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Trifluoromethylation of haloarenes with a new trifluoro-methylating reagent $Cu(O_2CCF_2SO_2F)_2$†

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A new trifluoromethylating reagent $Cu(O_2CCF_2SO_2F)_2$, which easily decomposes to generate active $CuCF_3$ species in DMF at room temperature, has been conveniently prepared from inexpensive starting materials on a large scale. This new reagent can be applied to efficiently trifluoromethylate a variety of haloarenes under mild conditions, providing good-to-excellent yields of the desired products.

1. Introduction

Trifluoromethyl-containing aromatic compounds are becoming increasingly important as privileged structural motifs in pharmaceuticals, agrochemicals and drug candidates due to the unique properties arising from the electron-withdrawing nature, unique lipophilicity and metabolic stability of the trifluoromethyl groups.[1] Hence, considerable effort has been made to synthesise them and considerable progress has been achieved in recent decades.[2] Representative aromatic trifluoromethylation during the last few decades includes transition-metal-promoted nucleophilic trifluoromethylation[2a–d,g–j] as well as radical trifluoromethylation.[2e,f,j] Among these methodologies, copper-mediated aromatic trifluoromethylation has been most extensively studied and applied[2,3] due to its good reactivity, relatively low cost of copper and good regiospecificity.[4] Various $CuCF_3$ reagents preformed or generated *in situ* from a variety of CF_3 sources have been developed recently and demonstrated good reactivity towards haloarenes or their analogues.[2] For example, Vicic,[5] Hartwig,[6] Grushin[7] and Weng[8] successively reported relatively stable and well defined complexes of $(L)_nCuCF_3$ based on Me_3SiCF_3 by treatment with a Cu(I) salt and an appropriate ligand. Grushin's group subsequently developed the first reaction of direct cupration of fluoroform by treatment with CuCl and KO^{t}Bu followed by stabilization with $Et_3N\cdot 3HF$ to generate highly active $CuCF_3$ reagents.[9] Hu[10] and Mikami[11] independently reported the preparation of $CuCF_3$ reagent from cuprate and phenyl trifluoromethyl sulfones and trifluoromethyl ketone derivatives, respectively. Xiao found that difluorocarbene derived from various carbene precursors could be decomposed by DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) to generate a fluoride ion and further converted to $CuCF_3$ in the presence of a Cu(I) salt to efficiently finish trifluoromethylation with iodoarenes.[12] Zhang reported a new reagent trimethylsilyl chlorodifluoroacetate for the efficient synthesis of trifluoromethyl-substituted arenes.[13] Very recently, Weng reported the synthesis and trifluoromethylation reactions of a decarboxylative trifluoromethylating reagent (phen)$Cu(O_2CCF_3)$ (phen = 1,10-phenanthroline).[14] Despite these notable accomplishments, it is still desirable to develop efficient and convenient reagents to access various trifluoromethylated arenes under mild conditions.

Because of our long-standing interest in various trifluoromethylation reactions, we have always been turning our attention and putting effort toward developing new trifluoromethylation methods, particularly by using tetrafluoroethene β-sultone-based fluorinating derivatives as reagents.[15] Tetrafluoroethylene β-sultone is a unique cyclic compound and can be conveniently synthesized from the reaction between cheap $CF_2{=}CF_2$ and SO_3 in nearly quantitative yield.[16] Dupont commercialized perfluorinated Nafion polymer (Nafion™), a key source of pendant perfluoroalkylsulfonate groups, which has been widely manufactured and used as a basic and important industrial product.[17] Hence, fluorinating reagents derived from it are inexpensive and readily available in large quantities. In 1989, to the best of our knowledge, we developed the first catalytic trifluoromethylation reaction of haloarenes with FSO_2CF_2COOMe (ref. 17) in DMF at 60–80 °C in the presence of catalytic amounts of CuI, leading to various trifluoromethylated arenes in good yields.[3h] Later on, several related trifluoromethylating reagents were developed to efficiently furnish a variety of desired trifluoromethylated arenes.[15] It has been proposed that the reaction pathway involves the formation of the corresponding Cu(I)$(O_2CCF_2SO_2F)$ as the intermediate, followed by decarboxylation and generation of difluorocarbene, which in combination with a fluoride ion produces a CF_3Cu species in the presence of Cu(I) (Scheme 1).[3h,15] However, this Cu(I)$(O_2CCF_2SO_2F)$ has not been isolated or detected spectroscopically in the reaction system. We then sought to isolate and characterize the intermediate Cu(I)$(O_2CCF_2SO_2F)$. During the study, it was

