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UV light irradiated trifluoromethylation of diheteroaryl disulfides with CF_3SO_2Na

Bao-Qian Cao,[a,b] [‡] Yi-Feng Qiu,[a,b] [‡] Xi Zhang, [a,b] Zheng-He Zhu, [a,b] Zheng-Jun Quan, *, [a,b] and Xi-Cun Wang*,[a,b]

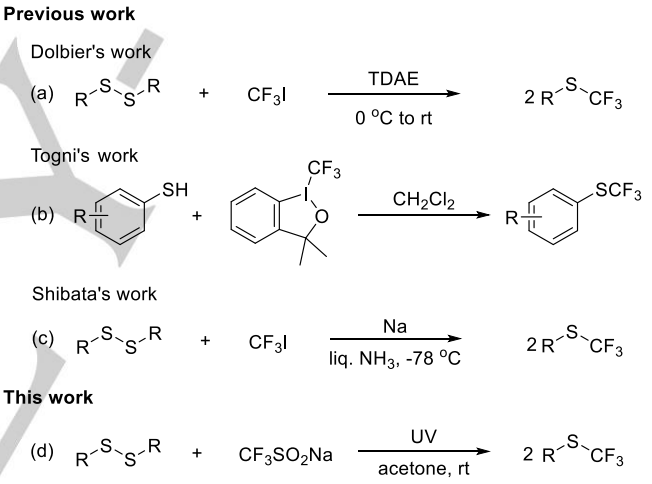
Dedication ((optional))

Abstract: A simple protocol for the UV light irradiated preparation of heteroaryl trifluoromethyl thioethers from disulfides and inexpensive, environmentally sodium triflinate (CF_3SO_2Na) is been developed. The features of simple and clean reaction conditions, in moderate to good yields, and broad substrate scope render this new approach synthetically attractive for the preparation of potentially pharmaceutically active compounds.

Introduction

Organofluorine has achieved considerable development during last decades, specifically in pharmaceutical research, pesticide chemistry, and material science.[1,2] Thus, the exploration for efficient strategies on the introduction of fluoroalkyl groups into organic compounds has become the present research focus.[3,4] Among such numerous fascinating fluorine-containing groups, the trifluoromethyl group (CF_3) and trifluoromethylthio group (SCF_3) have attracted much attention for desirable properties in biological and pharmacological activities.[5]

Disulfide has the advantages of being inexpensive, easy to prepare, and stable in air, which could provide two S-containing moieties via a facile S-S bond cleavage under mild conditions. [6] In recent years, our group has been working on the study of dipyrimidyl disulfide, and we have found that compounds containing pyrimidine structure have certain biological activity. In addition, the trifluoromethylation of sulfur-containing precursors has caused great interest among chemists.[7] Nevertheless, these methods suffer from various unavoidable drawbacks, such as tedious operations, harsh conditions, toxic metal catalysts, poor selectivity and functional group compatibility. Stimulated by advancing aspiration on new routes to introduce the trifluoromethyl group into sulfur-containing precursors, adequate advancements have been achieved in the development of various new reagents. In 2004, Dolbier and other researchers developed the addition of CF_3 anion, generated from the reduction of CF_3I by tetrakis-(dimethylamino)ethylene (TDAE), onto disulfides (Scheme 1a).[8] In 2007, Togni and co-workers used their hypervalent iodine(III)–CF_3 reagent to perform the trifluoromethylation of sulphydryl compounds (Scheme 1b).[9] After that, Shibata described the reductive trifluoromethylation of homocystine and cystine to provide corresponding trifluoromethyl thioethers through the CF_3I/Na/Liq.NH_3 system (Scheme 1c).[10] Still, the exploration of safety, operationally simple, and environmentally friendly (metal and oxidant free) synthetic methods with high efficiency on trifluoromethylation of sulfur-containing precursors is fueled by strong and increasing aspiration.



Scheme 1. Strategies for trifluoromethylation of sulfur-containing precursors and our new anticipation.

As a stable and cheap trifluoromethylation reagent, sodium triflinate (Langlois reagent) is widely used in the field of organic fluorine chemistry.[11] In 2016, the Li group reported a simple and clean strategy for direct trifluoromethylation of arenes/heteroarenes under ultraviolet/visible light irradiation.[12] By taking into consideration of our current interests in the transformation of sulfur-containing organic compounds,[13] as well as the continued anticipation of new approaches to skeletons of pharmaceutical molecule, we designed a UV light irradiated trifluoromethylation of disulfides with CF_3SO_2Na (Scheme 1d). The conversion has relatively good functional group compatibility, and the disulfide has fully utilized while constructing two S-CF_3 bonds. Inexpensive and commercially available CF_3SO_2Na provided CF_3 source without external photocatalyst, generating the corresponding products in moderate to good yields under mild conditions. Notably, the trifluoromethylthio group in the products would lead to a great promotion of membrane permeability and absorption rate in bioavailability for its high lipophilicity, electronegativity, and metabolic stability.[14] This

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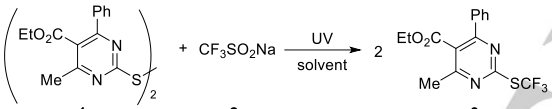
synthetic strategy may provide potential application of pharmaceutical synthesis in industrial production.

Results and Discussion

1,2-Di(pyrimidin-2-yl) disulfides (**1a**) was selected as the model substrate for the optimization of reaction conditions (Table 1). The initial attempt was conducted in CH_3CN under the irradiation of 365 nm UV light (300 W) under air at room temperature for 4 h, which gave the desired trifluoromethylation product **3a** in 30% isolated yield (Table 1, entry 1). A short survey on solvents revealed that acetone performed best for this reaction (entries 2-6). Changing the loadings of **2a** to 8 equivalents improved the yield of product **3a** to 85% (entries 7-9). The investigation on the light sources indicated that 100 W UV (365 nm) was the most effective light source with 86% yield of product **3a** obtained (entries 10-11). The subsequent control experiments verified that the light source made significant influences on this transformation since no reaction occurred in darkness. (entry 12). Prolonging the reaction time to 6 h gave a slight improvement of the yield to 88% (entry 13). After the above detailed investigations, the optimized reaction conditions were settled as the use of **1a** in the presence of CF_3SO_2Na **2a** (8 equivalents) in acetone at room temperature for 6 h.

