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Access to new (Cat)[Cu(CF_3)$_2$] complexes as efficient trifluoromethylating agents in the activation of aryl halides

Accés a nous complexos de tipus (Cat)[Cu(CF_3)$_2$] com a agents trifluorometilants eficients en l'activació d'halurs d'aril

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Abstract: In this paper, the formation of bis(trifluoromethyl)cuprate complexes through a transmetalation reaction using analogous silver complexes and different copper(I) sources is discussed. The rapid, selective and in situ synthesis of these complexes has been developed from the reaction of (Cat)[Ag(CF_3)$_2$] and CuI under mild reaction conditions. Subsequently, their potential as trifluoromethylating agents in the formation of C–CF_3 bonds using different model substrates such as aryl halides that contain C_{sp^2}–I, C_{sp^2}–Br and C_{sp^3}–Br bonds has been evaluated. It is worth mentioning that this is the first time that the capability of these species has been demonstrated, since their reactivity had been neglected to date.

Keywords: Organometallic chemistry, transmetalation, copper, organocuprate complexes, trifluoromethylation.

Resum: En aquest treball s'ha estudiat la formació de complexos de tipus bis(trifluorometil)cuprat a través d'una reacció de transmetal·lació utilitzant complexos de plata anàlegs i diferents fonts de coure(I). S'ha desenvolupat la síntesi in situ *d'aquests complexos de manera ràpida i selectiva a partir de (Cat)[Ag(CF_3)$_2$] i CuI en condicions de reacció suaus. Posteriorment se n'ha avaluat la capacitat com a agents trifluorometilants en la formació d'enllaços C–CF_3 utilitzant diferents substrats model, halurs d'aril que contenen enllaços C_{sp^2}–I, C_{sp^2}–Br i C_{sp^3}–Br. És important destacar que és la primera vegada que s'ha pogut demostrar el potencial d'aquestes espècies, ja que fins ara no se n'havia estudiat la reactivitat en profunditat.*

Paraules clau: Química organometàl·lica, transmetal·lació, coure, complexos organocuprats, trifluorometilació.

Introduction

In the last few decades, the addition of the CF_3 group to organic scaffolds has received special attention from the synthetic community [1]. The trifluoromethyl group (CF_3) is a prevalent structural motif in pharmaceuticals and agrochemicals due to its unique capability to modify physical, chemical and biological properties of organic molecules [2]. In particular, tremendous efforts have been devoted to the development of strategies for late-stage installation of this special functional group into diversely decorated molecules using transition metal (TM) catalysts [1]. Among the different methods described in literature, those that use trifluoromethylated copper complexes stand out since they are capable of functionalizing efficiently aryl halide derivatives (scheme 1) [3].

In most of these studies, the authors use neutral copper species such as $LCuCF_3$ (L = solvent or coordinating ligand). However, the reactivity of the trifluoromethylated derivatives such as (Cat)[Cu(CF_3)$_2$], analogous to Gilman reagents [4], has hardly been explored in this type of reactions. Although the groups of Vicic [3*a*, *b*] and Hartwig [3*c*] have described the formation of this type of complexes in equilibrium with neutral copper(I) species in the trifluoromethylation reactions of aryl halides, their participation in these transformations has not been investigated in detail (scheme 1*a*). In this context, the Mikami group has explored the trifluoromethylation of aryl iodides by using a mixture of homoleptic and heteroleptic cuprates, combining a copper(I) salt with a zinc transmetalating agent as the initial source of CF_3 [3*f*, *g*]. However, the complex mixture of compounds observed by the authors in the reaction media made it impossible to determine the actual potential of these proposed reactive species (scheme 1*b*).

Therefore, this study seeks to *(i)* investigate the efficient and selective access to the (Cat)[Cu(CF_3)$_2$] complexes from copper(I) sources and selective transmetalating agents, *(ii)* evaluate the reactivity of the (Cat)[Cu(CF_3)$_2$] species in the trifluoromethylation reactions of different representative aryl