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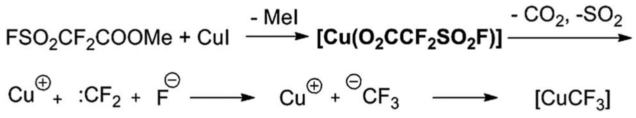


Scheme 1 Proposed decomposition mechanism of FSO_2CF_2COOMe in the presence of CuI in the literature.

found that fluorosulfonyldifluoroacetic acid copper(II) salt Cu(II)($FSO_2CF_2COO)_2$,[19] instead of Cu(I)($O_2CCF_2SO_2F$), was easily prepared in a large quantity and could be used as an efficient and mild trifluoromethylating agent. Herein, we present the results.

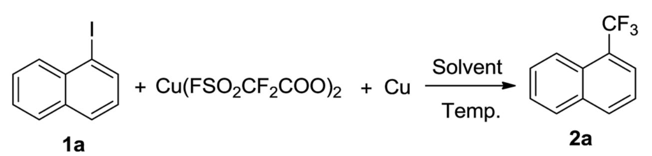
2. Results and discussion

At the beginning, we became aware of the potential to synthesize and isolate the key intermediate Cu(I)($O_2CCF_2SO_2F$) as a new trifluoromethylating reagent. Attempts were carried out to prepare it by mixing FSO_2CF_2COOH (ref. 18) with excess amounts of the corresponding Cu_2O in Et_2O. The color of the contents turned to dark-blue after stirring for 24 hours at room temperature. After filtration and evaporation of the solvent Et_2O and water generated during the reaction, a blue powder was obtained (Scheme 2). To our surprise, it was not the desired Cu(I)($O_2CCF_2SO_2F$) but Cu(II)$(O_2CCF_2SO_2F)_2$ after thorough characterization by ^{19}F NMR spectroscopy, elemental analysis and X-ray structural analysis. The redox processes involved in the reaction was unclear at this stage. The ^{19}F NMR spectrum shows a typical paramagnetic resonance due to the Cu(II) center. The single crystals obtained by solvent diffusion (Et_2O/hexane) were subjected to X-ray structural analysis. The copper(II) center is bound by two fluorosulfonyldifluoroacetic ions and four water molecules as ligands and demonstrates an axially-elongated octahedron configuration. As expected, the reaction of FSO_2CF_2COOH and a copper(II) salt $Cu_2(OH)_2CO_3$ under similar conditions afforded the corresponding $Cu(O_2CCF_2SO_2F)_2$ in almost quantitative yield. The reaction was run on a >50 gram scale, and the procedure was very simple. Both starting materials are commercially available and inexpensive. As such, $Cu(O_2CCF_2SO_2F)_2$ is very convenient to prepare on a large scale.

$Cu(O_2CCF_2SO_2F)_2$ is a stable and hygroscopic blue powder. No obvious decomposition occurred after storage for more than one month at 4 °C under dry air, and it displayed reactivity similar to that of a freshly prepared material. It is relatively stable in low polarity solvents such as CH_2Cl_2, acetone, toluene, THF and Et_2O at room temperature. However, it decomposes quickly in highly polar solvents such as CH_3CN, MeOH, DMF and DMSO at room temperature. Notably, it is highly soluble in Et_2O and THF, which is beneficial for the work-up. To our delight, both $[Cu(CF_3)]$ ($\delta = -26.6$ ppm) and $[Cu(CF_3)_2^-]$ ($\delta = -31.3$ ppm) species were detected in the reaction solution of $Cu(O_2CCF_2SO_2F)_2$ in DMF according to the ^{19}F NMR spectra, which matched well with the previous reported results.[3f,9,20]

