Accepted Manuscript

Title: Copper-mediated trifluoromethylation of diaryliodonium salts with TMSCF₃ at room temperature

Author: Jing-Yun Yang Xiu-Hua Xu Feng-Ling Qing



Please cite this article as: J.-Y. Yang, Х.-Н. Xu. F.-L. Qing, of Copper-mediated trifluoromethylation diaryliodonium salts with TMSCF₃ at room temperature, Journal Fluorine Chemistry (2015),of http://dx.doi.org/10.1016/j.jfluchem.2015.09.015

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Copper-mediated trifluoromethylation of diaryliodonium salts with TMSCF₃ at room temperature

Jing-Yun Yang^a, Xiu-Hua Xu^a, Feng-Ling Qing^{a,b*}flq@mail.sioc.ac.cn

^aKey Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Science, 345 Lingling Lu, Shanghai 200032, China

^bCollege of Chemistry, Chemical Engineering and Biotechnology, Donghua University, 2999 North Renmin Lu, Shanghai 201620, China

Tel.: 86-21-54925187; fax: 86-21-64166128

Abstract

A convenient method for the preparation of trifluoromethylated arenes from the reaction of diaryliodonium salts with $TMSCF_3$ in the presence of $CuBF_4$ ·(MeCN)₄ and KF at room temperature within 25 minutes was developed. This reaction provides a valuable complement to the previously established trifluoromethylation methods.

Keywords

Copper; Trifluoromethylation; Arene; Diaryliodonium salts; Synthetic methods

1. Introduction

Trifluoromethylated arenes have received increasing attention in the fields of pharmaceutical, agrochemical, and material sciences [1]. Accordingly, the development of methods to introduce CF_3 group into aromatic compounds has become a field of intense research effort [2]. Traditional methods to access benzotrifluorides, such as the Swarts reaction, typically require harsh conditions and have a low substrate scope [3]. Over the past few years, the mild and direct trifluoromethylation of aromatic compounds has blossomed dramatically. Trifluoromethylation of an aromatic C—H bond through a radical process has emerged as an attractive approach to trifluoromethylated arenes (Scheme 1a) [4]. Alternatively, direct C—H bond trifluoromethylation of arenes substituted with directing groups provides another highly economical and efficient access to these compounds (Scheme 1b) [5]. With respect to high regiochemical fidelity in aromatic substitution, the transition metal-promoted cross-coupling of aryl halides [6] or boronic acid derivatives [7] with trifluoromethylating reagents offers one of the most useful methods (Scheme 1c and 1d). Very recently, Sandmeyer type trifluoromethylation was also described by several groups (Scheme 1e) [8]. Although remarkable achievements have been made on aromatic trifluoromethylation, most current methods are limited by some combination of expensive reagents, long reaction time, high temperature, low regioselectivity, and limited substrate

^{*} Corresponding author. Tel.: +86 21 54925187; fax: +86 21 64166128.

E-mail address: flq@mail.sioc.ac.cn (F.-L. Qing).

scope. There is still great demand for the development of new trifluoromethylation methods that function under mild and simple conditions.

Diaryliodonium salts, owing to their highly electron-deficient nature and excellent leaving-group ability [9], have received considerable attention in the preparation of numerous aromatic compounds [10]. Recently, Sanford and co-workers disclosed the Cu-catalyzed fluorination of diaryliodonium salts for the preparation of aryl fluorides [11]. Inspired by their results, we wondered whether it might be possible to apply analogous transformations for the preparation of trifluoromethylated arenes. In continuation of our research interest in the development of new methods for trifluoromethylation reaction [7a,7k,12], we describe here the Cu-mediated trifluoromethylation of diaryliodonium salts with TMSCF₃ (Scheme 1f) [13].

2. Results and Discussion

As the mesityl group of arylmesityliodonium salts was widely used as a dummy ligand to selectively transfer the aryl group [14], [1,1'-biphenyl]-4-ylmesityliodonium triflate (1a) was chosen as the test substrate to optimize the reaction conditions (Table 1). The reaction of 1a with TMSCF₃ (2.0 equiv) in the presence of CuI (0.2 equiv) and KF (2.0 equiv) in MeCN at 80 °C gave the trifluoromethylated product 2a in 33% yield (Entry 1). To our delight, slightly higher yields were gained at 50 °C or room temperature (Entries 2 and 3). Importantly, this coupling reaction proceeded within a short time of 25 min. Encouraged by these results, different Cu salts, including CuBr, CuTc, CuSCN, CuBF₄·(MeCN)₄, and Cu(OAc)₂, were then screened (Entries 4-8). Among them, CuBF₄·(MeCN)₄ was superior than other Cu salts, affording product 2a in 45% yield (Entry 7). Switching to other initiators such as CsF, NaOAc, and *t*-BuOK led to a dramatic decrease in the reaction yield (Entries 9-11). To our disappointment, the addition of ligand 1,10-phenanthroline (phen) had a negative effect to the yield of compound 2a (Entry 12). To further improve the reaction yield, the amounts of TMSCF₃, CuBF₄·(MeCN)₄, and KF were increased to improve the yield to 73% (Entries 13-16). Finally, the solvents DMF and DMSO were investigated, but neither of them gave better result (Entries 17 and 18).

