A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

## Accepted Article

**Title:** Trifluoromethanesulfonic Anhydride as a Low-Cost and Versatile Trifluoromethylation Reagent

**Authors:** Feng-Ling Qing, Yao Ouyang, and Xiu-Hua Xu



**To be cited as:** *Angew. Chem. Int. Ed.* 10.1002/anie.201803566
*Angew. Chem.* 10.1002/ange.201803566

**Link to VoR:** http://dx.doi.org/10.1002/anie.201803566
http://dx.doi.org/10.1002/ange.201803566

WILEY-VCH

10.1002/anie.201803566


WILEY-VCH

# Trifluoromethanesulfonic Anhydride as a Low-Cost and Versatile Trifluoromethylation Reagent

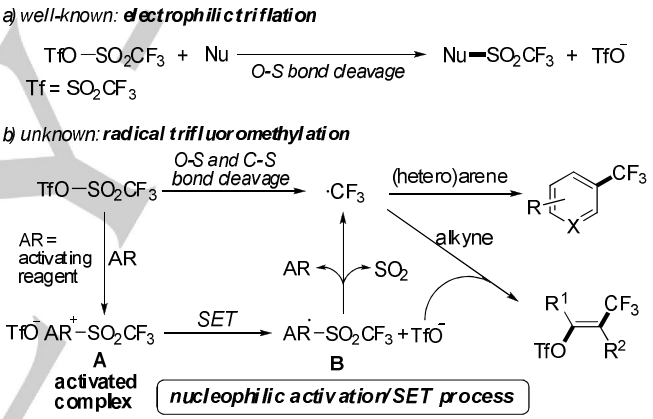
Yao Ouyang, Xiu-Hua Xu, and Feng-Ling Qing*

**Abstract:** A large number of reagents have been developed for the synthesis of trifluoromethylated compounds. However, an ongoing challenge in trifluoromethylation reaction is the use of less expensive and practical trifluoromethyl sources. We report herein the unprecedented direct trifluoromethylation of (hetero)arenes using trifluoromethanesulfonic anhydride as a radical trifluoromethylation reagent by merging photoredox catalysis and pyridine activation. Furthermore, the introduction of both of the $CF_3$ and OTf groups of trifluoromethanesulfonic anhydride into internal alkynes to access tetrasubstituted trifluoromethylated alkenes is developed. As trifluoromethanesulfonic anhydride is a low-cost and abundant chemical, this protocol provides a cost-efficient and practical route to trifluoromethylated compounds.

The prominent applications of trifluoromethylated compounds in pharmaceuticals, agrochemicals and advanced functional materials have triggered extensive efforts on introduction of trifluoromethyl group ($CF_3$) into organic molecules.[1] Over the past decade, impressive achievements have been made in the field[2-4] and radical trifluoromethylation has emerged as an attractive and straightforward strategy for the preparation of trifluoromethylated compounds.[2] Compared to the nucleophilic and electrophilic trifluoromethylations, radical trifluoromethylation can directly introduce $CF_3$ into organic molecules without requirement of additional step(s) to prepare functionalized substrates (e.g. organohalides and organometallic reagents), thus providing a more efficient route to access trifluoromethylated compounds. Among the developed radical trifluoromethylation methods, the photoredox- or transition-metal-catalyzed radical trifluoromethylation has received great attention recently. In this context, a large number of trifluoromethylation reagents have been recognized as the trifluoromethyl radical precursors, such as $CF_3X$ (X = I, Br),[5] $CF_3CO_2H$ and its derivatives,[6] $CF_3SO_2$-containing compounds ($CF_3SO_2Na$,[7] $Zn(SO_2CF_3)_2$,[8] $[CF_3SO_2Ag]$,[9] $CF_3SO_2Cl$,[10] triflones[11]), $TMSCF_3$,[12] Umemoto reagent,[13] and Togni reagent.[14] However, most of them are either expensive ($Zn(SO_2CF_3)_2$, Umemoto and Togni reagents), commercially unavailable ($[CF_3SO_2Ag]$, triflones), gaseous ($CF_3I$, $CF_3Br$) or volatile ($CF_3SO_2Cl$, $TMSCF_3$), which significantly restricts their widespread applications. Therefore, the searching for low-cost and practical radical $CF_3$ sources remains appealing.