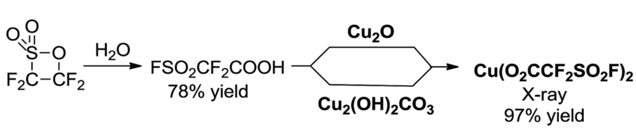
To assess the potential of $Cu(O_2CCF_2SO_2F)_2$ as a trifluoromethylation reagent, its reactivity with 1-iodonaphthalene (**1a**) was investigated under various conditions. As shown in Table 1, treatment of **1a** with 1.5 equivalent of $Cu(O_2CCF_2SO_2F)_2$ in DMF at room temperature for 3 hours resulted in smooth formation of the desired 1-trifluoromethylnaphthalene (**2a**) in 50% yield. As the Cu(I)CF_3 species is widely considered to be the real active intermediate, we attempted to convert Cu(II) to Cu(I) by adding an equal equivalent of Cu in the reaction system. To our delight, the reaction yield increased significantly to 96% in the presence of an equal equivalent of Cu. A survey of stoichiometry of $Cu(O_2CCF_2SO_2F)_2$/Cu and reaction temperatures showed that 1.5 equivalents and room temperature were the best choices. DMF stood out to be a more effective solvent than DMSO, DMAc, NMP and CH_3CN. It should be mentioned that in some cases 1-(pentafluoroethyl)naphthalene was observed as a side-product in trace amounts. The role of some additives was also investigated. KF, NEt_3 and DBU had no significant effect on the reaction. In addition, prolonging the reaction time to 12 hours was not beneficial. In brief, a combination of 1.5 equivalents of

Table 1 Optimization of trifluoromethylation reactions of $Cu(O_2CF_2SO_2F)_2$ with **2a** under various conditions[a]



Entry	Solvent	Temp. (°C)	Additives	Yield[b] (**2a**)
1[c]	DMF	25	—[d]	50%
2	DMF	25	—[d]	96%
3[e]	DMF	25	—[d]	96%
4[f]	DMF	25	—[d]	85%
5[g]	DMF	25	—[d]	85%
6	DMF	0	—[d]	74%
7	DMF	−5	—[d]	68%
8	DMF	−10	—[d]	57%
9	DMF	−20	—[d]	30%
10	DMSO	25	—[d]	0
11	NMP	25	—[d]	82%
12	DMAc	25	—[d]	83%
13	CH_3CN	25	—[d]	0
14	DMF	25	KF	90%
15	DMF	25	Et_3N	96%
16	DMF	25	DBU	87%

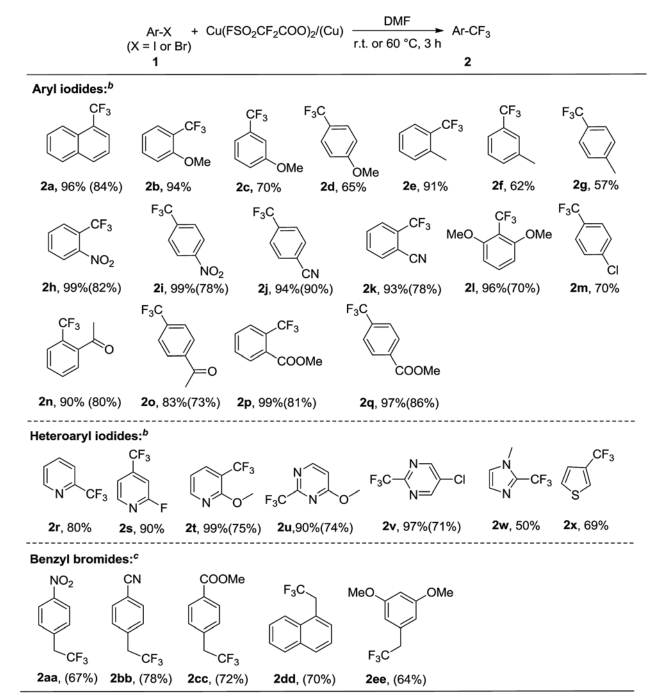
[a] Reaction conditions: 1-iodonaphthalene (0.2 mmol, 1.0 equiv.), $Cu(FSO_2CF_2COO)_2$ (0.3 mmol, 1.5 equiv.), Cu (0.3 mmol, 1.5 equiv.) in solvent (2 mL) under a nitrogen atmosphere for 3 hours at the reaction temperatures indicated above. [b] Yields were determined by ^{19}F NMR with trifluorotoluene as an internal standard. [c] Without Cu. [d] No additive was used. [e] 2.5 equiv. of $Cu(O_2CCF_2SO_2F)_2$/Cu was used. [f] 1.0 equiv. of $Cu(O_2CCF_2SO_2F)_2$/Cu was used. [g] Reaction time: 12 hours.