Table 1. Optimization of Reaction Conditions[a]

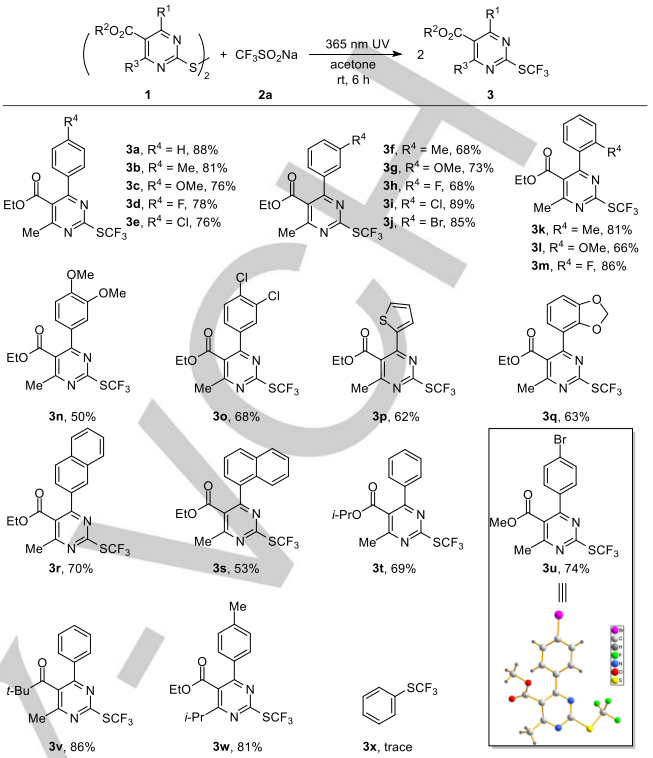


1a **2a** **3a**

Entry	Solvent	Light source	Yield (%)[b]
1	CH_3CN	300 W UV	30
2	1,4-dioxane	300 W UV	40
3	acetone	300 W UV	68
4	DCE	300 W UV	45
5	DMSO	300 W UV	62
6	EtOH	300 W UV	trace
7[c]	acetone	300 W UV	76
8[d]	acetone	300 W UV	85
9[e]	acetone	300 W UV	83
10	acetone	100 W UV	86
11[f]	acetone	300 W UV	72
12	acetone	-	0
13[g]	**acetone**	**100 W UV**	**88**
14[h]	acetone	100 W UV	85

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.4 mmol), solvent (2.0 mL) at room temperature under 365 nm UV light (300 W) irradiation under air for 4 h. [b] Isolated yields. [c] 6 equiv of **2a** were added. [d] 8 equiv of **2a** were added. [e] 10 equiv of **2a** were added. [f] This reaction was conducted under 254 nm UV light irradiation. [g] This reaction was conducted for 6 h. [h] This reaction was conducted for 8 h.

With the optimized reaction conditions in hand, as depicted in Scheme 2, different kinds of disulfides, including 1,2-di(pyrimidin-2-yl) disulfides and quinoline-2-disulfides were then synthesized to investigate the substrate scope. To our delight, a



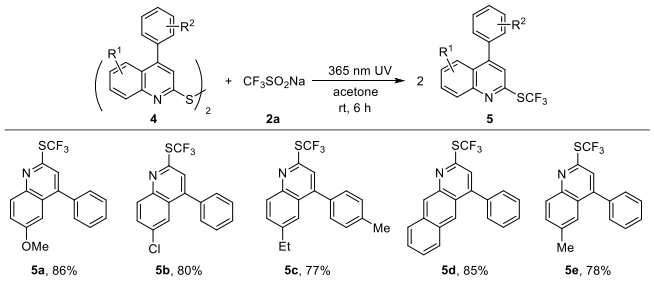
Scheme 2. Substrate scope of 1,2-di(pyrimidin-2-yl) disulfides.

wide range of disulfides could be tolerated under the optimal reaction conditions, generating the corresponding trifluoromethyl thioethers products in moderate to good yields (50%–89%). As for the 1,2-di(pyrimidin-2-yl) disulfides part (Scheme 2), both electron-rich (Me and OMe) and -deficient (F, Cl and Br) groups at the *para*-position and *meta*-position of the aromatic ring gave good yields of the corresponding trifluoromethylation products (**3b**–**3j**). The substituents at the *ortho*-position such as Me and F afforded the corresponding products **3k**, **3m** in 81%−86% yields, except for OMe, with a slight decrease (**3l**). Poly-substituted disulfides could also give moderate yields under the standard reaction conditions (**3n**, **3o**). When the disulfides possess a multiple-ring group or heterocyclic-group at the C4 position, such as 2-thiopheny, 2-piperonyl, *α/β*-naphthyl group, the desired products **3p-3s** could be obtained in 53%-70% yield, respectively. Subsequently, the effect of substituent at the C5 position was also investigated. Products with substituent groups on R^2 could be converted into the corresponding products in moderated to good yields (**3t**, **3u** and **3v**). The substituent of *i*-Pr at the C6 position also afforded the desired product **3w** in satisfactory yield. Unfortunately, diphenyl disulfide **1x** failed to give the corresponding trifluoromethyl thioethers product in this condition. It gives a complex mixture and the raw materials disappeared. We believed this may due to PhS• redical has a redox potential out of range from the redox potential of the Langlois' reagent.

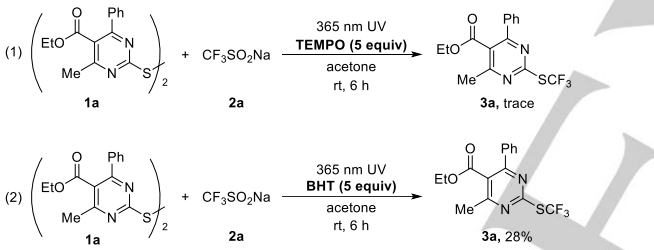
Subsequently, the reactions of a variety of substituted quinoline-2-disulfides derivatives with CF_3SO_2Na (**2a**) were also

investigated under the optimized reaction conditions. As shown in Scheme 3, a series of functional groups on the quinoline rings were tolerated, leading to the desired products in good to excellent yields(**5a**-**5e**).