With the optimized reaction conditions in hand (Table 1, Entry 15), we next investigated the substrate scope of this transformation. As shown in Table 2, various diaryiodonium salts, including [Mes—I—Ar]OTf and [Mes—I—Ar]BF4, were conveniently converted into the corresponding trifluoromethylated products in moderate to excellent yields. In all cases, the products 2 arose from the reaction of less sterically hindered aryl group. No product of MesCF₃ could be detected by the ¹⁹F NMR and GC-MS. This preferred reactivity of less sterically hindered aryl groups is consistent with reported Cu-catalyzed reactions of diaryliodonium salts with other nucleophiles [10a,11]. Substrates bearing both electron-donating and electron-withdrawing substituents on the aryl ring were compatible in this process. In general, the electron-rich diaryiodonium salts afforded lower yields than electron-poor substrates. A range of functional groups, including esters, ethers, ketones, and nitriles, were tolerated in this transformation. It was particularly noteworthy that the tolerance of a halo substituent (Cl, Br, and I) provided a complementary platform for further transformations. Interesting, dibenzo [b,d] furan derivative was also applicable for the trifluoromethylation reaction under the standard conditions to provide 20 in moderate yield. It was noteworthy that the symmetrical diaryliodonium salt was also effective for this transformation. For example, the reaction of diphenyliodonium triflate and $TMSCF_3$ in the presence of CuI and KF gave trifluoromethylbenzene in 90% yield.

In conclusion, we have developed a copper-mediated trifluoromethylation reaction of diaryliodonium salts with TMSCF₃. This reaction proceeds under mild conditions for a short time. A range of synthetically useful functional groups are well-tolerated. Thus, we believe that this new protocol can be potentially applied in the rapid preparation of trifluoromethylated arenes.

4. Experimental Section

4.1. General information

¹H NMR (TMS as the internal standard) was recorded on a Bruker AM300 spectrometer. ¹⁹F NMR (CFCl₃ as the outside standard and low field is positive) and ¹³C NMR spectra were recorded on a Bruker AM400 spectrometer. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q =quartet, m = multiplet. HRMS using EI were obtained on a GC-TOF mass spectrometer. The diaryliodonium salts were prepared from the corresponding iodoarenes or arylboronic acids [11,15]. All starting materials and reagents were purchased from commercial sources and used without further purification. Compounds 2a-2o are all known compounds.

4.2. General procedure for the synthesis of diaryliodonium salts

Procedure A: Preparation of diaryliodonium triflates. To a 100 mL round-bottom flask equipped with a stir bar was added the indicated iodoarene (9.0 mmol), *m*CPBA (1.20 g, 10.0 mmol), CH₂Cl₂ (40 mL) and mesitylene (1.39 mL, 10.0 mmol). The solution was cooled to 0 °C and TfOH (1.33 mL, 1.6 eq) was added dropwise over 3 minutes and the reaction was allowed to warm to room temperature. After stirring for 2 hours, the solvent was removed *in vacuo* and Et₂O (20 mL) was added. The mixture was cooled to -20 °C for at least 0.5 hour. The diaryliodonium triflates was filtered, washed with Et₂O and dried under vacuum.

Procedure B: Preparation of diaryliodonium tetrafluoroborates. To a 250 mL round-bottom flask equipped with a stir bar was added the indicated arylboronic acid (3.5 mmol) and CH_2Cl_2 (30 mL). The mixture was cooled to 0 °C and BF₃·OEt₂ (0.48 mL, 3.9 mmol) was added. The mixture was stirred for 10 minutes before a solution of 2-(diacetoxyiodo)mesitylene (1.42 g, 3.9 mmol) in CH_2Cl_2 (15 mL) was added dropwise over 2 minutes. The reaction was allowed to warm to room temperature and stirred for 2 hours. Then saturated aqueous NaBF₄ (70 mL) was added with rapid stirring. After stirring for 45 minutes, the aqueous layer was extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were dried over Na₂SO₄ and evaporated. Et₂O (20 mL) was added and the mixture was cooled to -20 °C for at least 0.5 hour. The diaryliodonium tetrafluoroborates was filtered, washed with Et₂O and dried under vacuum.

4.3. General procedure for trifluoromethylation of diaryliodonium salts

An over-dried 50 mL Schlenk tube equipped with a magnetic stir bar was charged with diaryliodonium salt (0.5 mmol, 1.0 eq), CuBF₄·(MeCN)₄ (157.3 mg, 0.5 mmol, 1.0 eq) and KF (58.1 mg, 1.0 mmol, 2.0 eq). The seal tube was evacuated and backfilled with N₂. Then TMSCF₃ (296 μ L, 2.0 mmol, 4.0 eq) and MeCN (5.0 mL) were added by syringes. The mixture was stirred at room temperature for 25 minutes. Then the reaction was quenched by H₂O and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated under reduced vacuum. The resulting residue was purified by silica gel column chromatography to provide the desired product.