Scheme 2 Preparation of $Cu(O_2CCF_2SO_2F)_2$.

$Cu(O_2CCF_2SO_2F)_2$ and Cu in DMF at room temperature for 3 hours was established as the optimal reaction conditions for the trifluoromethylation.

Under these optimal reaction conditions, the scope of iodoarenes was carefully examined. As shown in Scheme 3, a variety of aryl iodides could be subjected to trifluoromethylation under mild conditions, giving the corresponding trifluoromethylated products in good-to-excellent yields. In general, electron-deficient aryl iodides (**1h–k**, **1n–q**) demonstrated better reactivity and yields than electron-rich aryl iodides (**1b–g**). Remarkably, the enhanced reactivity of *ortho*-substituted haloarene substrates was observed (**1b**, **1e**, **1l**, **1n**, **1p**), which is consistent with the previously reported ortho-effect.[9b,c] This ortho-effect is characteristic of copper-mediated aromatic substitution reactions in general. Moreover, ether, nitro, acetyl, halide, ester and nitrile were tolerated under the standard conditions. In addition, we explored the scope of the trifluoromethylation reaction by utilizing heteroaryl iodides. Iodopyridenes, iodopyrimidines, iodoimidazole and iodothiofuran (**1r–1x**) were all suitable substrates, resulting in the desired trifluoromethylated products in good yields. In addition, it should be noted that in many cases, the isolated yields of the desired trifluoromethylated products were much lower than what could be detected by NMR spectroscopy, which may be attributed to their high volatility or similar polarity to the starting iodoarenes.

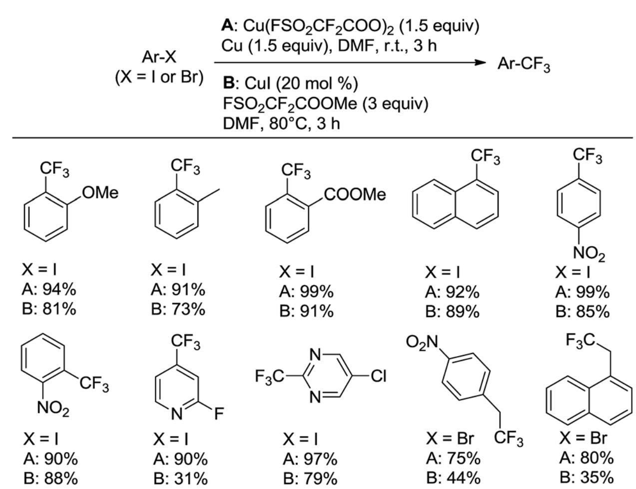


Scheme 3 Scope of the trifluoromethylation of various iodoarenes[a]. [a]Yields were determined by ^{19}F NMR with trifluorotoluene or 4-(trifluoromethoxy)benzotrifluoride as the internal standard. Isolated yields are given in parentheses. [b]Reaction conditions: substrate **1** (0.4 mmol, 1.0 equiv.), $Cu(O_2CCF_2SO_2F)_2$ (0.6 mmol, 1.5 equiv.), Cu (0.6 mmol, 1.5 equiv.) in DMF (4 mL) under a nitrogen atmosphere at room temperature for 3 hours. [c]Reaction conditions: substrate **1** (0.5 mmol, 1.0 equiv.), $Cu(O_2CCF_2SO_2F)_2$ (1.0 mmol, 2 equiv.) in DMF (5 mL) under nitrogen atmosphere at 60 °C for 3 hours.