[*] Y. Ouyang, Dr. X.-H. Xu, Prof. Dr. F.-L. Qing
Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecules Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Science, 345 Lingling Lu, Shanghai 200032 (China)
E-mail: flq@mail.sioc.ac.cn
Prof. Dr. F.-L. Qing
College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, 2999 North Renmin Lu, Shanghai, 201620
Supporting information for this article is given via a link at the end of the document.

Trifluoromethanesulfonic anhydride ($(CF_3SO_2)_2O$, $Tf_2O$) is an inexpensive and abundant chemical,[15] and thus represents an attractive and practical trifluoromethylation reagent. However, the use of $Tf_2O$ as trifluoromethyl source has not been reported. Due to its significant electrophilic characteristic,[16] $Tf_2O$ normally reacts with *O*-nucleophiles to produce the triflates, a class of widely used coupling partners for cross-coupling reactions (Scheme 1a). In this way, the O-S bond of $Tf_2O$ is cleaved via a two-electron addition-elimination process. We envisioned that if $Tf_2O$ could serve as a $CF_3$ radical precursor by cleavage of the $CF_3$-S bond via a single-electron-transfer (SET) pathway, it would provide a new and easily available trifluoromethylation reagent for cost-efficient synthesis of trifluoromethylated compounds.



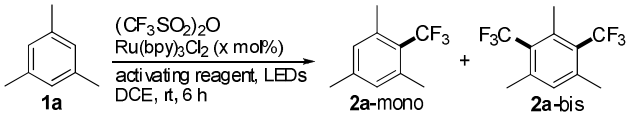

**Scheme 1.** The reaction of $Tf_2O$.

In view of the weakness of S-O bond of $Tf_2O$, which is prone to acceptance of a nucleophile, we hypothesized that if a nucleophile can serve as a $Tf_2O$ activating reagent (AR) for the formation of a triflated complex **A** ($AR^+$-$SO_2CF_3$·$TfO^-$), in which complex **A** could readily facilitate the cleavage of $CF_3$-S bond via a SET pathway by photoredox catalysis, and thus it would be feasible to use $Tf_2O$ for the radical trifluoromethylation (Scheme 1b). It was noteworthy that this activation mode was similar to Stephenson's the activation of $(CF_3CO)_2O$ with pyridine *N*-oxide.[6b] In continuation of our research interest in visible-light-induced fluoroalkylation reactions,[17] we herein disclose the unprecedented application of $Tf_2O$ as radical $CF_3$ source for the direct trifluoromethylation of (hetero)arenes by a combination of the pyridine activation with photoredox catalysis. The reaction system is also extended to a simultaneous trifluoromethylation and trifluoromethanesulfonyloxylation (triflation) of alkynes.

On the basis of our hypothesis, firstly, several activating reagents including $NEt_3$, pyridine and PhSPh that $Tf_2O$ was activated for the formation of complex **A** were identified.[18] Then, the direct trifluoromethylation of mesitylene (**1a**) with $Tf_2O$ in the presence of activating agent and catalytic $Ru(bpy)_3Cl_2$ under visible-light irradiation was investigated (Table 1, entries 1-3). To

our delight, the trifluoromethylation reaction proceeded smoothly to give the trifluoromethylated product **2a** in high yield when pyridine was used as the activating agent (entry 1). In contrast, $NEt_3$ and PhSPh were ineffective (entries 2-3). Further optimization of reaction conditions by examining a series of pyridine derivatives, photocatalysts and solvents diminished the reaction efficiency (see the supporting information). Decreasing the catalyst loading from 3 mol% to 2 mol% resulted in a comparable yield and better mono/bis-selectivity (entry 4), but a lower catalyst loading (1 mol%) reduced the yield of **2a** to 60% (entry 5). Additionally, only a trace of **2a** was formed in the presence of a catalytic amount of pyridine (entry 6). Finally, the control experiments demonstrated that both the photocatalyst and visible light were essential for the trifluoromethylation (entries 7 and 8).

