the highly fluorinated $-OC_7F_{14}$ ether **6** in 72 % yield.

These experiments demonstrate that the prepared silver(I) alcoholates are versatile and easy-to-handle reagents for the transfer of fluorinated ether moieties to various substrates with short reaction times.

Conclusions

In conclusion, we disclosed a general access to silver(I) perfluoroalcoholates by the reaction of AgF with the corresponding perfluorinated carbonyl compounds in acetonitrile including $Ag[OCF_3]$, $Ag[OC_2F_5]$, $Ag[O(i\text{-}C_3F_7)]$, $Ag[O(n\text{-}C_3F_7)]$, and $Ag[OC_8F_{17}]$. These silver(I) perfluoroalcoholates are stable for months when stored at −18 °C. Investigation of the molecular structures by X-ray diffractometry revealed that the perfluorinated alcoholates serve as bridging ligands coordinating to two Ag(I) centers for dimeric and polymeric structures. In contrast, when dissolved in acetonitrile various structures of $Ag[OCF_3]$ could be observed by IR spectroscopy.

Notably, we found that the acetonitrile solutions of the silver(I) perfluoroalcoholates serve as easy-to-handle reagents for the transfer of perfluoroalcoholates. We first investigated transmetalation reactions to other coinage metals providing $Cu[OCF_3]$, $Cu[OC_2F_5]$, and $[PPh_4][Au(CF_3)_3(OCF_3)]$. In contrast to the corresponding silver(I) salts, in the molecular structures of $[Cu(MeCN)_4][OCF_3]$ and $[Cu(MeCN)_4][OC_2F_5]$ the perfluoroalcoholate anions are separated from the metal centers. Additionally, we demonstrated that acetonitrile solutions of the prepared silver(I) perfluoroalcoholates can be used to introduce perfluoroalkoxy groups into organic molecules. We anticipate that these metal perfluoroalcoholates will become valuable reagents in future.

Experimental Section

Experiments with air sensitive compounds were conducted under exclusion of moisture and air using standard Schlenk techniques. Sensitive solids were handled inside an MBRAUN UNIlab plus glovebox with an argon atmosphere ($c(O_2)$ < 0.5 ppm, $c(H_2O)$ < 0.5 ppm). All purchased chemicals were used without further treatment. Pentane used for column chromatography was redistilled prior to use. Solvents were dried using an MBRAUN SPS-800 solvent system and stored over 3 Å molecular sieves. Thin-layer chromatography was performed on silica gel coated aluminium plates ALUGRAM® Xtra SIL G/UV254 (Macherey-Nagel). The product spots were detected by UV light (254 nm) or as permanganate stains. Flash column chromatography was performed with silica gel 60 M (0.040–0.063 mm, 230–400 mesh, Ma-cherey-Nagel). $[PPh_4][Au(CF_3)_3F]$ and $[PPh_4][Au(CF_3)_3I]$ were prepared via literature-known procedures.[38] IR spectra of moisture and temperature sensitive solids were measured under a cooled nitrogen stream using a Nicolet iS50 FTIR spectrometer with a diamond ATR attachment with 32 scans and a resolution of 4 cm^{-1}. IR spectra of air insensitive solids were measured with a NICOLET iS10 FTIR spectrometer equipped with an ATR unit (NICOLET SMART DuraSamplIR) and only diagnostic absorption bands are reported. IR spectra of air sensitive solutions were measured at room temperature using a Vertex70 with external MCT detector and an ATR Fiber Probe IN-350-T. IR spectra were processed using OPUS 7.5 and Origin 2022 was used for their graphical representation. NMR spectra were recorded using a Varian INOVA 600 (600 MHz), JEOL (ECZ–R 400, ECS 400, ECA 400, ECX 400, ECP 500, ECZ 600), or BRUKER (AVANCE III 500, AVANCE III 700) spectrometer and all chemical shifts are referenced using the X values given in the IUPAC recommendations of 2008 and the ^2H signal of the deuterated solvent as internal reference.[39] For external locking, acetone-d6 was flame sealed in a glass capillary and the lock oscillator frequency was adjusted to give $\delta(^1H) = 7.26$ ppm for a $CHCl_3$ sample locked on the capillary. MestReNova 14.2 was used for processing the spectra and for their graphical representation. ^1H NMR yields were measured using CH_2Br_2 as an internal standard. X-ray diffraction measurements were performed on a Bruker D8 Venture diffractometer with MoK α (λ = 0.71073 Å) radiation at 100 K. Single crystals were picked in perfluoroether oil at −40 °C under a nitrogen atmosphere and mounted on a 0.15 mm Mitegen micromount. They were solved using the ShelXT structure solution program with intrinsic phasing and were refined with the refinement package ShelXL using least squares minimizations by using the program OLEX2 Diamond 3 and POV-Ray 3.7 were used for their graphical representation. ESI mass spectrum of $[PPh_4][Au(CF_3)_3(OCF_3)]$ was recorded using a Synapt G2-S HDMS mass spectrometer by Waters Co., MA, USA. The ionization and transfer conditions of the mass spectrometer were optimized for maximal intensity of instable inorganic molecules. Negative ESI with a capillary voltage of 1.6 kV was used. The source temperature was set to 40 °C, the desolvation temperature was set to 80 °C. Sampling cone and source offset voltages were set to 25 and 50 V. The desolvation gas flow was 350.0 L/hr. For the analysis, dry acetonitrile and Pressurized Sample Infusion ESI[40] was used to establish inert source conditions. LockSpray correction (LeuEnk, m/z