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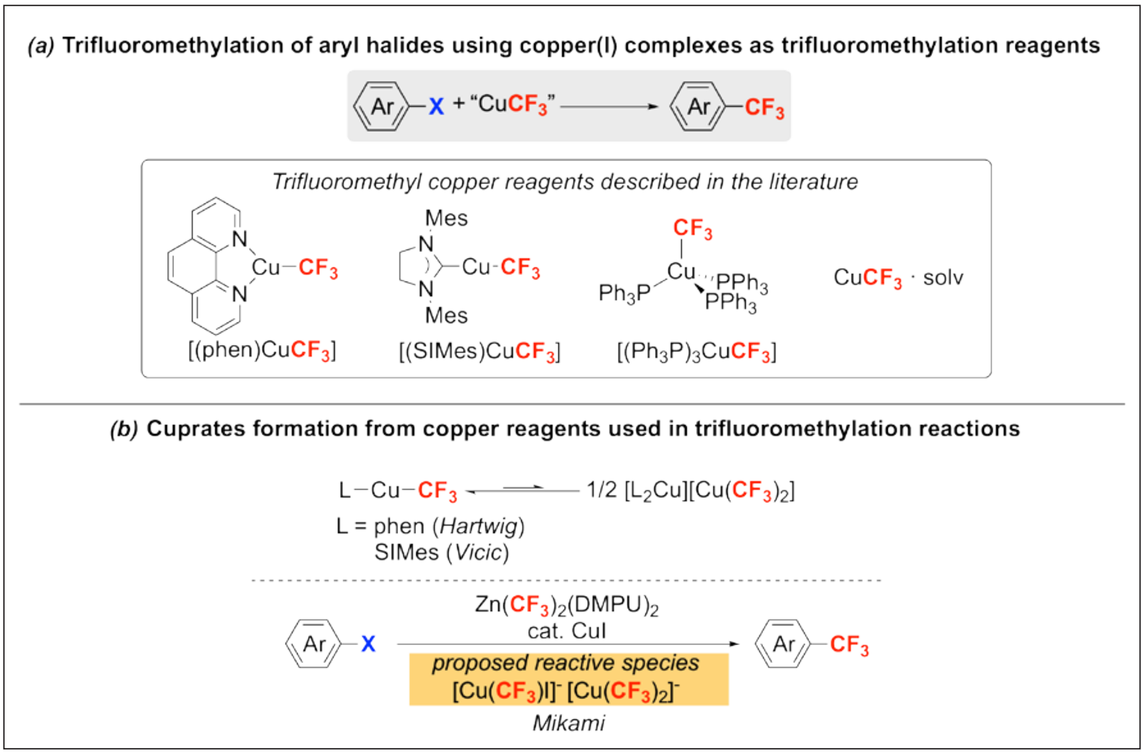


Scheme 1. Functionalization of aryl halides with copper(I) trifluoromethyl sources. Source: Prepared by the authors.

halides, and *(iii)* elucidate the mechanism involved in the trifluoromethylation reaction of organic substrates.

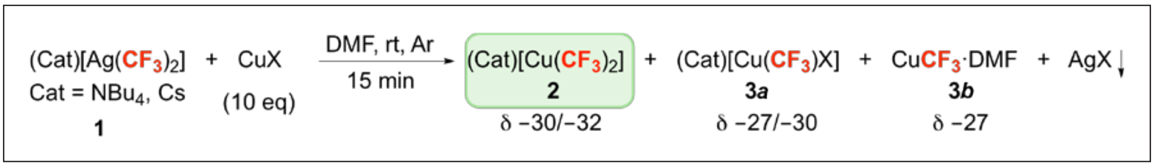
Results and discussion

Synthesis of copper complexes of the (Cat)[Cu(CF$_3$)$_2$] type

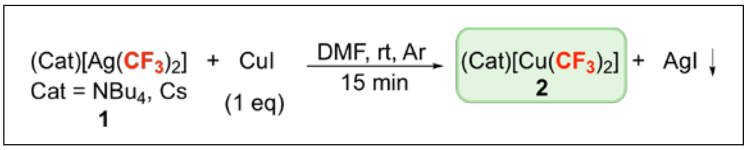
The first goal was to design an efficient synthetic route for accessing the targeted homoleptic cuprate species. In this context, Pérez-Temprano and co-workers have reported the efficient capability of (Cat)[Ag(CF$_3$)$_2$] (Cs = Cs or NBu$_4$) as transmetalating agents to transition metals, such as palladium [5].

We began by establishing the general conditions for the transmetalation reaction: *(i)* the use of 10 equivalents of CuX; *(ii)* the use of DMF as a solvent, based on the studies described in the literature on the trifluoromethylation reaction with different aryl halides [6]; and *(iii)* mild reaction conditions, including short reaction time (15 minutes) and room temperature (rt). Based on Mikami's work described in the introduction [3*f*, *g*], we envisioned the possible formation of different CuCF$_3$ compounds. These species could be assigned to: *(a)* $[Cu(CF_3)_2]^-$ (**2**), whose chemical shift values in ^{19}F NMR range from –30 to –32 ppm, and *(b)* $[Cu(CF_3)(X)]^-$ (3*a*) (δ = –27 to –30 ppm) or CuCF$_3$•S (3*b*) (S = coordinating solvents such as DMF, NMP, ACN...), whose δ in ^{19}F NMR spectra is assigned to values close to –27 ppm [1*b*, 4].

Different copper(I) sources were tested to explore the reactivity of this transformation. The copper(I) salts CuX (X = I, Br and Cl) were used to test the influence of the halogen and [Cu(NCMe)$_4$][BF$_4$], to evaluate the presence of the acetonitrile



Scheme 2. General procedure of the transmetalation reaction with 10 equivalents of the copper source. Source: Prepared by the authors.



Scheme 3. General procedure of the transmetalation reaction with 1 equivalent of CuI.
Source: Prepared by the authors.

ligand in the copper coordination sphere. In all cases, by ^{19}F NMR spectroscopy, one or two species in the region corresponding to CuCF$_3$ (from δ –25 to –32 ppm) were observed. One of the species unambiguously corresponds to the cuprate $[Cu(CF_3)_2]^-$ (**2**) (δ ≈ –30.7 ppm in all cases) and the other species whose δ is in the range of –26.04 to –26.95 ppm could not be conclusively identified as species **3***a* or **3***b*. The use of $[Cu(NCMe)_4][BF_4]$ and CuBr as copper sources was discarded since species **2** and **3** were not formed selectively, and a mixture of different major species was obtained. On the other hand, when performing the same reaction with CuCl, the species **3** was formed quantitatively without detecting the cuprate (Cat)$[Cu(CF_3)_2]$ (**2**) (entries 5 and 6, table 1). Finally, the reaction of the complexes (Cat)$[Ag(CF_3)_2]$ (**1**) (Cat = Cs or NBu$_4$) with 10 equivalents of CuI in DMF during 15 minutes at room temperature led to a mixture of the species (**2**:**3**) in proportion [66:34 (Cat = Cs); 52:48 (Cat = NBu$_4$)] (entries 7 and 8, table 1).