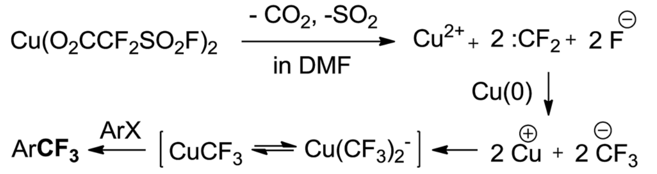
We next extended trifluoromethylation on various benzyl bromides under the abovementioned standard conditions. Although the reaction proceeded smoothly and successfully produced the desired product, the yield was not good (<30%). After further screening of the reaction conditions, it was found that the trifluoromethylation reactions of benzyl bromides proceeded better without the use of copper and at higher reaction temperatures (60 °C). Various benzyl bromides (Scheme 3, **1aa–ee**) were efficiently and conveniently subjected to smooth triflurometylation under these conditions, providing the desired products in good yields (Scheme 3).

Subsequently, a comparison of the reactivity of the new trifluoromethylating reagent $Cu(O_2CCF_2SO_2F)_2$ with our previously reported trifluoromethylating reagent FSO_2CF_2COOMe (ref. 3*h* and 18) with various haloarenes was performed (Scheme 4). The results clearly suggest that $Cu(O_2CCF_2SO_2F)_2$ demonstrates higher reactivity and better yields than FSO_2CF_2COOMe.

To determine the mechanism of trifluoromethylation with $Cu(O_2CCF_2SO_2F)_2$, we first carefully examined the decomposition of $Cu(O_2CCF_2SO_2F)_2$ in DMF using ^{19}F NMR analysis (see the ESI†). A singlet peak at −31.3 ppm assigned to $[Cu(CF_3)_2]^-$ was detected in 10 minutes. One hour later, a broad singlet peak at −26.5 ppm, which is considered to be the reactive mono-$CuCF_3$ species according to the literature,[3f,9,20] appeared and the intensity of the signal at −31.3 ppm decreased. Two hours later, the singlet at −26.5 ppm further increased, whereas the signal at −31.3 ppm further decreased. Based on these experimental results and the literature, we proposed a plausible mechanism (Scheme 5). First, $Cu(O_2CCF_2SO_2F)_2$ in DMF decomposes into Cu^{2+}, $:CF_2$ and fluoride with the release of SO_2 and CO_2. Then, difluorocarbene and fluoride combine into a $CuCF_3$ species in the presence of Cu^{2+} and Cu. $CuCF_3$ generated *in situ* reacts with the haloarenes to provide the desired trifluoromethylated products. It should be mentioned that $CuCF_3$ generated in our reaction system is a 'ligandless' species according to the



Scheme 4 Comparison of trifluoromethylating reagent $Cu(O_2CCF_2SO_2F)_2$ with FSO_2CF_2COOMe on various haloarenes. Yields were determined by ^{19}F NMR with trifluorotoluene or 4-(trifluoromethoxy) benzotrifluoride as the internal standard.



Scheme 5 Proposed mechanism of trifluoromethylation reactions with $Cu(O_2CCF_2SO_2F)_2$.

stoichiometry of the overall process and has excellent reactivity, which is in agreement with the literature.[12]

3. Conclusions

In summary, we developed a new trifluoromethylating reagent $Cu(O_2CCF_2SO_2F)_2$, which efficiently trifluoromethylates various haloarenes under mild conditions. It is a blue solid and can be conveniently prepared from inexpensive starting materials on a large scale. Its decomposition in DMF at room temperature readily affords highly active $CuCF_3$ species, and the corresponding trifluoromethylation reactions of various haloarenes proceeded smoothly and efficiently at room temperature in good to excellent yields with good functional group compatibility. Moreover, there is no need for an added ligand, which is in contrast with the vast majority of previously reported copper-mediated trifluoromethylation reactions of haloarenes in which the reaction proceeds efficiently only in the presence of a special ligand. Further investigation on the other fluorosulfonyldifluoroacetic acid metal salts is ongoing in our lab, and the results will be reported in due time.