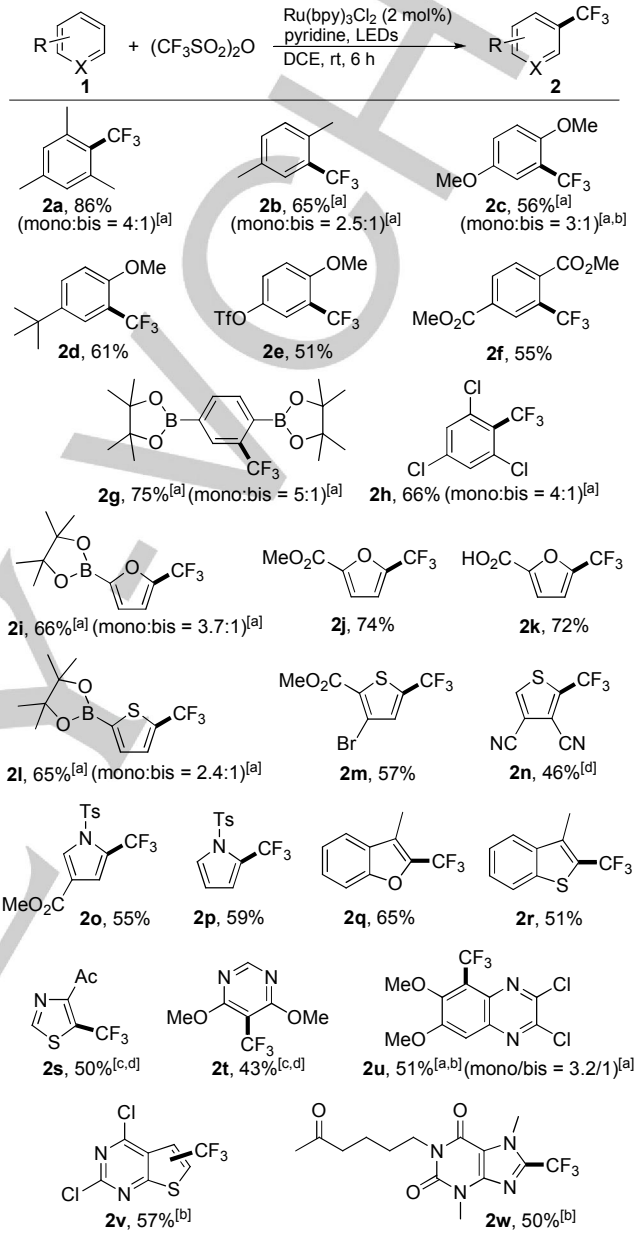
***Table 1.*** Optimization of reaction conditions[a]




| Entry | Activating reagent | x | Yield (**2a**-mono/**2a**-bis, %)[b] |
|---|---|---|---|
| 1 | pyridine | 3.0 | 56/32 |
| 2 | $NEt_3$ | 3.0 | 0 |
| 3 | PhSPh | 3.0 | 0 |
| 4 | pyridine | 2.0 | 67/20 |
| 5 | pyridine | 1.0 | 54/6 |
| 6[c,e] | pyridine | 2.0 | trace |
| 7[d] | pyridine | 2.0 | 0 |
| 8[e] | pyridine | 2.0 | 0 |

[a] Reaction conditions: **1a** (0.2 mmol), $(CF_3SO_2)_2O$ (0.6 mmol), activating reagent (0.6 mmol), $Ru(bpy)_3Cl_2$ (x mol%), DCE (2.0 mL), LEDs, $N_2$, rt, 6 h. [b] Yields determined by $^{19}F$ NMR spectroscopy using trifluoromethoxybenzene as an internal standard. [c] Pyridine (0.04 mmol). [d] Without $Ru(bpy)_3Cl_2$. [e] No light.