Table 1. Transmetalation reaction with different copper sources.

Entry	Ag source	Cu source	δ species 3	Ratio 2:3	Comment
1	1_{Cs}	$[Cu(NCMe)_4][BF_4]$	–26.04	2:98	Mixture major species
2	1_{NBu4}		–26.05	0:100	
3	1_{Cs}	CuBr	–26.75	1:99	Mixture major species
4	1_{NBu4}		–26.71	1:99	
5	1_{Cs}	CuCl	–26.46	0:100	
6	1_{NBu4}		–26.46	0:100	
7	1_{Cs}	CuI	–26.95	66:34	
8	1_{NBu4}		–26.86	52:48	

In view of these results, we evaluated the transmetalation reactions using stoichiometric amounts of CuI, in order to find a more selective synthesis for the complexes (Cat)$[Cu(CF_3)_2]$ (**2**). Thus, using 1 equivalent of CuI, the complexes (Cat)$[Cu(CF_3)_2]$ (**2**) (Cat = Cs or NBu$_4$) were obtained quantitatively, confirming their structure through ^{19}F NMR (δ = –30.66 ppm in both cases) (scheme 3). These compounds have not been isolated due to their instability, since when using the common Schlenk techniques, a rapid decomposition was observed. It is important to note that this is the first time that these bis(trifluoromethyl)cuprate species can be prepared in situ quantitatively under mild reaction conditions.

Study of the reactions in C-CF$_3$ bond formation using CuCF$_3$ to functionalize aryl halides

A first evaluation of the potential of these cuprate species as trifluoromethylating agents in the reaction of C-CF$_3$ bond formation was performed using 4-iodobiphenyl (4_I) as the model substrate. This was chosen not only because the C_{sp^2}-I bond is the most accessible within the aryl halides [6], but also because Vicic *et al.* have recently performed an exhaustive evaluation of the efficiency of the most active CuCF$_3$ species to date, using this substrate as a model to establish an objective comparison of their reactivity (figure 1) [1*j*].

Firstly, the conditions of the transmetalation reaction previously described were used (1 equivalent of CuI, 15 minutes at room temperature and DMF as solvent). Then, once (Cat)$[Cu(CF_3)_2]$ (**2**) (Cat = Cs or NBu$_4$) species were formed, 0.8 or 1.6 equivalents of the substrate were added and the reaction mixture was heated at 50 °C for 24 hours (scheme 4). It is important to mention that the substrate and copper source CuCF$_3$ ratio described by Vicic *et al.* is 0.8:1. In our case, as the complexes contain two trifluoromethyl groups, different substrate/copper source ratios were tested (0.8:1 and 1.6:1).

In all the cases evaluated, the bis-(trifluoromethyl)cuprate species (**2**) outperformed the copper species described by Vicic (figure 1), affording excellent yields of the targeted product, 4-trifluoromethylbiphenyl (4_{CF_3}), by ^{19}F NMR spectroscopy (table 2). It should be noted that the activity of **2** is independent of the nature of the cation. Finally, it is important to remark that when using 1.6 equivalents of substrate (entries 2 and 4,

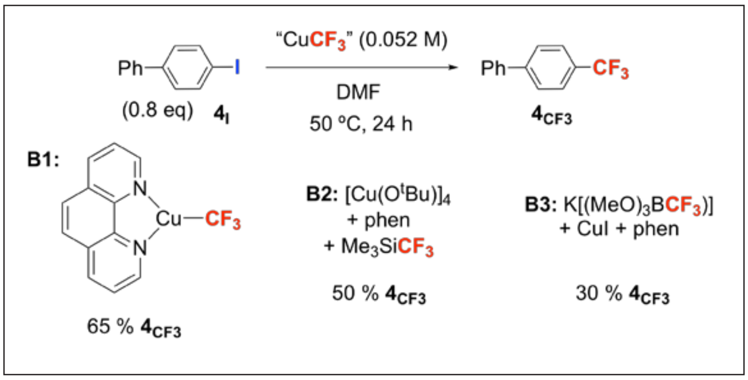
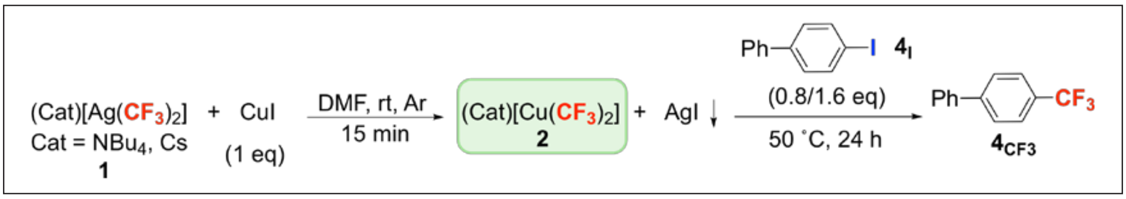


Figure 1. Copper complexes that provided best results in the trifluoromethylation reaction of 4_{I}.
Source: Prepared by the authors.