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Notes and references

1 (*a*) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320–330; (*b*) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. D. Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, *Chem. Rev.*, 2014, **114**, 2432–2506.
2 Selected recent reviews: (*a*) O. A. Tomashenko and V. V. Grushin, *Chem. Rev.*, 2011, **111**, 4475–4521; (*b*) S. Roy, B. T. Gregg, G. W. Gribble, V.-D. Le and S. Roy, *Tetrahedron*, 2011, **67**, 2161; (*c*) T. Besset, C. Schneider and D. Cahard, *Angew. Chem., Int. Ed.*, 2012, **51**, 5048–5050; (*d*) T. Liu and Q. Shen, *Eur. J. Org. Chem.*, 2012, 6679–6687; (*e*) A. Studer, *Angew. Chem., Int. Ed.*, 2012, **51**, 8950–8958; (*f*) C. Zhang, *Adv. Synth. Catal.*, 2014, **356**, 2895–2906; (*g*) L. Chu and F.-L. Qing, *Acc. Chem. Res.*, 2014, **47**, 1513; (*h*) X. Liu, C. Xu, M. Wang and Q. Liu, *Chem. Rev.*, 2015, **115**, 683–730; (*i*) C. Ni, M. Hu and J. Hu, *Chem. Rev.*, 2015, **115**, 765–825; (*j*) C. Alonso, E. M. Marigorta, G. Rubiales and F. Palacios, *Chem. Rev.*, 2015, **115**, 1847–1935; (*k*) A. T. Herrmann, L. L. Smith and A. Zakarian, *J. Am. Chem. Soc.*, 2012, **134**, 6976–6979; (*l*) J. Alvarado, A. T. Herrmann and A. Zakarian, *J. Org. Chem.*, 2014, **79**, 6206–6220.
3 Selective examples: (*a*) V. C. R. McLoughlin and J. Thrower, *Tetrahedron*, 1969, **25**, 5921; (*b*) Y. Kobayashi and I. Kumadaki, *Tetrahedron Lett.*, 1969, 4095; (*c*) K. Sato, A. Tarui, M. Omote, A. Ando and I. Kumadaki, *Synthesis*, 2010, 1865; (*d*) N. V. Kondratenko, E. P. Vechirko and L. M. Yagupolskii, *Synthesis*, 1980, 932; (*e*) K. Matsui, E. Tobita, M. Ando and K. Kondo, *Chem. Lett.*, 1981, 1719; (*f*) D. M. Wiemers and D. J. Burton, *J. Am. Chem. Soc.*, 1986, **108**, 832; (*g*) J. G. MacNeil and D. J. Burton, *J. Fluorine Chem.*, 1991, **55**, 225; (*h*) Q. Chen and S. J. Wu, *J. Chem. Soc., Chem. Commun.*, 1989, 705; (*i*) H. Urata and T. Fuchikami, *Tetrahedron Lett.*, 1991, **32**, 91; (*j*) H. Urata and T. Fuchikami, *Tetrahedron Lett.*, 1991, **32**, 91–94; (*k*) F. Cottet and M. Schlosser, *Eur. J. Org. Chem.*, 2002, 327–330; (*l*) M. Oishi, H. Kondo and H. Amii, *Chem. Commun.*, 2009, 1909; (*m*) M. M. Kremlev, A. I. Musha, W. Tyrra, Y. L. Yagupolskii, D. Naumann and A. Moller, *J. Fluorine Chem.*, 2012, **133**, 67–71.
4 For related reviews, see: (*a*) D. J. Burton and Z. Y. Yang, *Tetrahedron*, 1992, **48**, 189; (*b*) D. J. Burton and L. Lu, *Top. Curr. Chem.*, 1997, **193**, 45; (*c*) M. A. García-Monforte, S. Martínez-Salvador and B. Menjón, *Eur. J. Inorg. Chem.*, 2012, 4945–4966.
5 (*a*) G. G. Dubinina, H. Furutachi and D. A. Vicic, *J. Am. Chem. Soc.*, 2008, **130**, 8600–8601; (*b*) G. G. Dubinina, J. Ogikubo and D. A. Vicic, *Organometallics*, 2008, **27**, 6233–6235; (*c*) H. Wang and D. A. Vicic, *Synlett*, 2013, **24**, 1887–1898.
6 (*a*) H. Morimoto, T. Tsubogo, N. D. Litvinas and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2011, **50**, 3793–3798; *Angew. Chem.*, 2011, **123**, 3877–3882; (*b*) N. D. Litvinas, P. S. Fier and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2012, **51**, 536–539; *Angew. Chem.*, 2012, **124**, 551–554; M. G. Mormino, P. S. Fier and J. F. Hartwig, *Org. Lett.*, 2014, **16**, 1744–1747.
7 O. A. Tomashenko, E. C. Escudero-Adan, M. M. Belmonte and V. V. Grushin, *Angew. Chem., Int. Ed.*, 2011, **50**, 7655–7659; *Angew. Chem.*, 2011, **123**, 7797–7801.
8 Y. Liu, C. Chen, H. Li, K.-W. Huang, J. Tan and Z. Weng, *Organometallics*, 2013, **125**, 1588–1592.
9 (*a*) A. Zanardi, M. A. Novikov, E. Martin and V. V. Grushin, *J. Am. Chem. Soc.*, 2011, **133**, 20901–20913; (*b*) A. Lishchynskyi, M. A. Novikov, E. Martin, P. Novák and V. V. Grushin, *J. Org. Chem.*, 2013, **78**, 11126–11146; (*c*) A. I. Konovalov, A. Lishchynskyi and V. V. Grushin, *J. Am. Chem. Soc.*, 2014, **136**, 13410–13425.
10 X. Li, J. Zhao, L. Zhang, M. Hu, L. Wang and J. Hu, *Org. Lett.*, 2015, **17**, 298–301.
11 H. Serizawa, K. Aikawa and K. Mikami, *Chem.–Eur. J.*, 2013, **19**, 17692–17697.
12 J. Zheng, J.-H. Lin, X.-Y. Deng and J.-C. Xiao, *Org. Lett.*, 2015, **17**, 532–535.
13 X. Zhang, J. Wang and Z. Wan, *Org. Lett.*, 2015, **17**, 2086–2089.