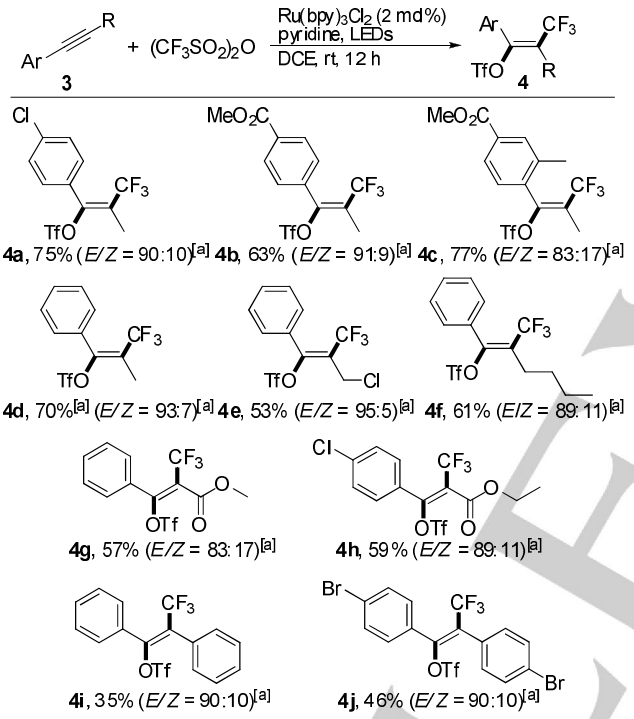
With the optimized reaction conditions in hand (Table 1, entry 4), the substrate scope of the C–H trifluoromethylation of (hetero)arenes with $Tf_2O$ was investigated (Scheme 2). Benzenes bearing either electron-donating or electron-withdrawing substituents (**1a**-**h**) underwent the current reaction smoothly with good regioselectivities to afford the corresponding trifluoromethylated products in moderate to excellent yields. However, phenols and anilines were not compatible with the reaction conditions. A variety of heteroarenes including furan (**1i**-**k**), thiophene (**1l**-**n**), pyrrole (**1o**,**p**), benzofuran (**1q**), benzo[*b*]thiophene (**1r**), thiazole (**1s**), pyrimidine (**1t**), quinoxaline (**1u**), and thieno[2,3-*d*]pyrimidine (**1v**) were all viable substrates under the reaction conditions, furnishing the corresponding $CF_3$-heteroaromatics with moderate efficiency. In most cases, good regioselectivities were observed. Electron-poor substrates (**1n**, **1s**, **1t**) afforded the products in slightly lower yields along with the recovery of some of the starting materials. Highly electron-deficient heteroarenes such as pyridines and pyrazines displayed minimal reactivity. Importantly, the synthetically useful triflate (**1e**), boronate (**1g**, **1i**, **1l**), and bromide (**1m**) were all tolerated under the reaction conditions. Remarkably, this protocol could be successfully applied to complex compound pentoxifylline (**1w**), thus demonstrating the potential utility of this reaction for late-stage trifluoromethylation.




**Scheme 2.** Substrate scope of C–H trifluoromethylation of (hetero)arenes. Reaction conditions: **1** (0.4 mmol), $(CF_3SO_2)_2O$ (1.2 mmol), pyridine (1.2 mmol), $Ru(bpy)_3Cl_2$ (0.008 mol), DCE (4.0 mL), LEDs, $N_2$, rt, 6 h, isolated yields. [a] Determined by $^{19}F$ NMR spectroscopy using trifluoromethoxybenzene as an internal standard. [b] 12 h. [c] 72 h. [d] Some of the starting material was recovered.

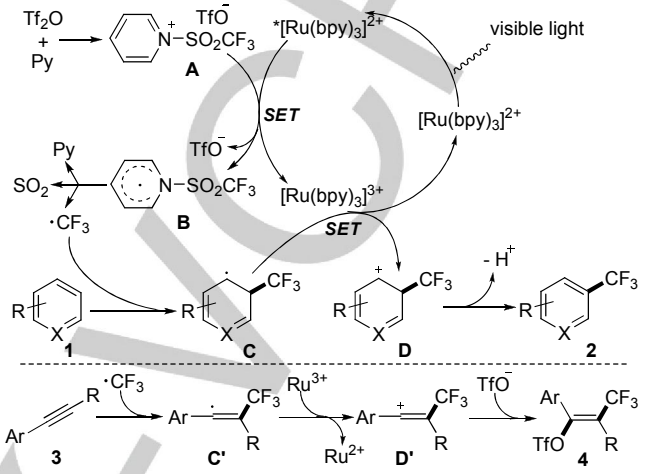
As the reaction design shown in Scheme 1b, $Tf_2O$ was transformed to the $CF_3$ radical and OTf anion. In the light of the atom economy, we wondered whether both of the $CF_3$ and OTf groups could be simultaneously introduced into organic molecules. Inspired by the recent advances of the trifluoromethylation functionalization reaction of alkenes and alkynes,[19] the internal alkynes were subjected to the