Scheme 4. Trifluoromethylation reaction of 4_{I} using 1 equivalent of CuI in the transmetalation reaction. Source: Prepared by the authors.

table 2), the bis-(trifluoromethyl)cuprate (**2**) species are capable of transferring the two trifluoromethyl groups. During the reaction, the accumulation of a transient intermediate, $[\mathrm{Cu(CF_3)I}]^-$ (**3***a*$_{\mathrm{I}}$), was observed in the range of –28.06 ppm to –28.29 ppm [3*f*, g] by ^{19}F NMR spectroscopy. Taking into account the amount of this species that is formed, it can be confirmed that it is also capable of transferring the trifluoromethyl group.

These preliminary results unambiguously confirm, for the first time, the capacity of the bis-(trifluoromethyl)cuprate species as trifluoromethylating agents in the activation of substrates with $\mathrm{C_{sp^2}}$-I bonds. Curious about the potential activity of **3**-type species, we decided to mimic the reaction conditions previously described, but using 10 equivalents of CuI in order to assess the effect of the presence of species **3** in the reaction media. In all the experiments, almost 100 % product conversion was achieved in 24 hours (entries 5-8, table 2).

Table 2. Trifluoromethylation reaction of 4_{I} using 1 or 10 equivalents of CuI in the transmetalation reaction.

Entry	Ag source	Equiv. substrate	Equiv. CuI	4_{CF3} yield (%)^a
1	1_{Cs}	0.8	1	100
2		1.6	1	90
3	1_{NBu4}	0.8	1	100
4		1.6	1	83
5	1_{Cs}	0.8	10	100
6		1.6	10	93
7	1_{NBu4}	0.8	10	100
8		1.6	10	100

a. The conversion value is calculated using two internal standards (see *Experimental section*).

In order to understand how the proportion between the $\mathrm{CuCF_3}$ species changes in the activation reaction of 4-iodobiphenyl (4_{I}) using 10 equivalents of CuI and $\mathrm{(Cs)[Ag(CF_3)_2]}$ (1_{Cs}), a monitorization of the reaction by ^{19}F NMR spectroscopy was performed (figure 2). The analysis of the kinetic profile after 3 hours shows the formation of $\mathbf{4}_{\mathrm{CF3}}$ in 73 % yield, while complex $\mathbf{2}_{\mathrm{Cs}}$ has decreased from an initial 60 % to 12 % and the complex $\mathbf{3}_{\mathrm{Cs}}$ from an initial 40 % to 29 %. These data confirm that species $\mathbf{2}_{\mathrm{Cs}}$ is involved in the trifluoromethylation of the aryl iodide (4_{I}), while more experiments would be necessary to determine the implication of the species $\mathbf{3}_{\mathrm{Cs}}$ in the reaction [7]. It is worth mentioning the variation of the chemical shift of species $\mathbf{3}_{\mathrm{Cs}}$ during the reaction, from –27.02 ppm to –28.18 ppm, due to the formation of $[\mathrm{CuI_2}]^-$. Hu and coworkers reported that the amount of $[\mathrm{CuI_2}]^-$ can affect the chemical shift of **3***a*-type species, so it is proposed that a more appropriate way of denominating these species would be $\{[\mathrm{Cu(CF_3)I}]_x\}^{x-}\ \{[\mathrm{CuI_2}]_y\}^{y-}$ [8].