4.3.1. 4-(Trifluoromethyl)-1,1'-biphenyl (2a)

Compound 2a was prepared following the general procedure in 70% yield, starting from [1,1'-biphenyl]-4-yl(mesityl)iodonium trifluoromethanesulfonate (274.2 mg, 0.5 mmol) prepared by procedure A. ¹H

NMR (300 MHz, CDCl₃): δ ppm 7.74-7.68 (m, 4H), 7.64-7.61 (m, 2H), 7.53-7.43 (m, 3H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -62.38 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 144.85, 139.90, 129.33 (q, *J* = 33.0 Hz), 129.13, 128.34, 127.56, 127.42, 125.84 (q, *J* = 3.7 Hz), 124.46 (q, *J* = 274.5 Hz). MS (EI): m/z (%) 222 (100). HRMS: Calculated for C₁₃H₉F₃: 222.0656; Found [M]⁺, 222.0654.

4.3.2. 1-(Benzyloxy)-4-(trifluoromethyl)benzene (2c

Compound 2c was prepared following the general procedure in 39% yield, starting from (4-(benzyloxy)phenyl)-(mesityl)iodonium tetrafluoroborate (258.1 mg, 0.5 mmol) prepared by procedure B. ¹H NMR (300 MHz, CDCl₃): δ ppm 7.56 (d, *J* = 8.7 Hz, 2H), 7.46-7.36 (m, 5H), 7.05 (d, *J* = 8.7 Hz, 2H), 5.12 (s, 2H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -61.47 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 161.29 (d, *J* = 1.6 Hz), 136.33, 128.86, 128.41, 127.62, 127.07 (q, *J* = 3.7 Hz), 124.57 (q, *J* = 272.6 Hz), 123.21 (q, *J* = 32.9 Hz), 114.96, 70.27. MS (EI): m/z (%) 252 (100). HRMS: Calculated for C₁₄H₁₁OF₃: 252.0755; Found [M]⁺, 252.0754.

4.3.3. 1-Phenoxy-4-(trifluoromethyl)benzene (2d)

Compound 2d was prepared following the general procedure in 34% yield, starting from mesityl(4-phenoxyphenyl)iodonium tetrafluoroborate (251.1 mg, 0.5 mmol) prepared by procedure B. ¹H NMR (300 MHz, CDCl₃): δ ppm 7.58 (d, *J* = 8.4 Hz, 2H), 7.40 (t, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.08-7.04 (m, 4H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -61.75 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 160.73 (d, *J* = 1.5 Hz), 155.90, 130.27, 127.31 (q, *J* = 3.8 Hz), 125.02 (q, *J* = 33.5 Hz), 124.70, 124.41 (q, *J* = 272.0 Hz), 120.14, 118.04. MS (EI): m/z (%) 238 (100). HRMS: Calculated for C₁₃H₉OF₃: 238.0605; Found [M]⁺, 238.0601.

4.3.4. 2-(Trifluoromethyl)naphthalene (2e)

Compound 2e was prepared following the general procedure in 80% yield, starting from mesityl(naphthalen-2-yl)iodonium tetrafluoroborate (230.0 mg, 0.5 mmol) prepared by procedure B. ¹H NMR (300 MHz, CDCl₃): δ ppm 8.19-8.14 (m, 1H), 8.00-7.89 (m, 3H), 7.67-7.56 (m, 3H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -62.26 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 134.55, 132.17, 128.98, 128.80, 128.05, 127.86, 127.70 (q, *J* = 32.4 Hz), 127.15, 125.68 (q, *J* = 4.5 Hz), 124.40 (q, *J* = 272.5 Hz), 121.43 (q, *J* = 3.4 Hz). MS (EI): m/z (%) 196 (100). HRMS: Calculated for C₁₁H₇F₃: 196.0500; Found [M]⁺, 196.0504.

4.3.5. 1-Methyl-4-(trifluoromethyl)naphthalene (2f)

Compound 2f was prepared following the general procedure in 76% yield, starting from mesityl(4methylnaphthalen-1-yl)iodonium tetrafluoroborate (237.0 mg, 0.5 mmol) prepared by procedure B. ¹H NMR (300 MHz, CDCl₃): δ ppm 8.30-8.27 (m, 1H), 8.11-8.08 (m, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.67-7.63 (m, 2H), 7.34 (d, *J* = 7.5 Hz, 1H), 2.74 (s, 3H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -59.25 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 139.72, 133.18, 129.17, 127.31, 126.53, 125.18 (q, *J* = 273.3 Hz), 125.05, 124.91, 124.87, 124.58 (q, *J* = 6.0 Hz), 124.56 (q, *J* = 30.1 Hz), 19.82. MS (EI): m/z (%) 210 (100). HRMS: Calculated for C₁₂H₉F₃: 210.0656; Found [M]⁺, 210.0651.

4.3.6. Methyl 2-(trifluoromethyl)benzoate (2g)

Compound 2g was prepared following the general procedure in 56% yield, starting from mesityl[2-(methoxycarbonyl)phenyl]iodonium trifluoromethanesulfonate (265.2 mg, 0.5 mmol) prepared by procedure A. ¹H NMR (300 MHz, CDCl₃): δ ppm 8.00-7.73 (m, 2H), 7.62-7.59 (m, 2H), 3.94 (s, 3H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -59.76 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 167.44, 131.85 (d, *J* = 2.2 Hz), 131.33, 130.30, 128.88 (q, *J* = 32.6 Hz), 126.81 (q, *J* = 5.6 Hz), 123.47 (q, *J* = 273.9 Hz), 52.98. MS (EI): m/z (%) 204 (100). HRMS: Calculated for C₉H₇O₂F₃: 204.0398; Found [M]⁺, 204.0399.