554.27) was used for exact mass measurement / internal recalibration mass spectra only since the lock spray solvent contained 0.1% Formic acid and led to led to fast degradation of the analysts. High-resolution mass spectra of organic substrates were measured with an Agilent (6210 ESI-TOF; 4 μL/min, 1.0 bar, 4 kV) or EI-MS (MAT 711, 80 eV). Quantum-chemical calculations were conducted using the HPC system provided by the ZEDAT (Freie Universität Berlin, Curta).[41] The program Orca 5.0.3[42] was used with PW6B95[43] or B3LYP[44] as functional and the basis sets def2-QZVPP.[45,46] The FIA values were calculated from the optimized structures at PW6B95-D3(BJ)/def2-QZVPP level of theory similar to the literature procedure.[35] For the solvation correction the difference of the single point energies at PW6B95-D3(BJ)/def2-QZVPP level of theory between the ones with solvation (c-pcm, MeCN) and without were used. (See Supporting Information for structures) Calorimetric measurements were performed with an EasyMax 102 Thermostat System by Mettler Toledo (100 mL glass reactor, temperature sensor: Pt100 FEP-coated) using the HFCal upgrade kit. (for details, see SI)

Preparation of Ag[OR^F] Solutions

AgF (1.27 g, 10 mmol) was suspended in MeCN or EtCN (10 mL). After degassing the suspension, an excess of the gaseous fluorinated acid fluoride or ketone was added at r.t. until the vessel retained a constant pressure (0.5–1.0 bara, normally less than 15 min.). Any excess of gas was removed by pumping off for 15 sec. After pressurizing the vessel with argon again, the solution was filtered with a syringe filter (PTFE, 0.45 μm). The obtained Ag[OR^F] solution (1 M) was stored in a glass vessel at −20 °C.

Ag[OCF_3]

^{19}F NMR (377 MHz, MeCN-d_3, 20 °C): $\delta = -25.9$ ppm (s, fwhm = 310 Hz, 3F).

Ag[OC_2F_5]

^{19}F NMR (377 MHz, MeCN-d_3, 16 °C): $\delta = -41.0$ (s, fwhm = 240 Hz, 2F, OCF_2), −84.5 ppm (s, 3F, CF_3).

Ag[O(i-C_3F_7)]

^{19}F NMR (377 MHz, MeCN-d_3, 21 °C): $\delta = -80.8$ (s, fwhm = 85 Hz, 1F, OCF), −82.0 ppm (s, 6F, CF_3).