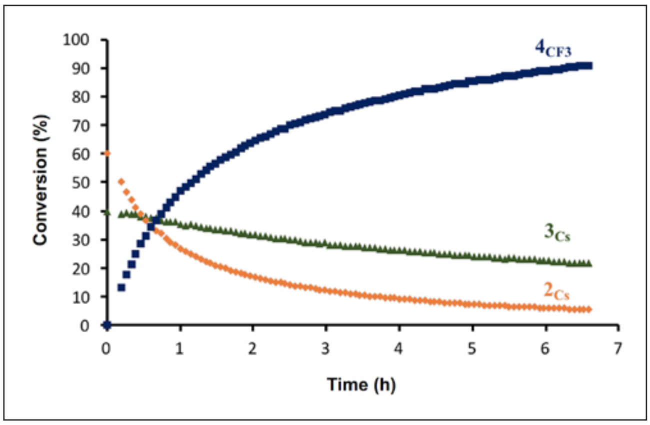
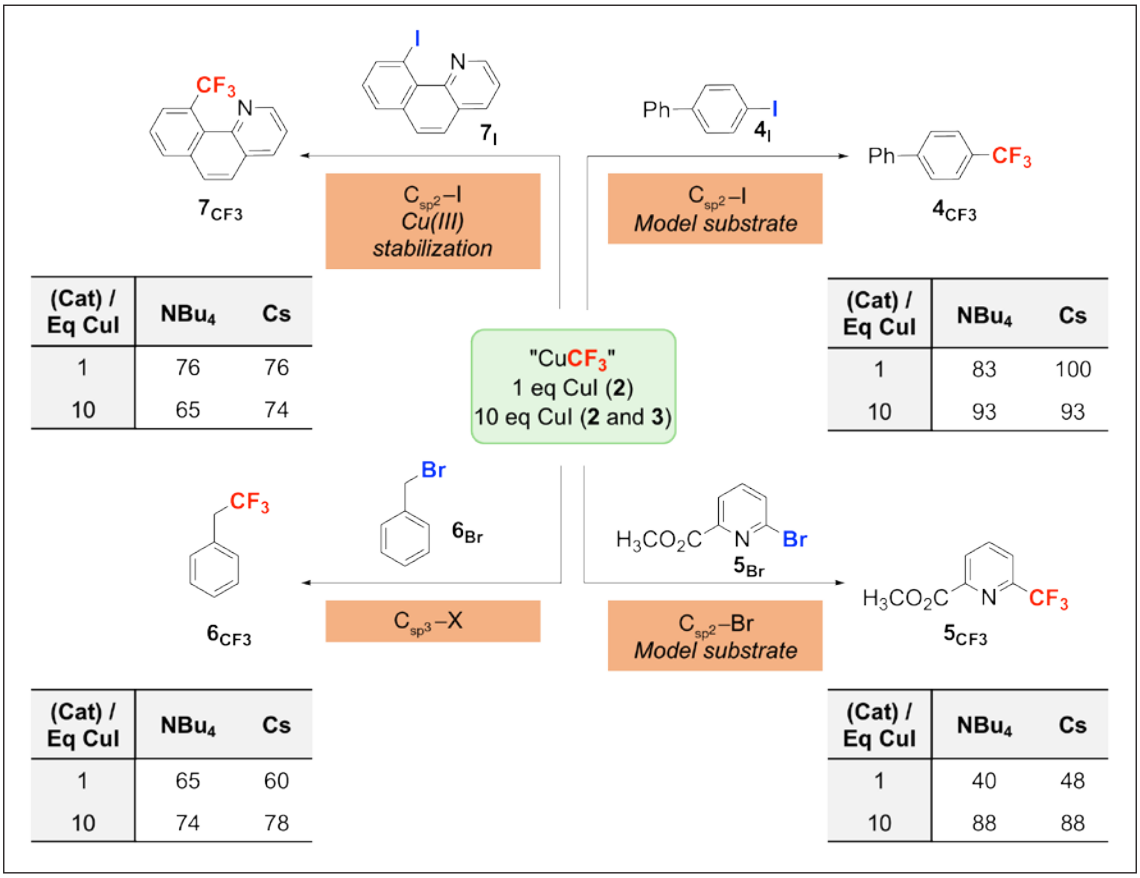


FIGURE 2. Formation of 4_{CF3} in the activation reaction of 4_I using (Cs)[Ag(CF_3)$_2$] and 10 equivalents of CuI in DMF at 50 °C. Source: Prepared by the authors.

Once the trifluoromethylation capability of the $CuCF_3$ species was verified using the model substrate, we decided to study its reactivity with different representative organic molecules such as methyl-6-bromopyridine-2-carboxylate (5_{Br}), benzyl bromide (6_{Br}) or 10-iodobenzo[h]quinoline (7_I). From this point on, the reactivity study is carried out with 1 or 10 equivalents of CuI and 1.6 equivalents of substrate to establish a comparison between the results.

The methyl-6-bromopyridine-2-carboxylate (5_{Br}) substrate was chosen not only for *(a)* the evaluation of the capability of copper species, and (2) to activate C_{sp2}–Br bonds, but also *(b)* to determine the efficiency of our system by comparing the results obtained with the ones reported by Hartwig and co-workers, who used different $CuCF_3$ species to functionalize this same substrate [9]. In this case, the reaction conditions are similar to those previously described, but they were carried out at 80 °C to compare our experimental results with the precedents in literature [9]. Hartwig *et al.* reported a 96 % conversion to 5_{Br} using 0.8 equivalents of substrate, (Phen) $CuCF_3$ as $CuCF_3$ source, DMF as solvent at 80 °C for 8 hours [9]. In our first preliminary studies, we performed the reaction with more diluted concentrations (0.052 vs 0.12 M) and 1.6 equivalents of substrate 5_{Br} for 24 hours. In this case, the



(Cat) / Eq CuI	NBu_4	Cs
1	76	76
10	65	74

(Cat) / Eq CuI	NBu_4	Cs
1	83	100
10	93	93

(Cat) / Eq CuI	NBu_4	Cs
1	65	60
10	74	78

(Cat) / Eq CuI	NBu_4	Cs
1	40	48
10	88	88

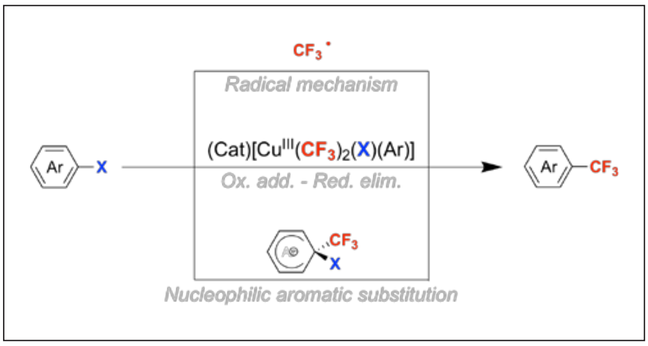
SCHEME 5. Evaluation of the capability of $CuCF_3$ (2 and 3) as trifluoromethylating agents in C-CF_3 bond formation, using different representative aryl halides. Source: Prepared by the authors.