14 X. Lin, C. Hou, H. Li and Z. Weng, *Chem.–Eur. J.*, 2016, **22**, 2075–2084.

15 (*a*) Q.-Y. Chen, *J. Fluorine Chem.*, 1995, **72**, 241–246; (*b*) C.-P. Zhang, Q.-Y. Chen, Y. Guo, J.-C. Xiao and Y.-C. Gu, *Coord. Chem. Rev.*, 2014, **261**, 28–72.

16 (*a*) I. L. Knunyants and G. A. Sokolski, *Angew. Chem., Int. Ed.*, 1972, **11**, 583–595; (*b*) J. Mohtasham and G. L. Gard, *Coord. Chem. Rev.*, 1992, **112**, 47–79.

17 M. Yamabe and H. Miyake, in *Organofluorine Chemistry Principles and Commercial Applications*, ed. R. E. Banks, B. E. Smart and J. C. Tatlow, Plenum Press, New York and London, 1994, pp. 403–411.

18 FSO_2CF_2COOMe (CAS No. 680-15-9) and FSO_2CF_2COOH (CAS No. 1717-59-5) are easily prepared on scale by reaction of tetrafluoroethylene β-sultone with methanol and water, respectively (for detailed preparation procedures, see the ESI†). They are also commercially available, such as from Sigma-Aldrich.

19 Q.-Y. Chen, G. Zhao, C. Liu, Y. Guo, J.-C. Xiao, S. Zhao, W. Wang and D. Jiang, Preparation and application of new trifluoromethylating reagents, CN201310077629.1, March 11 2013.

20 M. Hu, C. Ni and J. Hu, *J. Am. Chem. Soc.*, 2012, **134**, 15257–15260.