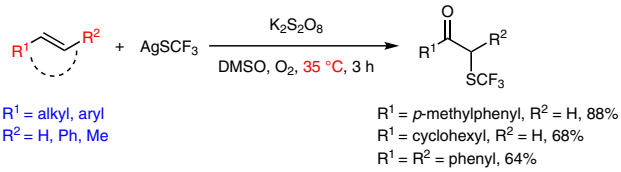
Synlett C. Zheng et al. Letter

# Ag(I)-Mediated Oxidative Radical Trifluoromethylthiolation of Alkenes

**Changge Zheng** *[a,b]
**Yang Liu**[a]
**Jianquan Hong**[a]
**Shuai Huang**[a]
**Wei Zhang**[b]
**Yupeng Yang**[a]
**Ge Fang**[b]

[a] Key Laboratory of Synthetic and Biological Colloids, Ministry of Education, School of Chemical and Material Engineering, Jiangnan University, Wuxi, Jiangsu 214122, P. R. of China
cgzheng@jiangnan.edu.cn
[b] School of Chemical Engineering, Xinjiang Agricultural University, Urumqi 830052, Xinjiang Uygur Autonomous Region, P. R. of China




Received: 11.03.2019
Accepted after revision: 29.04.2019
Published online: 15.05.2019
DOI: 10.1055/s-0037-1611546; Art ID: st-2019-l0143-l

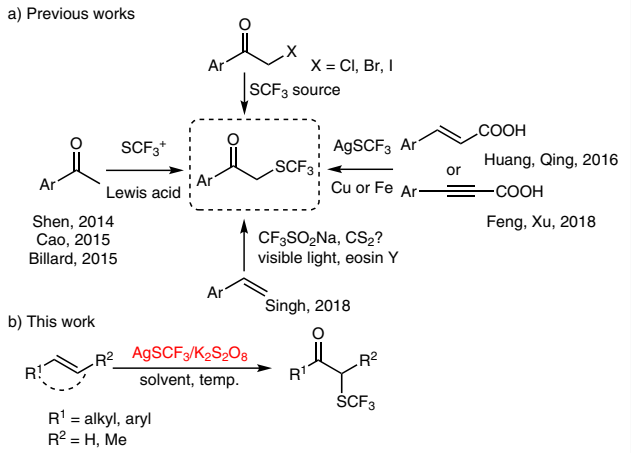
**Abstract** A simple, mild, and efficient method for an oxidative radical trifluoromethylthiolation of alkenes through $AgSCF_3/K_2S_2O_8$ system has been developed. This reaction provides a straightforward way to synthesize a variety of useful α-$SCF_3$-substituted ketone compounds from a wide range of alkenes in moderate to good yields.

**Key words** trifluoromethylthiolation, alkenes, $AgSCF_3$, α-$SCF_3$-substituted ketone, radical pathway

The trifluoromethylthio ($SCF_3$) group exhibits many unique properties in extremely high lipophilicity, strong electron-withdrawing effect, and desirable bioactivities,[1] with the highest Hansch parameter ($\pi R = 1.44$) among common fluorine-containing groups.[2] Introducing the $SCF_3$ group into the small molecules efficiently can bring great effects to its physical and chemical properties as well as metabolic stability.[3] The trifluoromethylthiolated compounds show increasingly important application prospects in medicine, pesticide, and materials.[4] Therefore, the new effective approach for trifluoromethylthiolation of organic molecules has always drawn great attention in considerable progress of synthetic methods. Many trifluoromethylthiolation approaches have been developed by using nucleophilic,[5] electrophilic,[6] and free-radical $SCF_3$ reagents.[7] The trifluoromethylthiolation through the $SCF_3$ radical pathway has been a hot topic in this field very recently.[8] In 2014, the primitive $AgSCF_3/K_2S_2O_8$ system was developed and achieved addition/ring-closing reaction of activated alkenes through $SCF_3$ radical by Wang.[7c] Due to the biological activities of drug molecules with the α-$SCF_3$-substituted ketone motifs, the α-$SCF_3$-substituted ketone analogues have been important structural motifs in medicinal chemistry, such as cefazaflur and cephalosporin derivatives.[9] Numerous α-$SCF_3$-substituted ketone compounds have been synthesized and achieved significant advances in the field of organofluorine and medicinal chemistry.