conversion values obtained using 1 equivalent of CuI were moderate (scheme 5) and this can be explained by the unknown potential reactivity of the $[Cu(CF_3)Br]^-$ species formed during the reaction (δ ≈ –27.10 ppm) (**3*a***$_{Br}$), that have not been described to date. These mixed species, although more reactive per se than bis-(trifluoromethyl)cuprate, could decompose in the reaction media at this temperature before activating the C_{sp^2}-Br bond. On the other hand, it should be mentioned that the yields obtained using 10 equivalents of CuI (scheme 5) are similar to those reported by Hartwig and co-workers [9]. Encouraged by the results obtained in the activation of C_{sp^2}-I and C_{sp^2}-Br bonds, we decided to extend the study and explore the functionalization of a substrate containing a C_{sp^3}-X bond. In particular, we chose benzyl bromide (**6**$_{Br}$) as the model system. The reactions were carried out at 50 °C for 24 hours under the same reaction conditions used for 4-iodobiphenyl (**4**$_{I}$). In all cases the yields obtained were similar when using 1 or 10 equivalents of CuI (> 50 %). These data suggest in this particular case that $[Cu(CF_3)Br]^-$ (**3*a***$_{Br}$) species are also capable of transferring the second CF_3 molecule at 50 °C (scheme 5). These results are comparable to those obtained using other $CuCF_3$ complexes [3*a*, *b*, 10]. At the end of the reactions, one species at δ = –34.01 ppm was observable by ^{19}F NMR spectroscopy, which is associated with Cu(III) species and in particular $[Cu(CF_3)_4]^-$ complexes, which are inactive in the activation of aryl halides [3*f*].

Finally, a more specific substrate was studied: 10-iodobenzo[h]quinoline (**7**$_{I}$). This scaffold presents a unique structure capable of stabilizing metals in high oxidation states [11]. In the case that the reaction mechanism would take place through oxidative addition-reductive elimination steps [6], this type of substrate could be used as a model to isolate highly reactive Cu(III) species. Therefore, the first step was to evaluate the activation of **7**$_{I}$ by species **2** and **3**. These preliminary studies were performed under optimized reaction conditions (1 or 10 equivalents of CuI, DMF, 50 °C, 24 hours and 0.052 M CF_3). In all cases, the yields obtained were promising [12], so this substrate or similar ones could be used as a model in a more exhaustive study in order to gain further insight into the reaction mechanism.

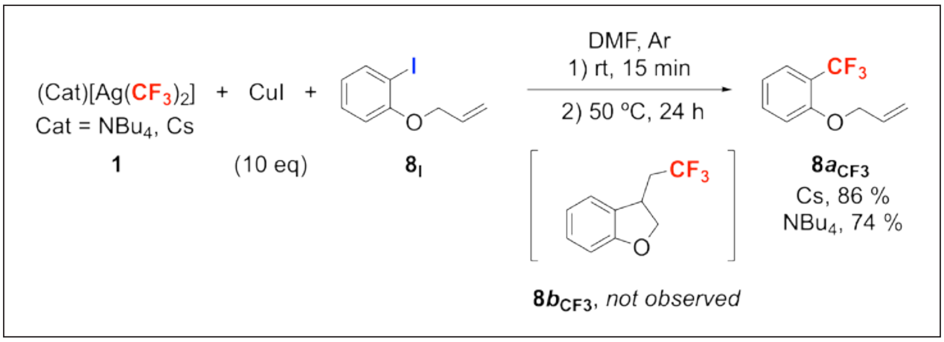
Preliminary studies of the trifluoromethylation reaction mechanism

Among the different proposed mechanisms for the activation reactions of C_{sp^2}-X through $CuCF_3$ complexes, the radical mechanism, nucleophilic aromatic substitution, and oxidative addition-reductive elimination (scheme 6) [6] were of special interest.

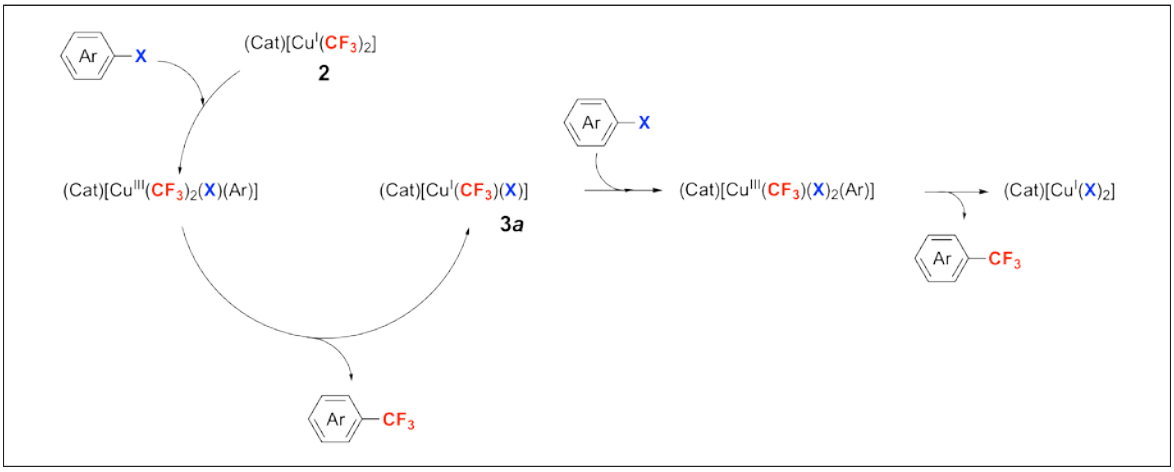


Scheme 6. Different proposed mechanisms for the activation reactions of C_{sp^2}–X through $CuCF_3$ complexes. Source: Prepared by the authors.