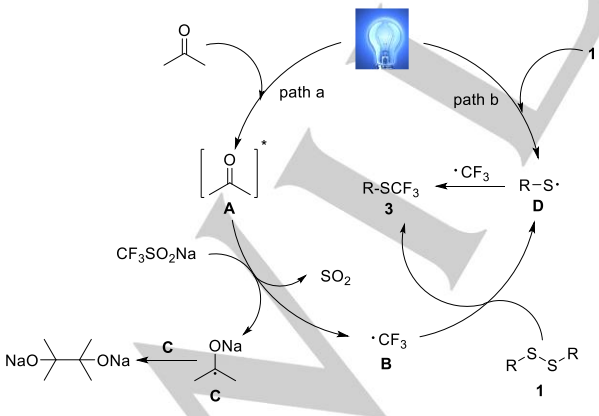
In order to probe the mechanism, some necessary inhibition experiments were performed (Scheme 4). When 5 equivalents of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or butylated hydroxytoluene (BHT) were added into the reaction system, only trace or 28% yield of product **3a** was detected, respectively [Scheme 4, eqn (1) and (2)], suggesting that the •CF_3 radical was likely involved as the reactive species in the transformation.



Scheme 3. Substrate scope of quinoline-2-disulfides.



Scheme 4. Control experiments.



Scheme 5. Proposed reaction mechanism.

Based on the above results and previous reports,[12,15] a plausible mechanism is outlined in Scheme 5. Two potential paths may achieve this result. As shown in path a, acetone is excited by ultraviolet light irradiation to generate the excited species **A**, which is reduced by CF_3SO_2Na and generate the •CF_3 radical **B** with concomitant release of one equivalent of SO_2 and sodium radical anion **C**. In the reaction end, two sodium radical anions **C** can couple to form a salt sodium 2,3-dimethylbutane-2,3-bis(olate).[16] Subsequently, the addition of disulfides **1** and the •CF_3 radical afforded the final product **3** with concomitant release of one equivalent of thiyl radicals **D**, which could also be generated by the hemolytic cleavage of S-S bond (path b), then coupled with a •CF_3 radical to give the final product **3**.

Conclusions

In summary, we have developed a UV light irradiation promoted trifluoromethylation of disulfides. In this reaction, a series of trifluoromethyl thioethers products including pyrimidinyl-2-trifluoromethyl thioethers and quinoline-2-trifluoromethyl thioethers were synthesized smoothly. This transformation process proved to involve a •CF_3 radical pathway which avoided the addition of external photocatalyst and could be easily operated under an air atmosphere. In addition, the synthetic utility of our developed reaction system has been demonstrated by its applicability to synthetically useful heteroaromatic disulfides.

Experimental Section

Typical Procedure for the Synthesis of 3a: Under an atmosphere of air, diethyl 2,2'-disulfanediylbis(6-methyl-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate) **1a** (0.1 mmol, 0.0546 g), $NaSO_2CF_3$ **2a** (8 equivalent 0.8 mmol, 0.1248 g) were added to a tube. Acetone (2.0 mL) was added by dropper and the mixture was stirred for 6 h at rt. 100 W UV light and the reaction was monitored by TLC analysis. The residue was purified by column chromatography on silica gel (ethyl acetate/ petroleum ether = 1:20) to give the corresponding product **3a**. All of the products were synthesized according to above described procedure.

Ethyl 4-methyl-6-phenyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3a). Colourless oil (60.2 mg, 88%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.68–7.65 (m, 2H), 7.51–7.43 (m, 3H), 4.20 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.28, 166.68, 165.10 (q, $J_{C\text{-}F}$ = 3.15 Hz, C-SCF_3), 164.08, 136.53, 130.68, 128.59, 128.47, 128.20 (q, $J_{C\text{-}F}$ = 306.3 Hz, SCF_3), 123.30, 62.08, 22.51, 13.58. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.09. HRMS (ESI) m/z: Calcd for $C_{15}H_{13}F_3N_2O_2S$: 343.0723 $[M+H]^+$, Found: 343.0728.

Ethyl 4-methyl-6-(*p*-tolyl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3b). Colourless oil (57.6 mg, 81%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.60–7.58 (m, 2H), 7.27–7.24 (m, 2H), 4.24 (q, J = 7.2 Hz, 2H), 2.57 (s, 3H), 2.40 (s, 3H), 1.14 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.50, 166.45, 164.95 (q, $J_{C\text{-}F}$ = 3.0 Hz, C-SCF_3), 163.88, 141.24, 133.62, 129.34, 128.49, 128.22 (q, $J_{C\text{-}F}$ = 306.4 Hz,

SCF_3), 123.05, 62.06, 22.47, 21.39, 13.66. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.10. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_2S$: 357.0879 $[M+H]^+$, Found: 357.0883.

Ethyl 4-(4-methoxyphenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3c). Colourless oil (56.6 mg, 76%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.71–7.65 (m, 2H), 6.98–6.93 (m, 2H), 4.26 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 2.55 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.72, 166.33, 164.81 (q, $J_{C\text{-}F}$ = 3.15 Hz, C-SCF_3), 163.13, 161.90, 130.32, 128.25 (q, $J_{C\text{-}F}$ = 306.0 Hz, SCF_3), 128.70, 122.58, 114.08, 62.07, 55.37, 22.44, 13.75. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.09. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_3S$: 373.0828 $[M+H]^+$, Found: 373.0823.IR

Ethyl 4-(4-fluorophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3d). Colourless oil (56.2 mg, 78%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.71–7.67 (m, 2H), 7.16–7.12 (m, 2H), 4.24 (q, J = 7.2 Hz, 2H), 2.58 (s, 3H), 1.14 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.21, 166.79, 165.18, 165.12 (q, J = 3.0 Hz, C-SCF_3), 163.51, 162.73, 132.60 (d, J = 3.2 Hz), 130.71 (d, J = 8.7 Hz), 128.15 (q, J = 306.5 Hz, SCF_3), 123.08, 62.18, 22.48, 13.65.^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.14, -109.43–-109.51 (m). HRMS (ESI) m/z: Calcd for $C_{15}H_{12}F_4N_2O_2S$: 361.0628 $[M+H]^+$, Found: 361.0630.