In general, synthetic methods of α-$SCF_3$-substituted ketone compounds were developed mainly through reaction of different $SCF_3$ sources and corresponding starting materials such as α-halo ketones,[10] aryl ketones,[11] carboxylic acids,[12] and others[13] (Scheme 1, a). In view of some shortcomings of these synthetic methods, such as preactivation being required for the substrate, harsh reaction conditions, poor substrate tolerance, and no high reaction yield, an efficient trifluoromethylthiolation method has always been the key pursuing goal for the synthesis of α-$SCF_3$-substituted ketone compounds, especially in using readily available substrates under mild conditions.

Recently, Singh reported the synthesis of α-$SCF_3$-substituted ketone through reaction of alkene substrates, with Langlois' reagent in the presence of $CS_2$ and eosin Y (Scheme 1, a).[14] Unfortunately, these results cannot be supported by the $^{19}F$ NMR spectroscopy in its Supporting Information. The chemical shift of –61 ppm ($^{19}F$ NMR spectroscopy) in that paper suggests the α-$CF_3$-substituted ketone compounds rather than α-$SCF_3$-substituted ketone compounds.[15] Inspired by the above inadequate research status, we have been trying to develop the effective approaches for convenient synthesis of the α-$SCF_3$-substituted ketone compounds through readily available raw material styrene and more stable $AgSCF_3$. Herein, we report a simple mild synthetic method for α-$SCF_3$-substituted ketone compounds through trifluoromethylthiolation of alkenes with $AgSCF_3$ (Scheme 1, b).

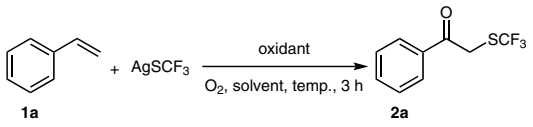



**Scheme 1** Syntheses of α-$SCF_3$-substituted ketones

Initially, our investigation is carried out to optimize the reaction conditions by treating the model substrate styrene (**1a**) with $AgSCF_3$ in the presence of various oxidants (Table 1). Selecting $K_2S_2O_8$ as the oxidant and DMSO as the solvent, the reaction system provided a 72% yield of the desired product **2a** (entry 1) under air atmosphere at room temperature. Since the molecular oxygen is essential for the formation of α-$SCF_3$-substituted ketones, the reaction under $O_2$ atmosphere gave the corresponding α-$SCF_3$-substituted ketone in unsurprisingly significant higher yield even at room temperature (86%, entry 2). With the slightly increase of reaction temperature to 35 °C, the reaction achieved an excellent yield (92%, entry 3). Testing the other solvents such as MeCN, DMF, NMP, and dioxane, the lower or worse yields show that these solvents had no efficiency to improve the reaction (entries 4–7). No observable reaction occurred in other solvents such as DCE, MeOH, and toluene (entries 8–10). Obviously, trifluoromethylthio ($SCF_3$) radical can be conveniently generated by mixing $AgSCF_3$ and $K_2S_2O_8$ together in polar solvents such as MeCN, DMSO, and DMF. The evaluation about other $S_2O_8^{2-}$ salt indicate that $Na_2S_2O_8$ and $(NH_4)_2S_2O_8$ were less efficient than $K_2S_2O_8$ (entries 11 and 12). No reaction occurred by using the other oxidants such as Selectfluor, TBHP, and NFSI (entries 13–15). This transformation was completely inhibited under $N_2$ or in the absence of $S_2O_8^{2-}$. It demonstrated that $O_2$ and $S_2O_8^{2-}$ were indispensable in this reaction system.

Based on the optimized reaction conditions (Table 1, entry 3), the substrate scope of oxidative trifluoromethylthiolation for aryl alkenes was investigated (Scheme 2). The substrates with electron-donating groups such as methyl, phenyl, *tert*-butyl, naphthalene ring, methoxy, ethoxy, and phenoxy (**1b–h**,**t**,**u**) were compatible with the reaction system to afford the corresponding products in good yields (**2b–h**,**t**,**u** 67–88%, Scheme 2). The higher yield with the methyl substituent in *para* position compared to *ortho* or *meta* position (**2b**, 88%; **2c**, 75%; **2d**, 73%) indicated that steric hindrance can also be used for understanding the reaction of the substrates with electron-donating groups. The substrates with electron-withdrawing groups such as halides, cyano, nitro, ester, and carboxyl (**1i–s**) can also be tolerated in this reaction system with slightly lower yields (**2i–s**, 56–71%, Scheme 2). Generally, aromatic substrate with electron-donating substituent (**1a–h**) can stabilize the reactive intermediate efficiently to give the products in higher yield than those of the electron-withdrawing substituents (**1i–s**). Comparing with aromatic substrates with fluorine atom substituent in *ortho* (**2m**, 67%) and *para* position (**2i**, 67%), the pretty lower yield of the electron-withdrawing substituent in *meta* position (**2n**, 60%) indicated that the electronic effect remains a key influence factor to the reaction. With the strongest electron-withdrawing nitro substituent, nitrostyrene **1q**,**v**,**w** generated **2q**,**v**,**w** in a lower yield (56–65%) than all other products. Furthermore, the reaction system can be suitable for the heteroaryl substrate 2-vinylpyridine (**1x**) to give the desired product **2x** in good yield of 75%.