In order to evaluate the presence of radical species, the trifluoromethylation reaction of the substrate 1-(allyloxy)-2-iodobenzene (**8**$_{I}$) was performed [3*c*, 6, 13]. The aryl radical



Scheme 7. Trifluoromethylation reaction of 8_I using 10 equivalents of CuI in the transmetalation reaction. Source: Prepared by the authors.



Scheme 8. Proposed oxidative addition/reductive elimination mechanism. Source: Prepared by the authors.

derived from this iodoarene cyclizes with a rate constant of 10^{10} s^{-1} [14]. Thus, in case that trifluoromethylation took place through an aryl radical, the product $\mathbf{8}\boldsymbol{b}_{\mathrm{CF3}}$ would be observed. However, if the product $\mathbf{8}\boldsymbol{a}_{\mathrm{CF3}}$ is obtained, the presence of radical species can be discarded. Both compounds can be easily identified by ^{19}F NMR spectroscopy since the product $\mathbf{8}\boldsymbol{a}_{\mathrm{CF3}}$ appears as a singlet signal at −61.4 ppm, while $\mathbf{8}\boldsymbol{b}_{\mathrm{CF3}}$ is represented by a triplet signal at −65.2 ppm. The trifluoromethylation reaction was carried out, reproducing the optimal conditions for the rest of the iodide-containing substrates. In this case, only 10 equivalents of CuI were tested to promote the formation of species **2** and **3** in the reaction media.

Compound $\mathbf{8}\boldsymbol{b}_{\mathrm{CF3}}$ was not observed by ^{19}F NMR spectroscopy and the yields obtained for $\mathbf{8}\boldsymbol{a}_{\mathrm{CF3}}$ (scheme 7) are comparable to those obtained previously. These results show that these reactions proceed without the intermediacy of an aryl radical from electron transfer and iodide expulsion [3*c*, 6].

Finally, the mechanism represented in scheme 8 is proposed as a possible oxidative addition/reductive elimination mechanism, based on the precedents in literature and our experimental results [7, 15]. The real nature of the intermediates, their geometry or the presence of other steps among those represented remain unknown to date.

More experiments are necessary to gain further insight into this proposed mechanism. For example, substrate $\mathbf{7}_{\mathrm{I}}$ could be used as a model for a further investigation of the suggested $(Cat)[Cu^{III}(CF_3)_2X(Ar)]$ intermediate [7].

Conclusions

In summary, a synthetic route that allows in situ, rapid and selective access to complexes of the bis-(trifluoromethyl)cuprate type has been established and the capacity of these complexes as trifluoromethylating agents in the C-CF_3 bond formation reactions has been evaluated using different representative aryl halides. The results obtained show the efficiency of these species, whose reactivity has been overlooked to date. Preliminary studies of the reaction mechanism have been carried out and the involvement of radical species can be discarded.

Experimental section

Materials and methods

Commercially available reagents AgF, AgOAc, NBu_4OAc, CsF, KF, Me_3SiCF_3, CuI, CuCl, CuBr, 4,4'-difluoro-1,1'-biphenyl, 4-iodobiphenyl, methyl-6-bromopyridine-2-carboxylate, benzyl bromide, 2-iodophenol, allyl bromide and K_2CO_3 were used without further purification, directly as received from the commercial supplier, and they were stored under inert gas and/or low temperature when required. When necessary, the solvents (THF, DMF) were used from a solvent purification system *pure-solv* (SPS-400, *Innovative Technology*) and stored under argon with 4 Å activated molecular sieves.

The copper source $[Cu(NCMe)_4][BF_4]$ [16], the $(Cat)Ag(CF_3)_2$ [5] complexes, and the organic compounds 10-iodobenzo[h]quinoline [10] and 1-(allyloxy)-2-iodobenzene

[17] were synthesized according to procedures described in literature.

All the silver complexes were light-sensitive so the reactions were performed in the dark to avoid photodecomposition.

General procedures

All reactions were carried out in an argon-filled glovebox (mBraun Unilab 4420) with concentrations of O_2 and $H_2O < 0.1$ ppm or oven-dried glassware (at 100 °C overnight and cooled under vacuum before use) using Schlenk techniques under argon atmosphere.

The reactions described in this report have been monitored by fluorine-19 nuclear magnetic resonance spectroscopy (^{19}F NMR). This same technique has been used for the characterization of copper complexes and trifluoromethylated organic compounds. NMR spectra were obtained on a Bruker 400 MHz. ^{1}H, ^{13}C and ^{19}F NMR chemical shifts are reported in parts per million (ppm), relative to tetramethylsilane (TMS) for ^{1}H and ^{13}C with the residual solvent peak used as an internal reference and relative to $CFCl_3$ (Freon) and 4,4'-difluoro-1,1'-biphenyl as internal standard for ^{19}F. In the ^{19}F spectra registered in non-deuterated solvents, a coaxial tube containing acetone-d_6 was used to maintain the lock 2H signal. Multiplicities are reported as follows: singlet (s), doublet (d), broad doublet (bd), triplet (t), doublet of quadruplet of quadruplets (dqq), and multiplet (m). The monitorization of the reaction and the product quantification were determined by internal calibration using 4,4'-difluoro-1,1'-biphenyl (d −116.8 ppm) and fluorobenzene (d −113.15 ppm) with 32 scans for data acquisition.