Ethyl 4-(4-chlorophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3e). Colourless oil (57.2 mg, 76%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.63–7.61 (m, 2H), 7.44–7.41 (m, 2H), 4.24 (q, J = 7.2 Hz, 2H), 2.58 (s, 3H), 1.14 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.09, 166.90, 165.24 (q, $J_{C\text{-}F}$ = 3.0 Hz, C-SCF_3), 162.70, 137.20, 134.90, 129.87, 129.12 (q, $J_{C\text{-}F}$ =306.3 Hz, SCF_3), 128.92, 123.12, 62.25, 22.54, 13.68. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.14. HRMS (ESI) m/z: Calcd for $C_{15}H_{12}ClF_3N_2O_2S$: 377.0333 $[M+H]^+$, Found: 377.0335.

Ethyl 4-methyl-6-(*m*-tolyl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3f). Colourless oil (48.4 mg, 68%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.49–7.43 (m, 2H), 7.33 (t, J = 7.8 Hz, 1H), 7.32–7.29 (m, 1H), 4.21 (q, J = 7.2 Hz, 2H), 2.58 (s, 3H), 2.40 (s, 3H), 1.10 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.34, 166.56, 165.02 (q, $J_{C\text{-}F}$ = 3.2 Hz, C-SCF_3), 164.25, 138.37, 136.45, 131.46, 128.99 (q, $J_{C\text{-}F}$ = 243.0 Hz, SCF_3), 129.07, 128.49, 125.59, 123.33, 62.03, 22.52, 21.37, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.09. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_2S$: 357.0879 $[M+H]^+$, Found: 357.0875.

Ethyl 4-(3-methoxyphenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3g). Colourless oil (54.4 mg, 73%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.34 (t, J = 7.8 Hz, 1H), 7.26 (t, J = 1.8 Hz, 1H), 7.21 (d, J = 7.8 Hz, 1H), 7.03 (dd, J = 2.4, 1.8 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.83 (s, 3H), 2.58 (s, 3H), 1.12 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.26, 166.63, 165.03 (q, $J_{C\text{-}F}$ = 3.0 Hz, C-SCF_3), 163.76, 159.77, 137.73, 129.61, 128.20 (q, $J_{C\text{-}F}$ =306.3 Hz, SCF_3), 123.39, 120.72, 116.91, 113.59, 62.12, 55.29, 22.47, 13.62. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.13. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_3S$: 373.0828 $[M+H]^+$, Found: 373.0830.

Ethyl 4-(3-fluorophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3h). Colourless oil (49.0 mg, 68%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.46–7.39 (m, 3H), 7.21–7.17 (m, 1H), 4.24 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.95 (d, J = 13.7 Hz), 165.27 (q, J = 3.2 Hz, C-SCF_3), 163.49, 162.56, 161.85, 138.55 (d, J = 7.7 Hz,), 130.22 (d, J = 8.1 Hz), 128.11 (q, J = 306.3 Hz), 124.18 (d, J = 3 Hz), 123.36, 117.65 (d, J = 21 Hz), 115.62 (d, J = 23.3 Hz), 62.24, 22.51, 13.57. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.13, -109.46–-114.65 (m). HRMS (ESI) m/z: Calcd for $C_{15}H_{12}F_4N_2O_2S$: 361.0628 $[M+H]^+$, Found: 361.0627.

Ethyl 4-(3-chlorophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3i). Colourless oil (67.0 mg, 89%); ^1H NMR (600 MHz, $CDCl_3$) δ = 7.65 (t, J = 1.8 Hz, 1H), 7.56–7.53 (m, 1H), 7.47–7.45 (m, 1H), 7.38 (t, J = 7.8 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 1.14 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.05, 166.83, 165.31 (q, J = 2.9 Hz, C-SCF_3), 162.51, 138.16, 134.67, 130.68, 129.89, 128.55, 128.10 (q, J = 306.5 Hz, SCF_3), 126.65, 123.35, 62.28, 22.56, 13.63. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -41.12. HRMS (ESI) m/z: Calcd for $C_{15}H_{12}ClF_3N_2O_2S$: 377.0333 $[M+H]^+$, Found: 377.0335.

Ethyl 4-(3-bromophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3j). Colourless oil (71.2 mg, 85%); ^1H NMR (600 MHz, $CDCl_3$) δ ppm = 7.80 (t, J = 1.8 Hz, 1H), 7.63–7.58 (m, 2H), 7.32 (t, J = 7.8 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 1.15 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm = 167.06, 166.82, 165.31 (q, $J_{C\text{-}F}$ = 2.9 Hz, C-SCF_3), 162.40, 138.38, 133.60, 131.41, 130.13, 128.09 (q, $J_{C\text{-}F}$ =306.5 Hz, SCF_3), 127.11, 127.07, 123.34, 122.62, 62.31, 22.58, 13.68. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -41.12. HRMS (ESI) m/z: Calcd for $C_{15}H_{12}BrF_3N_2O_2S$: 420.9828 $[M+H]^+$, Found: 420.9829.

Ethyl 4-methyl-6-(*o*-tolyl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3k). Colourless oil (57.7 mg, 81%); ^1H NMR (600 MHz, $CDCl_3$) δ ppm = 7.48 (s, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 2.58 (s, 3H), 2.40 (s, 3H), 1.10 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm = 167.33, 166.57, 165.01 (q, J = 3 Hz, C-SCF_3), 164.25, 138.37, 136.45, 131.46, 129.07, 128.49,128.20 (q, J = 306.5 Hz, SCF_3), 125.59, 123.34, 62.04, 22.51, 21.37, 13.60. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -41.09. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_2S$: 357.0879 $[M+H]^+$, Found: 357.0873.

Ethyl 4-(2-methoxyphenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3l). Colourless oil (49.2 mg, 66%); ^1H NMR (600 MHz, $CDCl_3$) δ ppm = 7.53 (dd, J = 7.8, 1.8 Hz, 1H), 7.44–7.40 (m, 1H), 7.07 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 4.08 (q, J = 7.2 Hz, 2H), 3.74 (s, 3H), 2.66 (s, 3H), 0.99 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm = 167.02, 166.13, 165.23 (q, $J_{C\text{-}F}$ = 3.2 Hz, C-SCF_3), 163.74, 156.38, 131.62, 130.96, 128.19 (q, $J_{C\text{-}F}$ =306.5 Hz, SCF_3), 126.61, 124.06, 121.04, 110.18, 61.20, 55.02, 23.34, 13.52. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -41.13. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_3S$: 373.0828 $[M+H]^+$, Found: 373.0829.