photoredox trifluoromethylation protocol (Scheme 3). Gratifyingly, the simultaneous trifluoromethylation and triflation of alkynes **3** proceeded smoothly to afford the tetrasubstituted trifluoromethylated alkenes **4** in high regio- and stereoselectivities. In some cases, the competing C–H trifluoromethylation of the benzene ring could be detected. Furthermore, neither terminal alkynes nor alkenes were suitable substrates for this transformation. To date, however, only Koike and Akita recently have reported the photoredox-catalyzed trifluoromethylation and triflation of alkynes,[20] but the more expensive *S*-(trifluoromethyl)diphenylsulfonium trifluoromethanesulfonate (Yagupol'skii-Umemoto reagent) was used as $CF_3$ source. Thus, this reaction provides a low-cost, atom-economy, and practical method for preparation of the tetrasubstituted trifluoromethylated alkenes.




**Scheme 3.** Trifluoromethyltriflation of alkynes. Reaction conditions: **3** (0.4 mmol), $(CF_3SO_2)_2O$ (1.2 mmol), pyridine (1.2 mmol), $Ru(bpy)_3Cl_2$ (0.008 mol), DCE (4.0 mL), LEDs, $N_2$, rt, 12 h, isolated yields. [a] Determined by $^{19}F$ NMR spectroscopy using trifluoromethoxybenzene as an internal standard.

On the basis of the above results and literature reports,[10a,14,18] a proposed reaction mechanism was depicted in Scheme 4. Irradiation of the photoredox catalyst $[Ru(bpy)_3]^{2+}$ with blue LEDs could generate the excited state $*[Ru(bpy)_3]^{2+}$, which is a strong reductant. Single-electron reduction of pyridinium complex **A** ($E_{pc}$ = -0.79 V vs SCE in $CH_3CN$, see the supporting information), formed in-situ from the reaction of $Tf_2O$ and pyridine,[18c] by $*[Ru(bpy)_3]^{2+}$ ($E_{1/2}*[Ru(bpy)_3]^{2+}/[Ru(bpy)_3]^{3+}$ = -0.81 V vs SCE in $CH_3CN$)[21] would give the radical species **B**[22] and $[Ru(bpy)_3]^{3+}$. This SET process was confirmed by fluorescence-quenching experiments (see the supporting information). The radical **B** would release the electrophilic $CF_3$ radical. Subsequently, the addition of $CF_3$ radical to arenes **1** provides radical intermediate **C**. Single-electron oxidation of intermediate **C** by $[Ru(bpy)_3]^{3+}$ would give the cation **D** and regenerate $[Ru(bpy)_3]^{2+}$ to close the catalytic cycle. Finally, the deprotonation of intermediate **D** affords the desired products **2**. In the cases of alkynes **3**, the similar $CF_3$-radical addition and then SET oxidation by $[Ru(bpy)_3]^{3+}$ gave vinylic cation **D'**. The reaction of intermediate **D'** with OTf anion provided products **4**.




**Scheme 4.** Proposed reaction mechanism.

In conclusion, we have developed an unprecedented photoredox-catalyzed trifluoromethylation of (hetero)arenes using the low-cost and abundant $Tf_2O$ as a trifluoromethyl radical source in the presence of pyridine. This reaction is compatible with a range of arenes and heteroarenes. Furthermore, internal alkynes underwent the simultaneous trifluoromethylation and trifluoromethanesulfonyloxylation in this protocol to access tetrasubstituted trifluoromethylated alkenes. The relative cost and versatile reactivities of $Tf_2O$ render this protocol highly attractive for the synthesis of trifluoromethylated compounds.