Ag[O-nC_3F_7]

^{19}F NMR (377 MHz, MeCN-d_3, 21 °C): $\delta = -34.5$ (s, fwhm = 530 Hz, 2F, OCF_2), −82.0 (s, 3F, CF_3), −126.3 ppm (s, 2F, CF_2).

Preparation of Ag[$OCF_2C(O)F$]

AgF (0.25 g, 2 mmol, 1 eq.) was suspended in MeCN (2 mL) and FC(O)C(O)F (2 mmol, 1 eq.) was condensed into the reaction vessel at −196 °C. After warming up to r.t. the suspension was stirred for 15 min. The obtained Ag[$OCF_2C(O)F$] solution (1 M) was stored in a glass vessel at −20 °C.

^{19}F NMR (377 MHz, MeCN-d_3, 18 °C): $\delta = -0.3$ ppm (s, fwhm = 130 Hz).

Preparation of Ag[OC_8F_{17}] Solution

AgF (1.27 g, 10 mmol, 1 equiv) was suspended in MeCN (5 mL) and $ClC(O)C_7F_{15}$ (2.16 g, 5 mmol, 0.5 equiv) was added at r.t. After stirring the suspension for 15 min, the precipitate was filtered off with a syringe filter (PTFE, 0.45 μm). The obtained Ag[OC_8F_{17}] solution (1 M) was stored in a glass vessel at −20 °C.

^{19}F NMR (377 MHz, MeCN-d_3, 21 °C): $\delta = -33.2$ (s, fwhm = 400 Hz, 2F, OCF_2), −81.7 (s, 3F, CF_3), −122.1 (m, 2F, CF_2), −122.5 (m, 6F, CF_2), −123.3 (m, 2F, CF_2), −126.7 (m, 2F, CF_2) ppm.

Preparation of [$Ag(bpy)_2$][OCF_3]

Bpy (0.6 g, 4 mmol, 2 equiv) was added to an Ag[OCF_3] solution in MeCN (2 mL, 2 mmol, 1 equiv). After stirring the suspension for 30 min the solvent was removed in vacuum resulting in an off-white crystalline powder of [$Ag(bpy)_2$][OCF_3] (1.0 g, 99%).

^{19}F NMR (377 MHz, DCM-d_2, 19 °C): $\delta = -21.6$ ppm (s, fwhm = 200 Hz).

^{1}H NMR (401 MHz, DCM-d_2, 19 °C): $\delta = 8.64$ - 8.55 (m, 4H), 8.35 - 8.23 (m, 4H), 8.10 - 7.97 (m, 4H), 7.60 - 7.46 (m, 1H) ppm.

Preparation of [NEt_3Me][OCF_3]

A solution of Ag[OCF_3] in MeCN (1 M, 21 mL, 21 mmol, 1.06 equiv) was added to a solution of [NEt_3Me]Cl (3.01 g, 19.8 mmol, 1 equiv) in MeCN, and a colorless precipitate formed. After the filtration with a syringe filter (PTFE, 0.45 μm) the solvent was removed in vacuum resulting in an off-white crystalline powder of [NEt_3Me][OCF_3] (99%).

^{19}F NMR (377 MHz, DCM-d_2, 19 °C): $\delta = -22.1$ ppm (s, 3F).

^{1}H NMR (401 MHz, DCM-d_2, 19 °C): $\delta = 1.33$ (pseudo-tt, 3F, $^3J(^1H, ^1H) = 7.3$ Hz, $^3J(^1H, ^{14}N) = 1.9$ Hz), 3.02 (s, 3F), 3.38 (q, 2F, $^3J(^1H, ^1H) = 7.3$ Hz) ppm.

Preparation of Cu[OR^F] Solutions

CuCl (97.9 mg, 1 mmol, 1 equiv) was dissolved in MeCN (1 mL) and an Ag[OR^F] stock solution (1 M, 1 mL, 1 equiv) was added. After stirring for 10 min the solution was filtered with a syringe filter (PTFE, 0.45 μm). The obtained Cu[OR^F] solution (0.5 M) was analysed directly. .

Cu[OCF_3]

^{19}F NMR (377 MHz, MeCN-d_3, 21 °C): $\delta = -24.2$ ppm (s, fwhm = 1500 Hz, 3F).