Ethyl 4-(2-fluorophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3m). Colourless oil (61.9 mg, 86%); ^1H NMR (600 MHz, $CDCl_3$) δ ppm = 7.63–7.59 (m, 1H), 7.48–7.43 (m, 1H), 7.29–7.25 (m, 1H), 7.12–7.08 (m, 1H), 4.19 (q, J = 7.2 Hz, 2H), 2.68 (s, 3H), 1.06 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ ppm = 167.83, 165.80,165.57 (q, J = 3.0 Hz, C-SCF_3), 161.12, 160.59, 158.94, 132.15 (d, J = 8.4 Hz), 132.19 (d, J = 2.7), 128.08 (q, J = 306.3 Hz, SCF_3), 125.19 (d, J = 14.0 Hz), 124.57 (d, J = 3.5 Hz), 115.43 (d, J = 21.6 Hz), 61.78, 23.43, 13.48. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -41.15, -114.71–-117.62 (m). HRMS (ESI) m/z: Calcd for $C_{15}H_{12}F_4N_2O_2S$: 361.0628 $[M+H]^+$, Found: 361.0625.

Ethyl4-(3,4-dimethoxyphenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3n). White solid (40.0 mg, 50%); m.p.: 89-91°C. ^1H NMR (600 MHz, $CDCl_3$) δ ppm = 7.38 (d, J = 1.8 Hz, 1H), 7.27 (dd, J = 7.2, 2.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 3.93 (s, 3H), 3.91 (s, 3H), 2.54 (s, 3H), 1.18 (t, J

= 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.80, 166.31, 164.77 (q, J_{C-F} = 3.0 Hz, C-SCF_3), 162.90, 151.52, 149.12, 128.84, 128.28 (q, J_{C-F} =306.3 Hz, SCF_3), 122.68, 121.84, 111.64, 110.73, 62.13, 55.99, 55.83, 22.39, 13.79. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.13. HRMS (ESI) m/z: Calcd for $C_{17}H_{17}F_3N_2O_4S$: 403.0934 $[M+H]^+$, Found: 403.0938.

Ethyl 4-(3,4-dichlorophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3o). Colourless oil (55.8 mg, 68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.78 (dd, J = 1.6, 0.8 Hz, 1H), 7.55–7.51 (m, 2H), 4.29 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.17, 166.76, 165.44 (q, J_{C-F} = 3.3 Hz, C-SCF_3), 161.35, 136.19, 135.35, 133.09, 130.69, 130.41, 127.70, 127.68, 128.05 (q, J_{C-F} =306.5 Hz, SCF_3), 123.18, 62.44, 22.60, 13.75. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.14. HRMS (ESI) m/z: Calcd for $C_{15}H_{11}Cl_2F_3N_2O_2S$: 410.9943 $[M+H]^+$, Found: 410.9945.

Ethyl 4-methyl-6-(thiophen-2-yl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3p). Colourless oil (43.2 mg, 62%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.93 (dd, J = 3.0, 1.2 Hz, 1H), 7.47 (dd, J = 5.4, 1.2 Hz, 1H), 7.37 (dd, J = 4.8, 3.0 Hz, 1H), 4.36 (q, J = 7.2 Hz, 2H), 2.52 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.60, 166.19, 164.92 (q, J = 3.2 Hz, C-SCF_3), 157.40, 137.74, 129.13, 128.24 (q, J = 306.3 Hz, SCF_3), 127.37, 126.46, 122.16, 62.36, 22.31, 13.82. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.15. HRMS (ESI) m/z: Calcd for $C_{13}H_{11}F_3N_2O_2S_2$: 349.0287 $[M+H]^+$, Found: 349.0286.

Ethyl 4-(benzo*[d]*[1,3]dioxol-4-yl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3q). Colourless oil (48.6 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.24–7.19 (m, 2H), 6.86 (d, J = 8.0 Hz, 1H), 6.03 (s, 2H), 4.28 (q, J = 7.2 Hz, 2H), 2.55 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ= 167.53, 166.44, 164.85 (q, J = 3.3 Hz, C-SCF_3), 162.96, 150.05, 148.18, 130.36, 128.20 (q, J = 306.3 Hz, SCF_3), 123.48, 122.81, 108.87, 108.35, 101.67, 62.15, 22.46, 13.78. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.10. HRMS (ESI) m/z: Calcd for $C_{16}H_{13}F_3N_2O_4S$: 387.0621 $[M+H]^+$, Found: 387.0625.

Ethyl 4-methyl-6-(naphthalen-2-yl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3r). Colourless oil (54.8 mg, 70%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.19 (s, 1H), 7.93–7.86 (m, 3H), 7.77 (dd, J = 8.4, 1.8 Hz, 1H), 7.58–7.51 (m, 2H), 4.21 (q, J = 7.2 Hz, 2H), 2.62 (s, 3H), 1.04 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.44, 166.72, 165.13 (q, J_{C-F} = 2.9 Hz, C-SCF_3), 163.93, 133.81, 132.80, 129.02, 128.83, 128.48, 127.72, 127.65, 128.22 (q, J_{C-F} = 306.5 Hz, SCF_3), 126.74, 125.17, 123.48, 62.15, 22.57, 13.66. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.03. HRMS (ESI) m/z: Calcd for $C_{19}H_{15}F_3N_2O_2S$: 393.0879 $[M+H]^+$, Found: 393.0877.

Ethyl 4-methyl-6-(naphthalen-1-yl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3s). Colourless oil (41.6 mg, 53%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.94 (d, J = 8.4 Hz, 1H), 7.90–7.88 (m, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.53–7.47 (m, 3H), 7.43 (dd, J = 6.6, 1.2 Hz, 1H), 3.81 (q, J = 7.2 Hz, 2H), 2.68 (s, 3H), 0.56 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.31, 166.20, 165.77, 165.24 (q, J = 3 Hz, C-SCF_3), 134.55, 133.46, 130.51, 130.19, 128.29, 128.13 (q, J = 306.5 Hz, SCF_3), 126.89, 126.37, 125.50, 124.99, 124.80, 61.60, 22.95, 13.07. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.03. HRMS (ESI) m/z: Calcd for $C_{19}H_{15}F_3N_2O_2S$: 393.0879 $[M+H]^+$, Found: 393.0881.