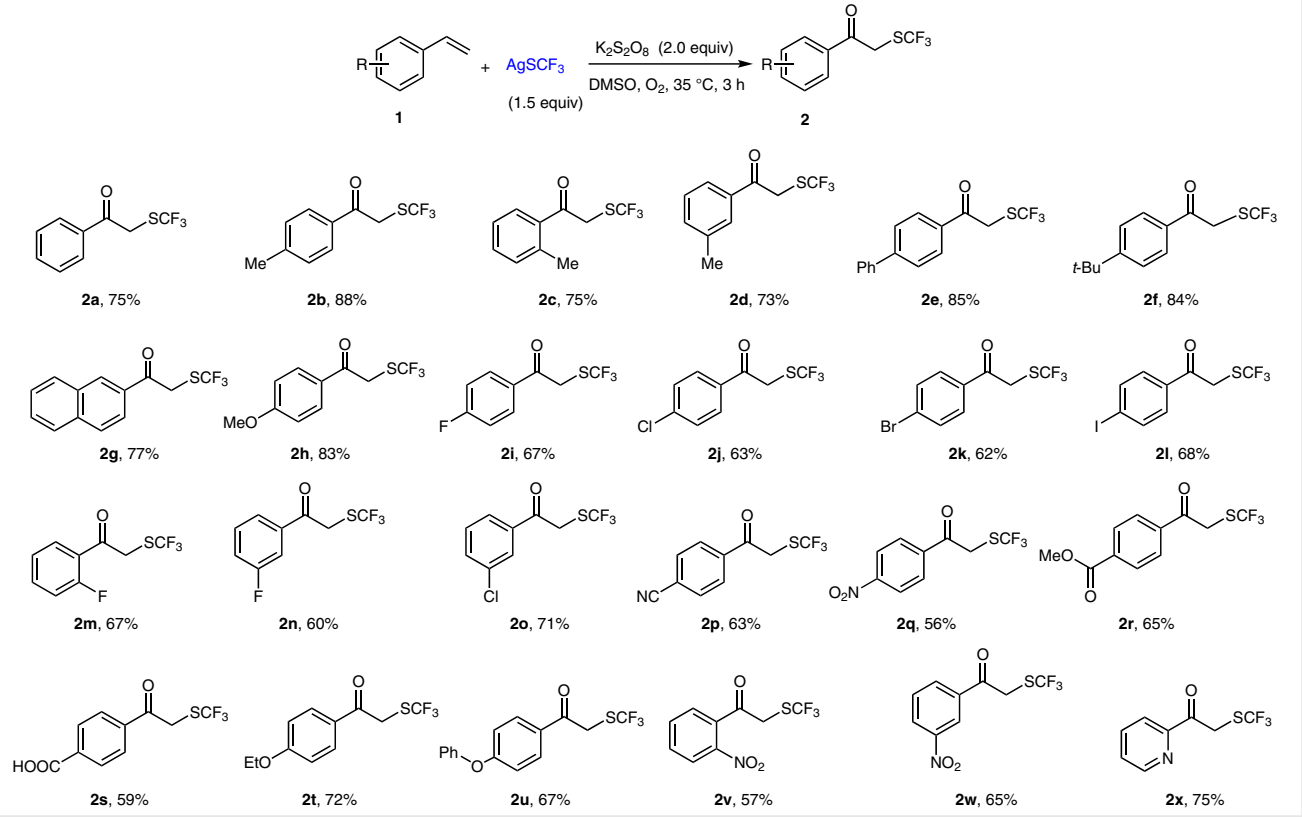
**Table 1** Optimization of Reaction Conditions[a]