4.3.7. Ethyl 4-(trifluoromethyl)benzoate (2h)

Compound 2h was prepared following the general procedure in 90% yield, starting from [4-(ethoxycarbonyl)phenyl](mesityl)iodonium trifluoromethanesulfonate (272.2 mg, 0.5 mmol) prepared by procedure A. ¹H NMR (300 MHz, CDCl₃): δ ppm 8.15 (d, *J* = 7.8 Hz, 2H), 7.69 (d, *J* = 7.8 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -63.16 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 165.53, 134.44 (q, *J* = 32.6 Hz), 133.83, 130.07, 125.48 (q, *J* = 3.8 Hz), 123.80 (q, *J* = 273.3 Hz), 61.68, 14.37. MS (EI): m/z (%) 218 (100). HRMS: Calculated for C₁₀H₉O₂F₃: 218.0555; Found [M]⁺, 218.0550.

4.3.8. 1-[4-(Trifluoromethyl)phenyl]ethanone (2i)

Compound 2i was prepared following the general procedure in 74% yield, starting from (4-acetylphenyl)(mesityl)iodonium trifluoromethanesulfonate (257.2 mg, 0.5 mmol) prepared by procedure A. ¹H NMR (300 MHz, CDCl₃): δ ppm 7.83 (d, J = 8.7 Hz, 2H), 7.66 (d, J = 8.7 Hz, 2H), 2.57 (s, 3H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -63.14 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 196.96, 139.70, 134.44 (q, J = 32.7 Hz), 128.63, 125.68 (q, J = 3.9 Hz), 123.61 (q, J = 272.7 Hz), 26.74. MS (EI): m/z (%) 188 (100). HRMS: Calculated for C₉H₇OF₃: 188.0449; Found [M]⁺, 188.0447.

4.3.9. 4-(Trifluoromethyl)benzonitrile (2j)

Compound 2j was prepared following the general procedure in 85% yield, starting from (4-cyanophenyl)(mesityl)iodonium trifluoromethanesulfonate (248.6 mg, 0.5 mmol) prepared by procedure A. ¹H NMR (300 MHz, CDCl₃): δ ppm 7.83 (d, J = 6.3 Hz, 2H), 7.76 (d, J = 6.3 Hz, 2H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -63.55 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 134.71 (q, J = 33.5 Hz), 132.84, 126.33 (q, J = 3.6 Hz), 123.24 (q, J = 273.1 Hz), 117.58, 116.21. MS (EI): m/z (%) 171 (100). HRMS: Calculated for C₈H₄NF₃: 171.0296; Found [M]⁺, 171.0298.

4.3.10. 4-(Trifluoromethyl)dibenzo[b,d]furan (20)

Compound 20 was prepared following the general procedure in 46% yield, starting from dibenzo[*b*,*d*]furan-4-yl(mesityl)iodonium tetrafluoroborate (250.0 mg, 0.5 mmol) prepared by procedure B. ¹H NMR (300 MHz, CDCl₃): δ ppm 8.11 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 8.9 Hz, 2H), 7.56-7.50 (m, 1H), 7.44-7.37 (m, 2H). ¹⁹F NMR (376 MHz, CDCl₃): δ ppm -61.06 (s, 3F). ¹³C NMR (100.7 MHz, CDCl₃): δ ppm 156.56, 152.24, 128.28, 126.13, 124.50, 124.05 (q, *J* = 4.6 Hz), 123.55, 123.44 (q, *J* = 272.0 Hz), 123.07, 122.49, 120.89, 115.09 (q, *J* = 34.2 Hz), 112.28. MS (EI): m/z (%) 236 (100). HRMS: Calculated for C₁₃H₇OF₃: 236.0449; Found [M]⁺, 236.0446.

Acknowledgement. We thank the National Natural Science Foundation of China (21421002, 21332010, 21272036) and the National Basic Research Program of China (2012CB21600) for funding this work.

References

[1] (a) K. Muller, C. Faeh, F. Diederich, Science 317 (2007) 1881-1886;

(b) S. Purser, P.R. Moore, S. Swallow, V. Gouverneur, Chem. Soc. Rev. 37 (2008) 320-330;

- (c) N.A. Meanwell, J. Med. Chem. 54 (2011) 2529-2591
- (d) M. Cametti, B. Crousse, P. Metrangolo, R. Milani, G. Resnati, Chem. Soc. Rev. 41 (2012) 31-42;

(e) J. Wang, M. Sanchez-Rosello, J.L. Acena, C. del Pozo, A.E. Sorochinsky, S. Fustero, V.A. Soloshonok, H. Liu, Chem. Rev. 114 (2014) 2432-2506.