Isopropyl 4-methyl-6-phenyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3t). Colourless oil (49.2 mg, 69%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.68–7.66 (m, 2H), 7.50–7.42 (m, 3H), 5.14–5.07 (m, 1H), 2.58 (s, 3H), 1.10 (d, J = 6.0 Hz, 6H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.73, 166.42, 164.92 (q, J_{C-F} = 3.0 Hz, C-SCF_3), 163.96, 136.53, 130.60, 128.19 (q, J_{C-F} = 306.5 Hz, SCF_3), 128.57, 128.55, 123.77, 70.10, 22.43, 21.25.^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.09. HRMS (ESI) m/z: Calcd for $C_{16}H_{15}F_3N_2O_2S$: 357.0879 $[M+H]^+$, Found: 357.0877.

Methyl 4-(4-bromophenyl)-6-methyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3u). White solid (60.0 mg, 74%); m.p.:118-120 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.61–7.58 (m, 2H), 7.56–7.52 (m, 2H), 3.76 (s, 3H), 2.57 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.63, 167.03, 165.46 (q, J_{C-F} = 3.0 Hz, C-SCF_3), 162.75, 135.28, 131.99, 129.95, 128.09 (q, J_{C-F} =306.3 Hz, SCF_3), 125.76, 122.72, 52.92, 22.60.^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.13. HRMS (ESI) m/z: Calcd for $C_{14}H_{10}BrF_3N_2O_2S$: 406.9671 $[M+H]^+$, Found: 406.9675.

Tert-butyl 4-methyl-6-phenyl-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3v). Colourless oil (63.6 mg, 86%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.71–7.68 (m, 2H), 7.51–7.47 (m, 1H), 7.47–7.43 (m, 2H), 2.59 (s, 3H), 1.38 (s, 9H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.21 (d, J = 11.0 Hz), 164.47 (q, J = 3.0 Hz, C-SCF_3), 163.70, 136.62, 130.51, 128.69, 128.47, 128.24 (q, J = 306.3 Hz, SCF_3), 124.74, 83.63, 27.64, 22.41. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -41.09. HRMS (ESI) m/z: Calcd for $C_{17}H_{17}F_3N_2O_2S$: 371.1036 $[M+H]^+$, Found: 371.1039.

Ethyl 4-isopropyl-6-(*p*-tolyl)-2-((trifluoromethyl)thio)pyrimidine-5-carboxylate (3w). Colourless oil (62.2 mg, 81%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.57 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 9.0 Hz, 2H), 4.22 (q, J = 7.2 Hz, 2H), 3.19–3.12 (m, 1H), 2.40 (s, 3H), 1.30 (d, J = 6.6 Hz, 6H), 1.13 (t, J = 7.2 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 174.25, 167.56, 165.34 (q, J = 3.2 Hz, C-SCF_3), 164.12, 141.00, 133.87, 129.31, 128.40, 128.35 (q, J = 306.2 Hz, SCF_3), 122.40, 62.03, 33.35, 21.55, 21.36, 13.65 ^{19}F NMR (376 MHz, $CDCl_3$) δ = -41.09. HRMS (ESI) m/z: Calcd for $C_{18}H_{19}F_3N_2O_2S$: 385.1192 $[M+H]^+$, Found: 385.1195.

6-methoxy-4-phenyl-2-((trifluoromethyl)thio)quinoline (5a). Yellow solid (57.6 mg, 86%); m.p.: 95-97 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 (d, J = 9.2 Hz, 1H), 7.59–7.49 (m, 6H), 7.42 (dd, J = 9.2, 2.8 Hz, 1H), 7.17 (d, J = 2.8 Hz, 1H), 3.79 (s, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 158.88, 148.91, 145.74 (q, J_{C-F} = 2.4 Hz, C-SCF_3), 145.18, 137.23, 131.36, 19.64 (q, J_{C-F} = 306.9 Hz, SCF_3), 129.21, 128.85, 128.83, 127.23, 124.99 (d, J_{C-F} = 1.8 Hz, C-$CSCF_3$), 122.87, 103.62, 55.49. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -39.99. HRMS (ESI) m/z: Calcd for $C_{17}H_{12}F_3NOS$: 336.0664 $[M+H]^+$, Found: 336.0666.

7-chloro-4-phenyl-2-((trifluoromethyl)thio)quinoline (5b). Yellow solid (54.2 mg, 80%); m.p.: 287-289 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.08 (dd, J = 9.0, 3.2 Hz, 1H), 7.86 (t, J = 2.4 Hz, 1H), 7.69 (dt, J = 9.0, 2.4 Hz, 1H), 7.58–7.54 (m, 3H), 7.52 (d, J = 3.0 Hz, 1H), 7.49–7.46 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 150.07 (q, J_{C-F} = 2.4 Hz, C-SCF_3), 149.56, 147.23, 136.26, 133.75, 131.36, 131.26, 139.27 (q, J_{C-F} = 307.1 Hz, SCF_3), 129.33, 129.23, 128.96, 126.51, 124.74, 123.89 (d, J_{C-F} = 2.1 Hz, C-SCF_3, it should be quartet, but only doublet was observed.). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -39.55. HRMS (ESI) m/z: Calcd for $C_{16}H_9ClF_3NS$: 340.0169 $[M+H]^+$, Found: 340.0166.

6-ethyl-4-(*p*-tolyl)-2-((trifluoromethyl)thio)quinoline (5c). Yellow solid (53.4 mg, 77%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.08 (d, J = 8.4 Hz, 1H), 7.70 (s, 1H), 7.63 (dd, J = 9.0, 2.4 Hz, 1H), 7.50 (s, 1H), 7.42–7.39 (m, 2H), 7.36 (d, J = 7.8 Hz, 2H), 2.77 (q, J = 7.2 Hz, 2H), 2.48 (s, 3H), 1.25 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 149.89, 148.04 (q, J_{C-F} = 2.6 Hz, C-SCF_3), 147.81, 144.11, 138.85, 134.23, 131.45, 129.93 (q, J_{C-F} = 108.5 Hz, SCF_3), 129.63, 129.43, 129.37, 126.04, 124.02 (d, J_{C-F} = 2.3 Hz, C-SCF_3), 123.48, 29.16, 21.31, 15.45. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -39.77. HRMS (ESI) m/z: Calcd for $C_{19}H_{16}F_3NS$: 348.1028 $[M+H]^+$, Found: 348.1030.