## Acknowledgements

National Natural Science Foundation of China (21332010, 21421002), the Strategic Priority Research Program of the Chinese Academy of Sciences (XDB20000000), and Youth Innovation Promotion Association CAS (No. 2016234) are greatly acknowledged for funding this work. We are grateful to Professors Xingang Zhang and Lingling Chu for helpful discussion.

**Keywords:** trifluoromethylation • trifluoromethanesulfonic anhydride • photoredox catalysis • pyridine • radical

[1] a) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; b) N. A. Meanwell, *J. Med. Chem.* **2011**, *54*, 2529; c) M. Cametti, B. Crousse, P. Metrangolo, R. Milani, G. Resnati, *Chem. Soc. Rev.* **2012**, *41*, 31; d) J. Wang, M. Sanchez-Rosello, J. L. Acena, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432.

[2] a) W. R. Dolbier, Jr., *Chem. Rev.* **1996**, *96*, 1557; b) A. Studer, *Angew. Chem. Int. Ed.* **2012**, *51*, 8950; *Angew. Chem.* **2012**, *124*, 9082; c) T. Koike, M. Akita, *Acc. Chem. Res.* **2016**, *49*, 1937; d) T. Chatterjee, N. Iqbal, Y. You, E. J. Cho, *Acc. Chem. Res.* **2016**, *49*, 2284.

[3] a) G. K. S. Prakash, A. K. Yudin, *Chem. Rev.* **1997**, *97*, 757; b) X. Liu, C. Xu, M. Wang, Q. Liu, *Chem. Rev.* **2015**, *115*, 683.

[4] a) T. Umemoto, *Chem. Rev.* **1996**, *96*, 1757; b) J. Charpentier, N. Früh, A. Togni, *Chem. Rev.* **2015**, *115*, 650.

[5] a) Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034; b) N. Iqbal, J. Jung, S. Park, E. J. Cho, *Angew. Chem. Int. Ed.* **2014**, *53*, 539; *Angew. Chem.* **2014**, *126*, 549; c) F. Sladojevich, E. McNeill, J. Börgel, S.-L. Zheng, T. Ritter, *Angew. Chem. Int. Ed.* **2015**, *54*, 3712; *Angew. Chem.* **2015**, *127*, 3783; d) K. Natte, R. V. Jagadeesh, H. He, J. Rabeah, J. Chen, C. Taeschler, S. Ellinger, F. Zaragoza, H. Neumann, A. Brückner, M. Beller, *Angew. Chem. Int. Ed.* **2016**, *55*, 2782; *Angew. Chem.* **2016**, *128*, 2832; e) N. J. W. Straathof, S. E. Cramer, V. Hessel, T. Noël, *Angew. Chem. Int. Ed.* **2016**, *55*, 15549; *Angew. Chem.* **2016**, *128*, 15778.

[6] a) G. Shi, C. Shao, S. Pan, J. Yu, Y. Zhang, *Org. Lett.* **2015**, *17*, 38; b) J. W. Beatty, J. J. Douglas, K. P. Cole, C. R. J. Stephenson, *Nat. Commun.* **2015**, *6*, 7919; c) S. Kawamura, M. Sodeoka, *Angew. Chem. Int. Ed.* **2016**, *55*, 8740; *Angew. Chem.* **2016**, *128*, 8882; d) J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole, C. R. J. Stephenson, *Chem* **2016**, *1*, 456; e) J. Lin, Z. Li, J. Kan, S. Huang, W. Su, Y. Li, *Nat. Commun.* **2017**, *8,* 14353.

[7] a) Y. Ji, T. Brueckl, R. D. Baxter, Y. Fujiwara, I. B. Seiple, S. Su, D. G. Blackmond, P. S. Baran, *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 14411; b) X.-Y. Jiang, F.-L. Qing, *Angew. Chem. Int. Ed.* **2013**, *52*, 14177; *Angew. Chem.* **2013**, *125*, 14427; c) K. Matcha, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2014**, *53*, 11960; *Angew. Chem.* **2014**, *126*, 12154; d) L. Li, X. Mu, W. Liu, Y. Wang, Z. Mi, C.-J. Li, *J. Am. Chem. Soc.* **2016**, *138*, 5809; e) Z. Wu, D. Wang, Y. Liu, L. Huan, C. Zhu, *J. Am. Chem. Soc.* **2017**, *139*, 1388.