- [2] (a) O.A. Tomashenko, V.V. Grushin, Chem. Rev. 111 (2011) 4475-4521
- (b) T. Furuya, A.S. Kamlet, T. Ritter, Nature 473 (2011) 470-477
- (c) Z. Jin, G.B. Hammond, B. Xu, Aldrichim. Acta 45 (2012) 67-83;
- (d) T. Besset, C. Schneider, D. Cahard, Angew. Chem. Int. Ed. 51 (2012) 5048-5050;
- (e) A. Studer, Angew. Chem. Int. Ed. 51 (2012) 8950-8958
- (f) X.-F. Wu, H. Neumann, M. Beller, Chem. Asian J. 7 (2012) 1744-1754;
- (g) F.-L. Qing, Chin. J. Org. Chem. 32 (2012) 815-824;
- (h) Y. Macé, E. Magnier, Eur. J. Org. Chem. (2012) 2479-2494;
- (i) T. Liu, Q. Shen, Eur. J. Org. Chem. (2012) 6679-6687;
- (j) Y. Ye, M.S. Sanford, Synlett 23 (2012) 2005-2013;
- (k) H. Liu, Z. Gu, X. Jiang, Adv. Synth. Catal. 355 (2013) 617-626;
- (1) T. Liang, C.N. Neumann, T. Ritter, Angew. Chem. Int. Ed. 52 (2013) 8214-8264;
- (m) H. Wang, D.A. Vicic, Synlett 24 (2013) 1887-1898;
- (n) P. Chen, G. Liu, Synthesis 45 (2013) 2919-2939
- (o) D. L. Browne, Angew. Chem. Int. Ed. 53 (2014) 1482-1484;
- (p) C. Zhang, Org. Biomol. Chem. 12 (2014) 6580-6589
- (q) M. Sodeoka, H. Egami, Pure Appl. Chem. 86 (2014) 1247-1256
- (r) J. Xu, X. Liu, Y. Fu, Tetrahedron Lett. 55 (2014) 585-594
- (s) A.J. Cresswell, S.G. Davies, P.M. Roberts, J.E. Thomson, Chem. Rev. 115 (2015) 566-611
- (t) J. Charpentier, N. Fruh, A. Togni, Chem. Rev. 115 (2015) 650-682
- (u) X. Liu, C. Xu, M. Wang, Q. Liu, Chem. Rev. 115 (2015) 683-730
- (v) C. Ni, M. Hu, J. Hu, Chem. Rev. 115 (2015) 765-825;
- (w) C. Alonso, E. Martinez de Marigorta, G. Rubiales, F. Palacios, Chem. Rev. 115 (2015) 1847-1935.
- (x) S. Roy, B.T. Gregg, G.W. Gribble, V.-D. Le, S. Roy, Tetrahedron 67 (2011) 2161-2195.
- [3] F. Swarts, Bull. Soc. Chim. Belg. 24 (1892) 309.
- [4] (a) D.A. Nagib, D.W.C. MacMillan, Nature 480 (2011) 224-228

(b) Y. Ji, T. Brueckl, R.D. Baxter, Y. Fujiwara, I.B. Seiple, S. Su, D.G. Blackmond, P.S. Baran, Proc. Natl. Acad. Sci. U.S.A. 108 (2011) 14411-14415

- (c) Y. Ye, S.H. Lee, M.S. Sanford, Org. Lett. 13 (2011) 5464-5467;
- (d) E. Mejia, A. Togni, Acs Catal. 2 (2012) 521-527