4-phenyl-2-((trifluoromethyl)thio)benzo*[g]*quinoline (5d). Yellow solid (60.4 mg, 85%); m.p.: 81-83 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.01 (s, 2H), 7.87 (dd, J = 7.8, 1.2 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.57 (s, 1H), 7.55–7.49 (m, 4H), 7.42–7.40 (m, 2H), 7.19–7.16 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 150.24, 150.20, 147.72 (q, $J_{C\text{-}F}$ = 2.3 Hz, C-SCF_3), 141.53, 133.18, 132.60, 129.40, 129.21, 128.74, 128.64, 129.46 (q, $J_{C\text{-}F}$ = 306.9 Hz, SCF_3), 128.23, 128.19, 128.07, 127.29, 126.85 (d, $J_{C\text{-}F}$ = 2.0 Hz, C-SCF_3, it should be quartet, but only doublet was observed.), 125.94, 123.49. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -39.80. HRMS (ESI) m/z: Calcd for $C_{20}H_{12}F_3NS$: 356.0715 $[M+H]^+$, Found: 356.0718.

6-methyl-4-phenyl-2-((trifluoromethyl)thio)quinoline (5e). Yellow solid (49.8 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.06 (d, J = 8.4 Hz, 1H), 7.65 (s, 1H), 7.60 (dd, J = 8.4, 1.8 Hz, 1H), 7.57–7.52 (m, 3H), 7.51–7.46 (m, 3H), 2.47 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 149.65, 148.06 (q, $J_{C\text{-}F}$ = 2.4 Hz, C-SCF_3), 147.58, 138.01, 137.13, 132.64, 139.53 (q, $J_{C\text{-}F}$ = 306.9 Hz, SCF_3), 129.48, 129.43, 128.79, 128.71, 125.89, 124.56, 123.99 (d, $J_{C\text{-}F}$ = 2.1 Hz, C-SCF_3, it should be quartet, but only doublet was observed.), 21.87. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -39.76. HRMS (ESI) m/z: Calcd for $C_{17}H_{12}F_3NS$: 320.0715 $[M+H]^+$, Found: 320.0716.

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[1] (a) T. Furuya, A. S. Kamlet, T. Ritter, *Nature*. **2011**, *473*, 470-477. (b) O. Allemann, S. Duttwyler, P. Romanato, K. K. Baldridge, J. S. Siegel, *Science*. **2011**, *332*, 574-577. (c) J. Choi, D. Y. Wang, S. Kundu, Y. Choliy, T. J. Emge, J, K. Krogh, A. Goldman, *Science*. **2011**, *332*, 1545-1548.

[2] (a) E. Lee, A. S. Kamlet, D. C. Powers, C. N. Neumann, G. B. Boursalian, T. Furuya, D. C. Choi, J. M. Hooker, T. Ritter, *Science*. **2011**, *334*, 639-642. (b) V. Rauniyar, A. D. Lackner, G. L. Hamilton, F. D. Toste, *Science*. **2011**, *334*, 1681-1584. (c) C. Wakselman, M. Tordeux, *J. Org. Chem.* **1985**, *50*, 4047-4051.

[3] (a) V. V. Grushin, W. J. Marshall, *J. Am. Chem. Soc*. **2006**, *128*, 12644-12645. (b) K. Muller, C. Faeh, F. Diederich, *Science*. **2007**, *317*, 1881-1886. (c) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev*. **2008**, *37*, 320-330. (d) E. J. Cho, T. D. Senecal, T. Y. Kinzel, Y. Zhang, D. A. Watson, S. L. Buchwald, *Science*. **2010**, *328*, 1679-1681. (e) D. A. Nagib, D. W. C. MacMillan, *Natrue*. **2011**, *480*, 224-228. (f) F. Yang, P. Klumphu, Y.-M. Liang, *Chem. Commun*. **2014**, *50*, 936-938. (g) J. Zheng, J.-H. Lin, X.-Y. Deng, *Org. Lett.* **2015**, *17*, 532-535. (h) X.-H. Xu, K. Matsuzaki, and N. Shibata, *Chem. Rev*. **2015**, *115*, 731-764. (i) L. Zhu, L.-S. Wang, B. Li, *Chem. Commun*. **2016**, *52*, 6371-6374.

[4] (a) D. O'Hagan, *Chem. Soc. Rev*. **2008**,*37*, 308-319. (b) B. Manteau, S. Pazenok, J. P. Vors, F. R. Leroux, *J. Fluorine Chem*. **2010**, *131*, 140-158. (c) X. T. Li, Q.-S. Gu, X.-Y. Dong, X. Meng, and X.-Y. Liu, *Angew. Chem. Int. Ed*. **2018**, *57*, 7668-7672; *Angew. Chem*. **2018**, *130*, 7794 – 7798. (d) M. Mészáros, A. Székely, A. Stirling. Z. Novák, *Angew. Chem. Int. Ed*. **2018**, *57*, 6643-6647; *Angew. Chem*. **2018**, *130*, 6753 –6757.

[5] (a) A. Ferry, T. Billard, B. R. Langlois, E. Bacqué, *Angew. Chem.Int. Ed*. **2009**, *48*, 8551-8555; *Angew. Chem*. **2009**, *121*, 8703–8707. (b) C. Chen, L.-L. Chu, F.-L. Qing, *J. Am. Chem. Soc*. **2012**, *134*, 12454-12457. (c) Alazet, S.; Zimmer, L.; Billard, T. *Angew. Chem. Int. Ed*. **2013**, *52*, 10814-10817; *Angew. Chem*. **2013**, *125*, 11014–11017.

[6] (a) M. Arisawa, K. Fujimoto, S. Morinaka, and M. Yamaguchi, *J. Am. Chem. Soc*. **2005**, *127*, 12226-12227. (b) X.-S. Zhang, J.-Y. Jiao, X.-H. Zhang, B.-L. Hu, and X.-G. Zhang, *J. Org. Chem.* **2016**, *81*, 5710−5716. (c) W.-Q. Fu, T.-T. Liu, Z.-X. Fang, Y.-L. Ma, X. Zheng, W.-C. Wang, X.-J. Ni, M.-L. Hu, and T.-L. Tang, *Chem. Commun.* **2015**, *51*, 5890-5893. (d) H.-Y. Tu, B.-L. Hu, C.-L. Deng, and X.-G. Zhang, *Chem. Commun.* **2015**, *51*, 15558-15561.