Cu[OC_2F_5]

^{19}F NMR (377 MHz, MeCN-d_3, 21 °C): $\delta = -39.4$ (s, fwhm = 1600 Hz, 2F, OCF_2), −83.9 ppm (s, 3F, CF_3).

PPh_4[$Au(CF_3)_3(OCF_3)$]

a) from PPh_4[$Au(CF_3)_3I$] and $AgOCF_3$ in MeCN

PPh_4[$Au(CF_3)_3I$] (261.0 mg, 0.3 mmol, 1 equiv) was dissolved in MeCN (1 mL) and an Ag[OR^F] stock solution (1 M, 0.3 mL, 1 equiv) was added at $-30\,^{\circ}C$. After stirring for 15 min the solution was filtered with a syringe filter (PTFE, 0.45 μm).

^{19}F NMR (377 MHz, MeCN, 20 °C): $\delta = -28.0$ (hept, 3F, CF_3, $^{4}J(^{19}F, ^{19}F) = 6.3$ Hz), -36.8 (br, s, 3F, OCF_3), -39.4 (q, 6F, CF_3, $^{4}J(^{19}F, ^{19}F) = 6.3$ Hz) ppm.

MS (ESI−): $m\ z^{-1} = 488.9429$ ($[Au(CF_3)_3(OCF_3)]^-$, calc. 488.94286, $< 1\,\%$), 422.9569 ($[Au(CF_3)_3F]^-$, calc. 422.95113, 100 %).

b) from $PPh_4[Au(CF_3)_3F]$ and COF_2

$PPh_4[Au(CF_3)_3F]$ (76 mg, 0.1 mmol, 1 equiv) was dissolved in DCM or MeCN (0.6 mL) and the vessel was pressurized with exc. COF_2 (1 bara) at r.t. The mixture was agitated over 5 min and then analyzed by NMR spectroscopy.

^{19}F NMR (377 MHz, DCM-d$_2$, 19 °C): $\delta = -28.2$ (hept, 3F, CF_3, $^{4}J(^{19}F, ^{19}F) = 6.3$ Hz), -37.5 (br, pseudo-quint, 3F, OCF_3, $^{5}J(^{19}F, ^{19}F) = 2.3$ Hz), -39.6 (qq, 6F, CF_3, $^{4}J(^{19}F, ^{19}F) = 6.3$ Hz, $^{5}J(^{19}F, ^{19}F) = 2.3$ Hz) ppm.

Reactions with Organic Halides

A solution of $Ag[OR^F]$ in MeCN (1.0 м, 0.750 mL, 0.750 mmol, 1.5 equiv) was added to a heat gun-dried Schlenk tube and cooled to $-30\,^{\circ}C$. The alkyl halide (0.500 mmol, 1.0 equiv) was added to the solution and the mixture was stirred for 30 min at $-30\,^{\circ}C$. The solution was allowed to warm to r.t. over 1 h by removing the cooling bath. The suspension was filtered and washed with Et_2O, the filtrate was concentrated under reduced pressure, and the products **2a-6** were purified by flash column chromatography (SiO_2, *n*-pentane/Et_2O). The products were analysed by NMR spectroscopy and HRMS spectrometry.

(For details see SI).

Supporting Information

The authors have cited additional references within the Supporting Information.[47–54]

Deposition Number(s) 2326777 (for $[Ag(MeCN)_2(OCF_3)]_n$), 2326778 (for $[Ag(bpy)_2][OCF_3]$), 2326776 (for $[Ag(EtCN)_2(OC_2F_5)]_2$), 2326775 (for $[Ag(EtCN)_2(O^iC_3F_7)]_2$), 2326772 (for $[Cu(MeCN)_4][OCF_3]$), 2326773 (for $[Cu(MeCN)_4][OC_2F_5]$), 2326774 (for $[Cu^I(MeCN)_4]_2[Cu^{II}\{OC(CF_3)_2–O–C(CF_3)_2O\}_2]$) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Trifluormethoxy · Perfluoroalcoholates · Metal Salts · Fluorine Chemistry · Solvent Effects

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