[8] Y. Fujiwara, J. A. Dixon, F. O'Hara, E. D. Funder, D. D. Dixon, R. A. Rodriguez, R. D. Baxter, B. Herle, N. Sach, M. R. Collins, Y. Ishihara, P. S. Baran, *Nature* **2012**, *492*, 95.

[9] For the *in situ* generation of $CF_3SO_2Ag$ from $Ag(O_2CCF_2SO_2F)$, see: Y. Liu, H. Wu, Y. Guo, J.-C. Xiao, Q.-Y. Chen, C. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 15432; *Angew. Chem.* **2017**, *129*, 15634.

[10] a) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224; b) X.-J. Tang, W. R. Dolbier, Jr., *Angew. Chem. Int. Ed.* **2015**, *54*, 4246; *Angew. Chem.* **2015**, *127*, 4320; c) D. B. Bagal, G. Kachkovskyi, M. Knorn, T. Rawner, B. M. Bhanage, O. Reiser, *Angew. Chem. Int. Ed.* **2015**, *54*, 6999; *Angew. Chem.* **2015**, *127*, 7105; d) N. Noto, T. Koike, M. Akita, *Chem. Sci.* **2017**, *8*, 6375; e) J.-S. Lin, F.-L. Wang, X.-Y. Dong, W.-W. He, Y. Yuan, S. Chen, X.-Y. Liu, *Nat. Commun.* **2017**, *8*, 14841.

[11] a) J. Gong, P. L. Fuchs, *J. Am. Chem. Soc.* **1996**, *118*, 4486; b) J. Lei, X. Wu, Q. Zhu, *Org. Lett.* **2015**, *17*, 2322; c) H. Jiang, Y. He, Y. Cheng, S. Yu, *Org. Lett.* **2017**, *19*, 1240; d) J. Rong, L. Deng, P. Tan, C. Ni, Y. Gu, J. Hu, *Angew. Chem. Int. Ed.* **2016**, *55*, 2743; *Angew. Chem.* **2016**, *128*, 2793; e) P. Liu, W. Liu, C.-J. Li, *J. Am. Chem. Soc.* **2017**, *139*, 14315.

[12] a) Y. Ye, S. H. Lee, M. S. Sanford, *Org. Lett.* **2011**, *13*, 5464; b) A. Hafner, S. Bräse, *Angew. Chem. Int. Ed.* **2012**, *51*, 3713; *Angew. Chem.* **2012**, *124*, 3773; c) X. Wu, L. Chu, F.-L. Qing, *Angew. Chem. Int. Ed.* **2013**, *52*, 2198; *Angew. Chem.* **2013**, *125*, 2254; d) Y.-F. Wang, G. H. Lonca, S. Chiba, *Angew. Chem. Int. Ed.* **2014**, *53*, 1067; *Angew. Chem.* **2014**, *126*, 1085.

[13] a) Y. Yasu, T. Koike, M. Akita, *Angew. Chem. Int. Ed.* **2012**, *51*, 9567; *Angew. Chem.* **2012**, *124*, 9705; b) S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Médebielle, V. Gouverneur, *J. Am. Chem. Soc.* **2013**, *135*, 2505; c) B. Sahoo, J.-L. Li, F. Glorius, *Angew. Chem. Int. Ed.* **2015**, *54*, 11577; *Angew. Chem.* **2015**, *127*, 11740; d) Y. Xu, Z. Wu, J. Jiang, Z. Ke, C. Zhu, *Angew. Chem. Int. Ed.* **2017**, *56*, 4545; *Angew. Chem.* **2017**, *129*, 4616.

[14] a) A. E. Allen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2010**, *132*, 4986; b) Y. Li, A. Studer, *Angew. Chem. Int. Ed.* **2012**, *51*, 8221; *Angew. Chem.* **2012**, *124*, 8345; c) H. Egami, R. Shimizu, S. Kawamura, M. Sodeoka, *Angew. Chem. Int. Ed.* **2013**, *52*, 4000; *Angew. Chem.* **2013**, *125*, 4092; d) F. Wang, D. Wang, X. Mu, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2014**, *136*, 10202; e) J.-S. Lin, X.-Y. Dong, T.-T. Li, N.-C. Jiang, B. Tan, X.-Y. Liu, *J. Am. Chem. Soc.* **2016**, *138*, 9357.