- (e) Y.-D. Yang, K. Iwamoto, E. Tokunaga, N. Shibata, Chem. Commun. 49 (2013) 5510-5512
- (f) S. Seo, J.B. Taylor, M.F. Greaney, Chem. Commun. 49 (2013) 6385-6387
- (g) X. Wu, L. Chu, F.-L. Qing, Tetrahedron Lett. 54 (2013) 249-251
- (h) J. Xie, X. Yuan, A. Abdukader, C. Zhu, J. Ma, Org. Lett. 16 (2014) 1768-1771
- (i) F. Sladojevich, E. McNeill, J. Börgel, S.-L. Zheng, T. Ritter, Angew. Chem. Int. Ed. 54 (2015) 3712-3716
- (j) G. Shi, C. Shao, S. Pan, J. Yu, Y. Zhang, Org. Lett. 17 (2015) 38-41.
- [5] (a) X. Wang, L. Truesdale, J.-Q. Yu, J. Am. Chem. Soc. 132 (2010) 3648-3649
- (b) Y. Ye, N.D. Ball, J.W. Kampf, M.S. Sanford, J. Am. Chem. Soc. 132 (2010) 14682-14687
- (c) A. Hafner, S. Bräse, Angew. Chem. Int. Ed. 51 (2012) 3713-3715
- (d) X.-G. Zhang, H.-X. Dai, M. Wasa, J.-Q. Yu, J. Am. Chem. Soc. 134 (2012) 11948-11951
- (e) S. Cai, C. Chen, Z. Sun, C. Xi, Chem. Commun. 49 (2013) 4552-4554
- (f) L.-S. Zhang, K. Chen, G. Chen, B.-J. Li, S. Luo, Q.-Y. Guo, J.-B. Wei, Z.-J. Shi, Org. Lett. 15 (2013) 10-13
- (g) M. Miura, C.-G. Feng, S. Ma, J.-Q. Yu, Org. Lett. 15 (2013) 5258-5261
- (h) M. Nappi, G. Bergonzini, P. Melchiorre, Angew. Chem. Int. Ed. 53 (2014) 4921-4925
- (i) M. Shang, S.-Z. Sun, H.-L. Wang, B.N. Laforteza, H.-X. Dai, J.-Q. Yu, Angew. Chem. Int. Ed. 53 (2014) 10439-10442.
- [6] (a) M. Oishi, H. Kondo, H. Amii, Chem. Commun. (2009) 1909-1911
- (b) E.J. Cho, T.D. Senecal, T. Kinzel, Y. Zhang, D.A. Watson, S.L. Buchwald, Science 328 (2010) 1679-1681;
- (c) H. Kondo, M. Oishi, K. Fujikawa, H. Amii, Adv. Syn. Catal. 353 (2011) 1247-1252
- (d) C.-P. Zhang, Z.-L. Wang, Q.-Y. Chen, C.-T. Zhang, Y.-C. Gu, J.-C. Xiao, Angew. Chem. Int. Ed. 50 (2011) 1896-1900
- (e) H. Morimoto, T. Tsubogo, N.D. Litvinas, J.F. Hartwig, Angew. Chem. Int. Ed. 50 (2011) 3793-3798
- (f) O.A. Tomashenko, E.C. Escudero-Adán, M.M. Belmonte, V.V. Grushin, Angew. Chem. Int. Ed. 50 (2011) 7655-7659
- (g) T. Knauber, F. Arikan, G.-V. Röschenthaler, L.J. Gooßen, Chem.-Eur. J. 17 (2011) 2689-2697
- (h) A. Zanardi, M.A. Novikov, E. Martin, J. Benet-Buchholz, V.V. Grushin, J. Am. Chem. Soc. 133 (2011) 20901-20913
- (i) Y. Li, T. Chen, H. Wang, R. Zhang, K. Jin, X. Wang, C. Duan, Synlett (2011) 1713-1716
- (j) I.A. Sanhueza, M.C. Nielsen, M. Ottiger, F. Schoenebeck, Helv. Chim. Acta 95 (2012) 2231-2236
- (k) T. Schareina, X.-F. Wu, A. Zapf, A. Cotte, M. Gotta, M. Beller, Top. Catal. 55 (2012) 426-431

(1) M. Chen, S.L. Buchwald, Angew. Chem. Int. Ed. 52 (2013) 11628-11631

(m) A. Lishchynskyi, M.A. Novikov, E. Martin, E.C. Escudero-Adan, P. Novak, V.V. Grushin, J. Org. Chem. 78 (2013) 11126-11146

(n) M. Huiban, M. Tredwell, S. Mizuta, Z. Wan, X. Zhang, T.L. Collier, V. Gouverneur, J. Passchier, Nature Chemistry 5 (2013) 941-944

(o) T. Ruhl, W. Rafique, V.T. Lien, P.J. Riss, Chem. Commun. 50 (2014) 6056-6059

(p) M.G. Mormino, P.S. Fier, J.F. Hartwig, Org. Lett. 16 (2014) 1744-1747

(q) Z. Gonda, S. Kovacs, C. Weber, T. Gati, A. Meszaros, A. Kotschy, Z. Novak, Org. Lett. 16 (2014) 4268-4271

(r) K. Aikawa, Y. Nakamura, Y. Yokota, W. Toya, K. Mikami, Chem.-Eur. J. 21 (2015) 96-100

(s) X. Zhang, J. Wang, Z. Wan, Org. Lett. 17 (2015) 2086-2089

(t) Y. Liu, X. Shao, P. Zhang, L. Lu, Q. Shen, Org. Lett. 17 (2015) 2752-2755.

[7] (a) L. Chu, F.-L. Qing, Org. Lett. 12 (2010) 5060-5063

(b) J. Xu, D.-F. Luo, B. Xiao, Z.-J. Liu, T.-J. Gong, Y. Fu, L. Liu, Chem. Commun. 47 (2011) 4300-4302

(c) C.-P. Zhang, J. Cai, C.-B. Zhou, X.-P. Wang, X. Zheng, Y.-C. Gu, J.-C. Xiao, Chem. Commun. 47 (2011) 9516-9518

(d) T.D. Senecal, A.T. Parsons, S.L. Buchwald, J. Org. Chem. 76 (2011) 1174-1176

(e) T. Liu, Q. Shen, Org. Lett. 13 (2011) 2342-2345

(f) N.D. Litvinas, P.S. Fier, J.F. Hartwig, Angew. Chem. Int. Ed. 51 (2012) 536-539

(g) T. Liu, X. Shao, Y. Wu, Q. Shen, Angew. Chem. Int. Ed. 51 (2012) 540-543

(h) P. Novák, A. Lishchynskyi, V.V. Grushin, Angew. Chem. Int. Ed. 51 (2012) 7767-7770