1a 2a

| Entry | Oxidant | Solvent | Temp (°C) | Yield (%)[b] |
|---|---|---|---|---|
| 1[c] | $K_2S_2O_8$ | DMSO | 25 | 72 |
| 2 | $K_2S_2O_8$ | DMSO | 25 | 86 |
| 3 | $K_2S_2O_8$ | DMSO | 35 | 92 |
| 4 | $K_2S_2O_8$ | MeCN | 35 | 56 |
| 5 | $K_2S_2O_8$ | DMF | 35 | 67 |
| 6 | $K_2S_2O_8$ | NMP | 35 | 49 |
| 7 | $K_2S_2O_8$ | dioxane | 35 | 23 |
| 8 | $K_2S_2O_8$ | DCE | 35 | trace |
| 9 | $K_2S_2O_8$ | MeOH | 35 | 0 |
| 10 | $K_2S_2O_8$ | toluene | 35 | 0 |
| 11 | $Na_2S_2O_8$ | DMSO | 35 | 81 |
| 12 | $(NH_4)_2S_2O_8$ | DMSO | 35 | 49 |
| 13 | Selectfluor | DMSO | 35 | trace |
| 14 | TBHP | DMSO | 35 | 0 |
| 15 | NFSI | DMSO | 35 | 0 |
| 16[d] | $K_2S_2O_8$ | DMSO | 35 | 0 |

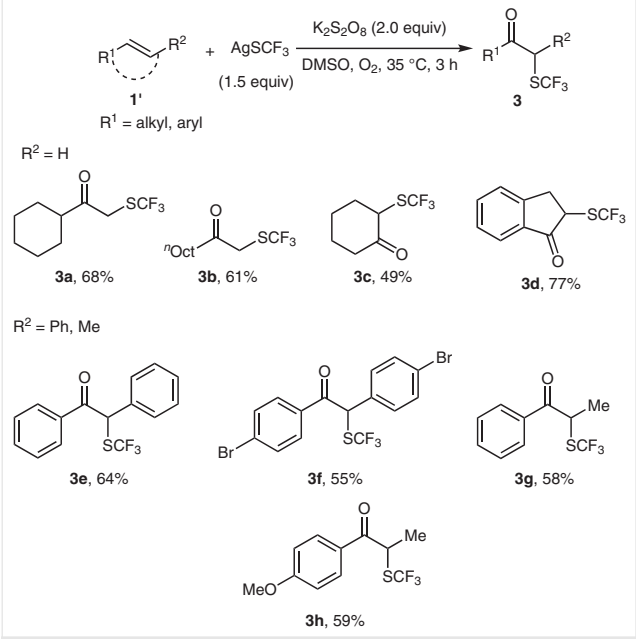
[a] Reaction conditions: **1a** (0.5 mmol), $AgSCF_3$ (0.75 mmol, 1.5 equiv), and oxidant (1.0 mmol, 2.0 equiv) in solvent (5.0 mL) at the given temperature for 3 h.
[b] Yields determined by $^{19}F$ NMR spectroscopy using 4,4-difluorobiphenyl as internal standard based on **1a**.
[c] Under air atmosphere.
[d] Under $N_2$.




**Scheme 2** Substrate scope with arylalkenes. *Reagents and conditions*: **1** (0.5 mmol), $AgSCF_3$ (0.75 mmol, 1.5 equiv), and $K_2S_2O_8$ (1.0 mmol, 2.0 equiv) in DMSO (5.0 mL) at 35 °C for 3 h. Isolated yields are given.

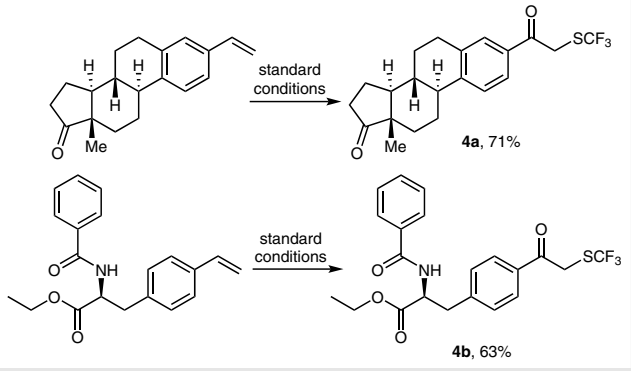
Inspired by these promising results, the aliphatic alkenes and less reactive β-substituted styrenes were examined to further broaden the scope of substrate under the standard reaction conditions (Scheme 3). Satisfactorily, these substrates can also be tolerated in the reaction system to afford the desired products. The terminal olefin, both 1-decene and cyclohexylethene, gave the desired compounds **3a** and **3b** in moderate yields. The lower yield of **3c** can be attributed to the larger steric hindrance of cyclohexene substrate than cyclohexylethene. A good yield of **3d** indicated that the aromatic nucleus always plays an important role in stabilizing the reaction intermediate. The less reactive β-substituted styrene substrate was also efficiently trifluoromethylthiolated through the reaction system to give the corresponding products **3e**,**f**,**g**,**h** in 55–64% yield, respectively, with excellent regioselectivity.