[7] (a) C. Ausı´n, J. S. Kauffman, R. J. Duff, S. Shivaprasad, S. L. Beaucage, *Tetrahedron*, **2010**, *66*, 68–79. (b) C. Pooput, W. R. Dolbier, Jr, M. Médebielle, *J. Org. Chem*. **2006**, *71*, 3564-3568. (c) H. Kawai, Z. Yuan, E. Tokunaga, N. Shibata, *Org. Biomol. Chem*. **2013**, *11*, 1446-1450.

[8] C. Pooput, M. Medebielle, and W. R. Dolbier, *Org. Lett.* **2004**, *6*, 301-303.

[9] H. Yasui, T. Yamamoto, E. Tokunaga, N. Shibata, *J. Fluorine. Chem*. **2011**, *132*, 186-189.

[10] I. Kieltsch, P. Eisenberger, and Togni, *Angew. Chem. Int. Ed*. **2007**, *46*, 754-757; *Angew. Chem*. **200**7, *119*, 768–771.

[11] (a) M. Tordeux, B. R. Langlois, C. Wakselman, *J. Org. Chem.* **1989**, *54*, 2452-2453. (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.* **2011**, *108*, 14411-14415. (c) Z. Hang, Z. Li, Z.-Q. Liu, *Org. Lett*. **2014**, *16*, 3648-3651. (d) B. Yang, X.-H. Xu, F. L. Qing, *Org. Lett*. **2015**, *17*, 1906-1909. (e) C. Liu, Q. Lu, Z. Huang, *Org. Lett*. **2015**, *17*, 6034-6037. (f) L. Zhu, L.-S. Wang, B. Li, *Chem. Commun*. **2016**, *52*, 6371-6374. (g) S. Jana, A. Verma, R. Kadu, S. Kumar, *Chem. Sci.* **2017**, *8*, 6633-6644. (h) R. Martin, Y. V. Reddy, Y. Shen, *Angew. Chem. Int. Ed.* **2017**, *56*,10915-10919; *Angew. Chem*. **2017**, *129*, 11055–11059. (i) L.-L. Zhao, P.-H. Li, X.-Y. Xie, and L. Wang, *Org. Chem. Front.* **2018**, *5*, 1689-1697. (j) C. C. Xia, K. Wang, G. D. Wang, and G. Y. Duan, *Org. Biomol. Chem.* **2018**, *16*, 2214-2218.

[12] L. Li, X.-Y. Mu, W.-B. Liu, Y.-C. Wang, Z.-T. Mi, and C.-J. Li. *J. Am. Chem. Soc*. **2016**, *138*, 5809-5812.

[13] (a) Z.-J. Quan, Y. Lv, F.-Q. Jing, X.-D. Jia, C.-D. Huo, X.-C. Wang, *Adv. Synth. Catal*. **2014**, *356*, 325-332. (b) Z.-F. Yan, Z.-J. Quan, Y.-X. Da, Z. Zhang. and X.-C. Wang, *Chem. Commun.* **2014**, *50*, 13555-13558. (c) B.-X. Du, Z.-J. Quan, Y.-X. Da, Z. Zhang, X.-C. Wang. *Adv. Synth. Catal*. **2015**, *357*, 1270-1276. (d) K.-J. Wei, Z.-J. Quan, Z. Zhang, Y.-X. Da, X.-C. Wang, *Org. Biomol. Chem.* **2016**, *14*, 2395-2398. (e) T.-L. Wang, X.-J. Liu, C.-D. Huo, X.-C. Wang, and Z.-J. Quan, *Chem. Commun.* **2018**, *54*, 499-502.

[14] (a) S.-Q. Zhu, X.-H. Xu, F.-L. Qing, *Eur. J. Org. Chem*. **2014,** 4453-4456. (b) Q.-H Deng, C. Rettenmeier, H. Wadepohl, L. H. Gade, *Chem.Eur. J.* **2014**, 20, 93-97. (c) G.-Y Yin, I Kalvet, F Schoenebeck, *Angew. Chem. Int. Ed*. **2015**, 54, 6809-6813; *Angew. Chem*. **2015**, *127*, 6913-6917 (d) H.-Li, S.-Liu, Y.-Y. Huang, X.-H Xu, F.-L Qing *Chem. Commun.* **2017**, *53*, 10136-10139 (e) S. Pan, Y.-Y Huang*, X-H Xu,* F. -L Qing, *Org. Lett.* **2017**, *19*, 4624-4627. (f) S.-Pan, Y.-Y Huang, F.-L Qing*, Chem. Asian J.* **2016**, *11*, 2854-2858. (g) S. Pan, H. Li, Y.-g Huang*,* X.-H Xu, F.-L Qing, *Org. Lett.* **2017**, *19*, 3247-3250.

[15] J.-B. Li, C. A. D. Caiuby, M. W. Paixão, and C.-J. Li. *Eur. J. Org. Chem*. **2018**, 2498-2503.

[16] (a) A. A. P. Schreibmann. *Tetrahedron Letters*. **1970**, *49*, 4271-4272. (b) A. Furstner, R. Csuk, C. Rohrer, H Weidmann, *J. Chem. Soc., Perkin Trans 1*, **1988**, 1729-1734. (c) Y.-J. Bian, S.-M. Liu, J-T. Li, T-S. Li, *synth commun*. **2002**, *32*, 1169-1173.

[17] The CCDC number of **3u** is 1855199.

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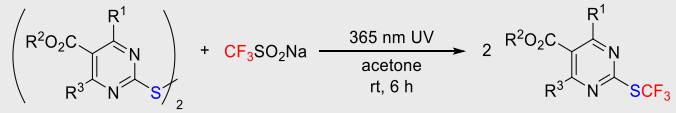

- Metal free
- Photocatalyst free
- Open to air
- Mild conditions

A trifluoromethylation of diheteroaryl disulfides with CF_3SO_2Na to afford the trifluoromethyl thioethers derivatives. The conversion has good functional group compatibility, without external photocatalyst, generating the corresponding products in moderate to good yields under mild conditions, and the disulfide is fully utilized while constructing two S-CF_3 bonds.

* Radical reactions Trifluoromethylation

Key Topic*

Bao-Qian Cao,[‡] Yi-Feng Qiu,[‡] Zheng-Jun Quan,, and Xi-Cun Wang**

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UV light irradiated trifluoromethylation of disulfides with CF_3SO_2Na