High resolution mass spectrometry (HRMS) data were recorded on an LCT-Premier (Waters) or a MicroTOF Focus (Bruker Daltonics) mass spectrometer using ESI ionization technique and tetrahydrofuran as solvent.

$CuCF_3$ species from the transmetalation reaction of $(Cat)[Ag(CF_3)_2]$ with different copper sources

In an argon atmosphere glovebox, a crimped vial was charged with $(Cat)[Ag(CF_3)_2]$ (0.016 mmol), the corresponding copper source (1 and 10 equivalents with respect to **1**) and a known amount of the internal standard, 4,4'-difluoro-1,1'-biphenyl. The mixture was dissolved in 0.6 mL of DMF and stirred at room temperature for 15 minutes. The solution was then filtered using a 0.2 mm PTFE filter and transferred to an NMR tube to be analyzed by ^{19}F NMR spectroscopy.

TABLE 3. Spectroscopic data obtained in the transmetalation reaction of 1_{Cs} and different copper sources

Cu source (equiv.)	^{19}F NMR (400 MHz, acetone-d_6 insert, 25 °C) δ:
CuI (10 equiv.)	−26.94 (s) (3_{Cs}), −30.65 (s) (2_{Cs}) ppm
CuI (1 equiv.)	−30.66 (s) (2_{Cs}) ppm
CuBr (10 equiv.)	−26.75 (s) (3_{Cs}), −30.70 (s) (2_{Cs}) ppm
CuCl (10 equiv.)	−26.46 (s) (3_{Cs}), −33.84 (s) (Cu(III)) ppm
$[Cu(NCMe)_4][BF_4]$ (10 equiv.)	−26.03 (s) (3_{Cs}), −30.68 (s) (2_{Cs}), −33.83 (s) (Cu(III)), −84.04 (s), −112.05 (s), −116.80 (s), −150.34 (s), −150.40 (s) ppm. The signals that range from −84.04 to −150.48 ppm are decomposition products.

TABLE 4. Spectroscopic data obtained in the transmetalation reaction of 1_{NBu4} and different copper sources

Cu source (equiv.)	^{19}F NMR (400 MHz, acetone-d_6 insert, 25 °C) δ:
CuI (10 equiv.)	−26.86 (s) (3_{NBu4}), −30.66 (s) (2_{NBu4}) ppm
CuI (1 equiv.)	−30.66 (s) (2_{NBu4}) ppm
CuBr (10 equiv.)	−26.71 (s) (3_{NBu4}), −30.68 (s) (2_{NBu4}) ppm
CuCl (10 equiv.)	−26.46 (s) (3_{NBu4}) ppm
$[Cu(NCMe)_4][BF_4]$ (10 equiv.)	−26.05 (s) (3_{NBu4}), −30.69 (s) (2_{NBu4}), −33.84 (s) (Cu(III)), −83.70 (d), 84.04 (s), −112.06 (s), −150.43 (s), −150.48 (s) ppm. The signals that range from −83.70 to −150.48 ppm are decomposition products.

Synthesis and characterization of the trifluoromethylated organic compounds 4_{CF3}, 5_{CF3}, 6_{CF3}, 7_{CF3} and 8_{CF3}

In an argon atmosphere glovebox, a crimped vial was charged with $(Cat)[Ag(CF_3)_2]$ [5.9 mg (Cat = Cs), 7.6 mg (Cat = NBu_4), 0.016 mmol] and the corresponding copper source (1 and 10 equivalents with respect to **1**). The mixture was dissolved in 0.6 mL of DMF and stirred at room temperature for 15 minutes. The solution was then filtered using a 0.2 mm PTFE filter and transferred to another crimped vial, that contained the organic substrate [0.0128 mmol (0.8 equiv.) or 0.0256 mmol

(1.6 equiv.)] and a known amount of the internal standard, 4,4'-difluoro-1,1'-biphenyl. The mixture was stirred at 50 °C (substrates $\mathbf{4}_{\mathrm{I}}$, $\mathbf{6}_{\mathrm{Br}}$, $\mathbf{7}_{\mathrm{I}}$ and $\mathbf{8}_{\mathrm{I}}$) or 80 °C (substrate $\mathbf{5}_{\mathrm{Br}}$) for the corresponding time (24 hours) and it was directly transferred to an NMR tube to obtain the ^{19}F NMR spectra.

The quantification of the trifluoromethylated substrate is determined by taking into account the limiting reagent (aryl halide) with respect to the known amount of the internal standard.

^{19}F NMR (400 MHz, acetone-d_6 insert, 25 °C): δ –62.05 ppm ($\mathbf{4}_{\mathrm{CF3}}$); δ –67.61 ppm ($\mathbf{5}_{\mathrm{CF3}}$); δ –65.70 ppm ($\mathbf{6}_{\mathrm{CF3}}$); δ –56.10 ppm ($\mathbf{7}_{\mathrm{CF3}}$); δ –61.89 ppm ($\mathbf{8}_{\mathrm{CF3}}$).

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