Known for its unique pharmacological activity, the $SCF_3$ group can generate some unexpected effects and unparalleled results. Exactly, direct trifluoromethylthiolation of organic molecular is still a fascinating strategy for a medicinal chemist in modifying the known and common drugs.[16] The feasible method could be also employed to introduce the $SCF_3$ group into complex molecules smoothly, such as 3-vinylestrone and *N*-benzoyl-L-tyrosine ethyl ester (Scheme 4).[17] The corresponding products **4a** and **4b** were obtained



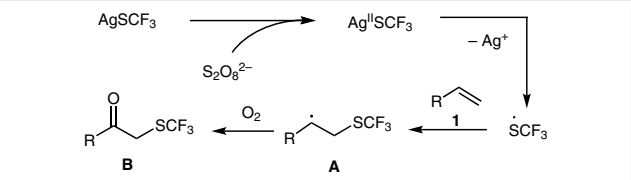

**Scheme 3** Scope with aliphatic alkenes and β-substituted styrenes. *Reagents and conditions*: **1'** (0.5 mmol), $AgSCF_3$ (0.75 mmol, 1.5 equiv) and $K_2S_2O_8$ (1.0 mmol, 2.0 equiv) in DMSO (5.0 mL) at 35 °C for 3 h. Isolated yields are given.

in 71% and 63% isolated yields, respectively. The results suggest that this method of oxidative trifluoromethylthiolation is convenient for natural products and drugs to provide the corresponding α-$SCF_3$-substituted ketone compounds.




**Scheme 4** The strategy to introduce $SCF_3$ groups to complex drug molecules. All reactions were performed under standard conditions.

The following experiment was carried out in order to elucidate a plausible reaction mechanism (Scheme 5). Firstly, we had known exactly that the presence of $O_2$ and $S_2O_8^{2-}$ was necessary to this reaction through condition optimization experiments (Table 1). When radical-trapping reagent 2,2,6,6-tetramethyl-1-oxylpiperidine (TEMPO) was added, the reaction was completely suppressed to give only trace products and the TEMPO-trifluoromethylthio adduct under the optimal conditions, which were detected by $^{19}F$ NMR spectroscopy and LC–MS (see the Supporting Information). This result suggests that the reaction may proceed *via* a radical pathway.



**Scheme 5** Plausible mechanism

Based on the above results and previous reported,[8] a plausible mechanism was proposed about the reaction process *via* a radical-type pathway as shown in Scheme 5. Initially, the $SCF_3$ radical was triggered by the Ag(II)$SCF_3$ species from the oxidation of Ag(I)$SCF_3$ by $S_2O_8^{2-}$. The reaction of alkenes **1** with $SCF_3$ radical gave the alkyl radical intermediates **A**. The participation of $O_2$ in the last step of reaction with **A** achieved the final products **B**.

In summary, we have developed a convenient and efficient method to provide a range of different α-$SCF_3$-substituted ketone compounds through oxidative trifluoromethylthiolation of alkenes with $AgSCF_3$.[18–21] A preliminary mechanistic investigation suggests that this reaction process *via* a radical pathway. With the extensive reaction tolerance, mild reaction conditions, and the easy-to-get raw material, this method achieve a useful and practical strategy for the synthesis of trifluoromethylthiolated ketones with great potential application of synthetic, medicinal, and agrochemical research.

## Funding Information

This work was supported by the National Natural Science Foundation of China (Grant No. 21562041 and 21502070) and the Fundamental Research Funds for the Central Universities.

## Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611546.

## References and Notes

(1) (a) Smart, B. E. *J. Fluorine Chem.* **2001**, *109*, 3. (b) Tlili, A.; Billard, T. *Angew. Chem. Int. Ed.* **2013**, *52*, 6818. (c) Wang, H.; Vicic, D. A. *Synlett* **2013**, *24*, 1887. (d) Landelle, G.; Panossian, A.; Pazenok, S.; Vors, J. P.; Leroux, F. R. *Beilstein J. Org. Chem.* **2013**, *9*, 2476. (e) Xu, X. H.; Matsuzaki, K.; Shibata, N. *Chem. Rev.* **2015**, *115*, 731. (f) Yang, X.; Wu, T.; Phipps, R. J.; Toste, F. D. *Chem. Rev.* **2015**, *115*, 826. (g) Zhang, P. P.; Lu, L.; Shen, Q. L. *Acta Chim. Sin.* **2017**, *75*, 744, DOI: 10.6023/A17050202.