(i) B.A. Khan, A.E. Buba, L.J. Gooßen, Chem.-Eur. J. 18 (2012) 1577-1581

(j) Y. Ye, M.S. Sanford, J. Am. Chem. Soc. 134 (2012) 9034-9037

(k) X. Jiang, L. Chu, F.-L. Qing, J. Org. Chem. 77 (2012) 1251-1257

(1) Y. Ye, S.A. Kuenzi, M.S. Sanford, Org. Lett. 14 (2012) 4979-4981

(m) Y. Huang, X. Fang, X. Lin, H. Li, W. He, K.-W. Huang, Y. Yuan, Z. Weng, Tetrahedron 68 (2012) 9949-9953

(n) Y. Li, L. Wu, H. Neumann, M. Beller, Chem. Commun. 49 (2013) 2628-2630

(o) H. Serizawa, K. Aikawa, K. Mikami, Chem.-Eur. J. 19 (2013) 17692-17697

(p) M. Presset, D. Oehlrich, F. Rombouts, G.A. Molander, J. Org. Chem. 78 (2013) 12837-12843

(q) D. van der Born, C. Sewing, J.D.M. Herscheid, A.D. Windhorst, R.V.A. Orru, D.J. Vugts, Angew. Chem. Int. Ed. 53 (2014) 11046-11050

(r) S.R. Dubbaka, M. Salla, R. Bolisetti, S. Nizalapur, RSC Adv. 4 (2014) 6496-6499

(s) X. Li, J. Zhao, L. Zhang, M. Hu, L. Wang, J. Hu, Org. Lett. 17 (2015) 298-301

(t) S. Arimori, N. Shibata, Org. Lett. 17 (2015) 1632-1635.

[8] (a) G. Danoun, B. Bayarmagnai, M.F. Grünberg, L.J. Gooßen, Angew. Chem. Int. Ed. 52 (2013) 7972-7975

(b) J.-J. Dai, C. Fang, B. Xiao, J. Yi, J. Xu, Z.-J. Liu, X. Lu, L. Liu, Y. Fu, J. Am. Chem. Soc. 135 (2013) 8436-8439

(c) X. Wang, Y. Xu, F. Mo, G. Ji, D. Qiu, J. Feng, Y. Ye, S. Zhang, Y. Zhang, J. Wang, J. Am. Chem. Soc. 135 (2013) 10330-10333

(d) B. Bayarmagnai, C. Matheis, E. Risto, L.J. Goossen, Adv. Synth. Catal. 356 (2014) 2343-2348

(e) A. Lishchynskyi, G. Berthon, V.V. Grushin, Chem. Commun. 50 (2014) 10237-10240

(f) X. Wang, Y. Xu, Y. Zhou, Y. Zhang, J. Wang, Synthesis 46 (2014) 2143-2148

(g) G. Danoun, B. Bayarmagnai, M.F. Gruenberg, C. Matheis, E. Risto, L.J. Goossen, Synthesis 46 (2014) 2283-2286.

[9] (a) E.A. Merritt, B. Olofsson, Angew. Chem. Int. Ed. 48 (2009) 9052-9070;

(b) Z. Xiao, C. Xia, Chin. J. Org. Chem. 33 (2013) 2119-2130;

(c) B. Zhang, X. Zhao, Q. Wu, Y. Guo, Pro. Chem. 25 (2013) 1142-1148.

[10] (a) R.J. Phipps, L. McMurray, S. Ritter, H.A. Duong, M.J. Gaunt, J. Am. Chem. Soc. 134 (2012) 10773-10776;

(b) J. Guo, S. Dong, Y. Zhang, Y. Kuang, X. Liu, L. Lin, X. Feng, Angew. Chem. Int. Ed. 52 (2013) 10245-10249

(c) L.Y. Chan, L. Cheong, S. Kim, Org. Lett. 15 (2013) 2186-2189

(d) N. Umierski, G. Manolikakes, Org. Lett. 15 (2013) 4972-4975

(e) J. Malmgren, A. Nagendiran, C.-W. Tai, J.-E. Backvall, B. Olofsson, Chem.-Eur. J. 20 (2014) 13531-13535

(f) F. Zhang, S. Das, A.J. Walkinshaw, A. Casitas, M. Taylor, M.G. Suero, M.J. Gaunt, J. Am. Chem. Soc. 136 (2014) 8851-8854

(g) P. Li, G. Cheng, H. Zhang, X. Xu, J. Gao, X. Cui, J. Org. Chem. 79 (2014) 8156-8162

(h) M. Iyanaga, Y. Aihara, N. Chatani, J. Org. Chem. 79 (2014) 11933-11939

(i) X. Pang, C. Chen, X. Su, M. Li, L. Wen, Org. Lett. 16 (2014) 6228-6231

(j) J. Chen, C. Chen, J. Chen, G. Wang, H. Qu, Chem. Commun. 51 (2015) 1356-1359

(k) B. Bhattarai, J.-H. Tay, P. Nagorny, Chem. Commun. 51 (2015) 5398-5401

(1) S.G. Modha, M.F. Greaney, J. Am. Chem. Soc. 137 (2015) 1416-1419

(m) A. Monastyrskyi, N.K. Namelikonda, R. Manetsch, J. Org. Chem. 80 (2015) 2513-2520

(n) W. Guo, S. Li, L. Tang, M. Li, L. Wen, C. Chen, Org. Lett. 17 (2015) 1232-1235.

[11] N. Ichiishi, A.J. Canty, B.F. Yates, M.S. Sanford, Org. Lett. 15 (2013) 5134-5137.