[15] For a cost comparison of $Tf_2O$ with the common trifluoromethylation reagents from Sigma Aldrich, TCI, and fluorochem on websites, see the Supporting Information.

[16] a) I. L. Baraznenok, V. G. Nenajdenko, E. S. Balenkova, *Tetrahedron* **2000**, *56*, 3077; b) B. A. Shainyan, L. L. Tolstikova, *Chem. Rev.* **2013**, *113*, 699; c) X.-H. Xu, K. Matsuzaki, N. Shibata, *Chem. Rev.* **2015**, *115*, 731.

[17] a) Q.-Y. Lin, X.-H. Xu, K. Zhang, F.-L. Qing, *Angew. Chem. Int. Ed.* **2016**, *55*, 1479; *Angew. Chem.* **2016**, *128*, 1501; b) Q.-Y. Lin, Y. Ran, X.-H. Xu, F.-L. Qing, *Org. Lett.* **2016**, *18*, 2419; c) W. Yu, X.-H. Xu, F.-L. Qing, *Org. Lett.* **2016**, *18*, 5130; d) B. Yang, X.-H. Xu, F.-L. Qing, *Org. Lett.* **2016**, *18*, 5956.

[18] a) T. Netscher, P. Bohrer, *Tetrahedron Lett.* **1996**, *37*, 8359; b) V. G. Nenajdenko, P. V. Vertelezkij, A. B. Koldobskij, I. V. Alabugin, E. S. Balenkova, *J. Org. Chem.* **1997**, *62*, 2483; c) R. A. Toscano, M. Hernández-Galindo, R. Rosas, O. García-Mellado, F. Portilla, C. Amábile-Cuevas, C. Álvarez-Toledano. *Chem. Pharm. Bull.* **1997**, *45*, 957.

[19] a) H. Egami, M. Sodeoka, *Angew. Chem. Int. Ed.* **2014**, *53*, 8294; *Angew. Chem.* **2014**, *126*, 8438; b) E. Merino, C. Nevado, *Chem. Soc. Rev.* **2014**, *43*, 6598.

[20] R. Tomita, T. Koike, M. Akita, *Angew. Chem. Int. Ed.* **2015**, *54*, 12923; *Angew. Chem.* **2015**, *127*, 13115.

[21] C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322.

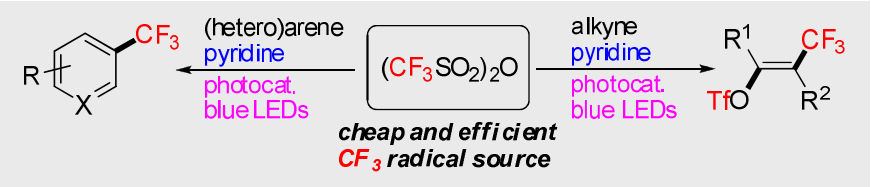
[22] a) F. Riboni, E. Selli, M. R. Hoffmann, A. J. Colussi, *J. Phys. Chem. A* **2015**, *119*, 4433; b) G. Wang, J. Cao, L. Gao, W. Chen, W. Huang, X. Cheng, S. Li, *J. Am. Chem. Soc.* **2017**, *139*, 3904.

10.1002/anie.201803566


WILEY-VCH

**Entry for the Table of Contents**

# COMMUNICATION




*Yao Ouyang, Xiu-Hua Xu, Feng-Ling Qing**

***Page No. – Page No.***

**Trifluoromethanesulfonic Anhydride as a Low-Cost and Versatile Trifluoromethylation Reagent**

An unprecedented application of trifluoromethanesulfonic anhydride as a radical trifluoromethylation reagent was developed by merging photoredox catalysis and pyridine activation. The synthetic utility of this protocol was exemplified by C–H trifluoromethylation of (hetero)arenes and trifluoromethyltriflation of alkynes.