(2) (a) Leo, A.; Hansch, C.; Elkins, D. *Chem. Rev.* **1971**, *71*, 525. (b) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(3) (a) Leroux, F.; Jeschke, P.; Schlosser, M. *Chem. Rev.* **2005**, *105*, 827. (b) Rossi, S.; Puglisi, A.; Raimondi, L.; Benaglia, M. *ChemCatChem* **2018**, *10*, 2717.

(4) (a) Toulgoat, F.; Alazet, S.; Billard, T. *Eur. J. Org. Chem.* **2014**, 2415. (b) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432. (c) Tlili, A.; Toulgoat, F.; Billard, T. *Angew. Chem. Int. Ed.* **2016**, *55*, 11726. (d) Meyer, F. *Chem. Commun.* **2016**, *52*, 3077. (e) Anselmi, E.; Simon, C.; Marrot, J.; Bernardelli, P.; Schio, L.; Pégot, B.; Magnier, E. *Eur. J. Org. Chem.* **2017**, 6319.

(5) (a) Adams, D. J.; Clark, J. H. *J. Org. Chem.* **2000**, *65*, 1456. (b) Teverovskiy, G.; David, S.; Surry, D. S.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 7312. (c) Zhang, C. P.; Vicic, D. A. *J. Am. Chem. Soc.* **2011**, *134*, 183. (d) Lefebvre, Q.; Fava, E.; Nikolaienko, P.; Rueping, M. *Chem. Commun.* **2014**, *50*, 6617. (e) Hu, M.; Rong, J.; Miao, W.; Ni, C.; Han, Y.; Hu, J. *Org. Lett.* **2014**, *16*, 2030. (f) Chu, L.; Qing, F. L. *Acc. Chem. Res.* **2014**, *47*, 1513.

(6) (a) Pluta, R.; Nikolaienko, P.; Rueping, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 1650. (b) Shao, X.; Xu, C.; Lu, L.; Shen, Q. L. *Acc. Chem. Res.* **2015**, *48*, 1227. (c) Chachignon, H.; Maeno, M.; Kondo, H.; Shibata, N.; Cahard, D. *Org. Lett.* **2016**, *18*, 2467. (d) Bu, M. J.; Lu, G. P.; Cai, C. *Org. Chem. Front.* **2017**, *4*, 266. (e) Song, H. X.; Han, Q. Y.; Zhao, C. L.; Zhang, C. P. *Green Chem.* **2018**, *20*, 1662.

(7) (a) Li, Y.; Koike, T.; Akita, M. *Asian J. Org. Chem.* **2017**, *6*, 445. (b) Dagousset, G.; Simon, C.; Anselmi, E.; Tuccio, B.; Billard, T.; Magnier, E. *Chem. Eur. J.* **2017**, *23*, 4282. (c) Yin, F.; Wang, X. S. *Org. Lett.* **2014**, *16*, 1128.

(8) (a) Guo, S.; Zhang, X.; Tang, P. *Angew. Chem. Int. Ed.* **2015**, *54*, 4065. (b) Wu, H.; Xiao, Z.; Wu, J.; Guo, Y.; Xiao, J. C.; Liu, C.; Chen, Q. Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 4070. (c) Wu, W.; Dai, W.; Ji, X.; Cao, S. *Org. Lett.* **2016**, *18*, 2918. (d) Chen, M. T.; Tang,

X. Y.; Shi, M. *Org. Chem. Front.* **2017**, *4*, 86. (e) Li, M.; Petersen, J. L.; Hoover, J. M. *Org. Lett.* **2017**, *19*, 638. (f) Ji, M. S.; Yu, J. J.; Zhu, C. *Chem. Commun.* **2018**, *54*, 6812.

(9) (a) Barata-Vallejo, S.; Bonesi, S.; Postigo, A. *Org. Biomol. Chem.* **2016**, *14*, 7150. (b) Cheng, Z. F.; Tao, T. T.; Feng, Y. S.; Tang, W. K.; Xu, J. J.; Dai, J.; Xu, H. J. *J. Org. Chem.* **2018**, *83*, 499.