[12] (a) L. Chu, F.-L. Qing, J. Am. Chem. Soc. 132 (2010) 7262-7263;

(b) L. Chu, F.-L. Qing, J. Am. Chem. Soc. 134 (2012) 1298-1304;

(c) L. Chu, F.-L. Qing, Org. Lett. 14 (2012) 2106-2109;

(d) X. Wu, L. Chu, F.-L. Qing, Angew. Chem. Int. Ed. 52 (2013) 2198-2202;

(e) X.-Y. Jiang, F.-L. Qing, Angew. Chem. Int. Ed. 52 (2013) 14177-14180;

(f) L. Chu, F.-L. Qing, Acc. Chem. Res. 47 (2014) 1513-1522;

(g) Q.-Y. Lin, X.-H. Xu, F.-L. Qing, J. Org. Chem. 79 (2014) 10434-10446;

(h) B. Yang, X.-H. Xu, F.-L. Qing, Org. Lett. 17 (2015) 1906-1909.

[13] The copper-mediated difluoromethylation of diaryliodonium salts with TMSCF₂H was also investigated, but the desired products were formed in low yields. For a Cu-mediated difluoromethylation of diaryliodonium salts with (NHC)Ag(CF₂H) complexes, see: Y. Gu, D. Chang, X. Leng, Y. Gu, Q. Shen, Organometallics 34 (2015) 3065-3071.

[14] The screening of other nontransferring ligands is currently under investigation in our lab.

[15] (a) A. Bigot, A.E. Williamson, M.J. Gaunt, J. Am. Chem. Soc. 133 (2011) 13778-13781;

(b) Á. Sinai, Á. Mészáros, T. Gáti, V. Kudar, A. Palló, Z. Novák, Org. Lett. 15 (2013) 5654-5657.

Scheme 1 Strategies for aryl trifluoromethylation.

Entry	X	Cu salt	У	Iniator	Z	Solvent	Temperature	Yield $(\%)^b$
1	2.0	CuI	0.2	KF	2.0	MeCN	80 °C	33
2	2.0	CuI	0.2	KF	2.0	MeCN	50 °C	39
3	2.0	CuI	0.2	KF	2.0	MeCN	rt	40
4	2.0	CuBr	0.2	KF	2.0	MeCN	rt	26
5	2.0	CuTc	0.2	KF	2.0	MeCN	rt	14
6	2.0	CuSCN	0.2	KF	2.0	MeCN	rt	11
7	2.0	$CuBF_4 \cdot (MeCN)_4$	0.2	KF	2.0	MeCN	rt	45
8	2.0	$Cu(OAc)_2$	0.2	KF	2.0	MeCN	rt	10
9	2.0	$CuBF_4 \cdot (MeCN)_4$	0.2	CsF	2.0	MeCN	rt	5
10	2.0	$CuBF_4 \cdot (MeCN)_4$	0.2	NaOAc	2.0	MeCN	rt	16
11	2.0	$CuBF_4 \cdot (MeCN)_4$	0.2	t-BuONa	2.0	MeCN	rt	0
17 ^c	20	CuRF.(MeCN)	02	KE	20	MeCN	rt	3

Table 1 Optimization of reaction conditions.^a

13	2.0	$CuBF_4 \cdot (MeCN)_4$	0.5	KF	2.0	MeCN	rt	53
14	2.0	$CuBF_4$ ·(MeCN) ₄	1.0	KF	2.0	MeCN	rt	60
15	4.0	$CuBF_4$ ·(MeCN) ₄	1.0	KF	2.0	MeCN	rt	73
16	4.0	$CuBF_4$ ·(MeCN) ₄	1.0	KF	4.0	MeCN	rt	73
17	4.0	$CuBF_4$ ·(MeCN) ₄	1.0	KF	2.0	DMF	rt	13
18	4.0	$CuBF_4$ ·(MeCN) ₄	1.0	KF	2.0	DMSO	rt	39

^aReaction conditions: 1a (0.1 mmol), TMSCF₃ (x equiv), Cu salt (y equiv), initiator (z equiv), solvent (1.0 mL), under N₂, 25 min.

^bYields were determined by ¹⁹F NMR spectroscopy using trifluoromethoxylbenzene as an internal standard.

^cPhen (0.2 equiv) was added.

Table 2 Scope of substrates.^a



^{*a*}Reaction conditions: 1 (0.5 mmol), TMSCF₃ (2.0 mmol), CuBF₄·(MeCN)₄ (0.5 mmol), KF (1.0 mmol), MeCN (5.0 mL), under N₂, rt, 25 min. Yields were determined by ¹⁹F NMR spectroscopy using trifluoromethoxylbenzene as an internal standard. Yields in parentheses were isolated yields.

^bProducts were obtained from the corresponding triflates.

[°]Products were obtained from the corresponding tetrafluoroborates.

Graphical Abstract

A rapid and efficient copper-mediated trifluoromethylation reaction of diaryliodonium salts with TMSCF_3 is described.

Highlights:

A novel copper-mediated trifluoromethylation of diaryliodonium salts was developed.

This reaction proceeded at room temperature with 25 min.

A wide range of functional groups were well tolerated.