(10) (a) Rueping, M.; Tolstoluzhsky, N.; Nikolaienko, P. *Chem. Eur. J.* **2013**, *19*, 14043. (b) Li, S. G.; Zard, S. Z. *Org. Lett.* **2013**, *15*, 5898. (c) Huang, Y.; He, X.; Lin, X.; Rong, M.; Weng, Z. *Org. Lett.* **2014**, *16*, 3284. (d) Jiang, M.; Zhu, F.; Xiang, H.; Xu, X.; Deng, L.; Yang, C. *Org. Biomol. Chem.* **2015**, *13*, 6935. (e) Zheng, J.; Cheng, R.; Lin, J. H.; Yu, D. H.; Ma, L.; Jia, L.; Liang, S. H. *Angew. Chem. Int. Ed.* **2017**, *56*, 3196.

(11) (a) Bayreuther, H.; Haas, A. *Chem. Ber.* **1973**, *106*, 1418. (b) Kolasa, A. *J. Fluorine Chem.* **1987**, *36*, 29. (c) Alazet, S.; Zimmer, L.; Billard, T. *Chem. Eur. J.* **2014**, *20*, 8589. (d) Glenadel, Q.; Alazet, S.; Billard, T. *J. Fluorine Chem.* **2015**, *179*, 89. (e) Alazet, S.; Ismalaj, E.; Glenadel, Q.; Bars, D. L.; Billard, T. *Eur. J. Org. Chem.* **2015**, 4607. (f) Shao, X. *Xu C., Lu L., Shen Q.* **2015**, *80*, 3012. (g) Wu, W.; Zhang, X. X.; Liang, F.; Cao, S. *Org. Biomol. Chem.* **2015**, *13*, 6992.

(12) (a) Pan, S.; Huang, Y.; Qing, F. L. *Chem. Asian J.* **2016**, *11*, 2854. (b) Pan, S.; Li, H.; Huang, Y.; Xu, X. H.; Qing, F. L. *Org. Lett.* **2017**, *19*, 3247.

(13) (a) Shao, X.; Wang, X.; Yang, T.; Lu, L.; Shen, Q. *Angew. Chem. Int. Ed.* **2013**, *52*, 3457. (b) Bootwicha, T.; Liu, X.; Pluta, R.; Atodiresei, I.; Rueping, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 12856. (c) Wang, X.; Yang, T.; Cheng, X.; Shen, Q. *Angew. Chem. Int. Ed.* **2013**, *52*, 12860. (d) Deng, Q. H.; Rettenmeier, C.; Wadepohl, H.; Gade, L. H. *Chem. Eur. J.* **2014**, *20*, 93. (e) Vinogradova, E. V.; Müller, P.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2014**, *53*, 3125. (f) Arimori, S.; Takada, M.; Shibata, N. *Org. Lett.* **2015**, *17*, 1063. (g) Guyon, H.; Chachignon, H.; Tognetti, V.; Joubert, L.; Cahard, D. *Eur. J. Org. Chem.* **2018**, 3756.

(14) Yadav, A. K.; Singh, K. N. *Chem. Commun.* **2018**, *54*, 1976.

(15) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 9747.

(16) (a) Liu, H.; Jiang, X. *Chem. Asian J.* **2013**, *8*, 2546. (b) Landelle, G.; Panossian, A.; Leroux, F. R. *Curr. Top. Med. Chem.* **2014**, *14*, 941. (c) Rueping, M.; Liu, X.; Bootwicha, T.; Pluta, R.; Merkens, C. *Chem. Commun.* **2014**, *50*, 2508.

(17) Yasu, Y.; Koike, T.; Akita, M. *Org. Lett.* **2013**, *15*, 2136.

(18) **1-(4-Iodophenyl)-2-[(trifluoromethyl)thio]ethanone (2l)**
In an oven-dried 25 mL Schlenk tube equipped with a stir bar were added 1-iodo-4-vinylbenzene (**1l**, 115.0 mg, 0.5 mmol), $AgSCF_3$ (156.7 mg, 0.75 mmol), and $K_2S_2O_8$ (270.3 mg, 1.0 mmol). The Schlenk tube was evacuated and refilled with oxygen balloon. DMSO (5 mL) was then added by syringe. The reaction mixture was stirred for 3 h at 35 °C. The crude reaction mixture was purified by column chromatography on silica gel to get product **2l**. Light yellow solid, 0.118 g, 68%. $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.87 (m, 2 H), 7.70–7.64 (m, 2 H), 4.48 (s, 2 H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 191.4 (s), 138.4 (s), 133.9 (s), 130.5 (q, *J* = 306.6 Hz), 129.6 (s), 102.5 (s), 38.0 (q, *J* = 1.9 Hz). $^{19}$F NMR (376 MHz, $CDCl_3$): δ = –41.39 (s, 3 F). HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_9H_7F_3IOS$: 346.9214; found: 346.9209.

(19) **1-[(Trifluoromethyl)thio]decan-2-one (3b)**
In an oven-dried 25 mL Schlenk tube equipped with a stir bar were added alkenes 1-decene **1'b** (70.1 mg, 0.5 mmol), $AgSCF_3$ (156.7 mg, 0.75 mmol), and $K_2S_2O_8$ (270.3 mg, 1.0 mmol). The Schlenk tube was evacuated and refilled with oxygen balloon. DMSO (5 mL) was then added by syringe. The reaction mixture was stirred for 3 h at 35 °C. The crude reaction mixture was purified by column chromatography on silica gel to get product **3b**. Light yellow oil, 0.078 g, 61%. $^1$H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 2 H), 2.59 (t, *J* = 7.4 Hz, 2 H), 1.30 (s, 11 H), 0.90 (t, *J* = 6.9 Hz, 4 H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 202.9 (s), 130.5 (q, *J* = 306.5 Hz), 41.2 (s), 40.0 (q, *J* = 1.8 Hz), 31.8 (s), 29.2 (s), 29.1 (s), 29.0 (s), 23.7 (s), 22.6 (s), 14.0 (s). $^{19}$F NMR (376 MHz, $CDCl_3$): δ = –41.68 (s, 3 F). HRMS (EI): *m/z* [M]$^+$ calcd for $C_{11}H_{19}F_3OS$: 256.1109; found: 256.1093

(20) **(8*R*,9*S*,13*S*,14*S*)-13-Methyl-3-{2-[(trifluoromethyl)thio]acetyl}-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (4a)[17]**
In an oven-dried 50 mL Schlenk tube equipped with a stir bar were added 3-vinylestrone (140.1 mg, 0.5 mmol), $AgSCF_3$ (156.7 mg, 0.75 mmol), and $K_2S_2O_8$ (270.3 mg, 1.0 mmol). The Schlenk tube was evacuated and refilled with oxygen balloon. DMSO (5 mL) was then added by syringe. The reaction mixture was stirred for 3 h at 35 °C. The crude reaction mixture was purified by column chromatography on silica gel to get product 4a. White solid, 0.141 g, 71%. $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.66 (m, 2 H), 7.44 (d, *J* = 8.2 Hz, 1 H), 4.51 (s, 2 H), 3.01 (d, *J* = 5.1 Hz, 2 H), 2.63–2.45 (m, 2 H), 2.38 (td, *J* = 10.7, 3.8 Hz, 1 H), 2.26–1.99 (m, 4 H), 1.75–1.45 (m, 6 H), 0.95 (s, 3 H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 191.8 (s), 146.9 (s), 137.5 (s), 132.4 (s), 130.7 (q, *J* = 306.4 Hz), 129.0 (s), 126.0 (s), 125.8 (s), 50.6 (s), 47.9 (s), 44.8 (s), 38.3 (q, *J* = 1.6 Hz), 37.7 (s), 35.8 (s), 31.5 (s), 29.3 (s), 26.2 (s), 25.5 (s), 21.6 (s), 13.8 (s). $^{19}$F NMR (376 MHz, $CDCl_3$): δ = –41.39 (s, 3 F). HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{24}F_3O_2S$: 397.1449; found: 397.1444

(21) **Radical Trapping Experiment**
Styrene (**1a**, 10.5 mg, 0.1 mmol), $AgSCF_3$ (31.3 mg, 0.15 mmol), $K_2S_2O_8$ (54.1 mg, 0.2 mmol), TEMPO (31.2 mg, 0.2 mmol), and 4,4′-difluorobiphenyl (19.0 mg, 0.1 mmol) were added to a Schlenk tube. The Schlenk tube was evacuated and refilled with oxygen balloon. Then DMSO (1.0 mL) was added by a syringe. The mixture was stirred at 35 °C for 3 h. Trace of the desired product **2a** and TEMPO-trifluoromethylthio adduct were detected by $^{19}$F NMR spectroscopy with 4,4′-difluorobiphenyl as the internal standard (δ = –115.78 ppm) based on **1a**. The same time, the reaction mixture was analyzed by LC–MS