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Synthetic Methods

Copper-Catalyzed Trifluoromethylation of Internal Olefinic C–H Bonds: Efficient Routes to Trifluoromethylated Tetrasubstituted Olefins and N-Heterocycles

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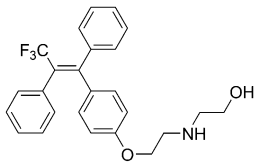
Abstract: The functionalization of internal olefins has been a challenging task in organic synthesis. Efficient Cu^{II}-catalyzed trifluoromethylation of internal olefins, that is, α-oxoketene dithioacetals, has been achieved by using $Cu(OH)_2$ as a catalyst and $TMSCF_3$ as a trifluoromethylating reagent. The push–pull effect from the polarized olefin substrates facilitates the internal olefinic C–H trifluoromethylation. Cyclic and acyclic dithioalkyl α-oxoketene acetals were used as the substrates and various substituents were tolerated. The internal olefinic C–H bond cleavage was not involved in the rate-determining step, and a mechanism that involves radicals is proposed based on a TEMPO-quenching experiment of the trifluoromethylation reaction. Further derivatization of the resultant CF_3 olefins led to multifunctionalized tetrasubstituted CF_3 olefins and trifluoromethylated N-heterocycles.

Introduction

The incorporation of a trifluoromethyl group into an organic molecule usually brings about remarkable alterations of its physical and biological properties, such as lipophilicity, metabolic stability, and conformational behaviors. Trifluoromethyl functionality is introduced into many pharmaceuticals (for example, panomifene,[1] which exhibits antiestrogenic and tumor-inhibiting activities superior to those of tamoxifen, which is widely used for the clinical treatment of breast cancer.), agrochemicals, and advanced materials.[2] Versatile methods have been developed to form C–CF_3 bonds.[3] Addition of trifluoromethylating reagents to C=O[4] and C=N[5] bonds, or olefins,[6] cross-coupling of the CF_3 reagents with prefunctionalized aromatics,[7] and other methods[8] have been applied for this purpose. Owing to the importance of the trifluoromethyl group in drug development, the synthesis of trifluoromethylated olefins has received considerable attention.

Trifluoromethylated olefins are usually prepared by reacting prefunctionalized olefins with trifluoromethylating reagents.[9] Addition of a trifluoromethylating reagent to terminal alkynes,[10] and other indirect routes,[11] can also be found to construct an olefinic C–CF_3 bond. C–H functionalization has recently been employed to realize both transition-metal-catalyzed[12] and metal-free[13] arene and heteroarene C–H trifluoromethylation. On comparison with the trifluoromethylation of (hetero)arenes,[14] the trifluoromethylation of an olefinic C–H bond is very challenging because trifluoromethylating reagents can readily react with terminal olefins to form trifluoromethylated alkanes[15] or allylic products.[6d, 8a, 16] To date, only a few reports on direct C–H trifluoromethylation of activated olefins, such as quinones[17a, b] and uracil,[17c] and terminal olefins[17d–f] have been documented. Under photocatalytic conditions, terminal olefins can also be trifluoromethylated.[17g, h] Direct C–H/C–X cross-coupling reactions between internal olefins and the usual coupling partners remains to be a challenge because of the low reactivity of the internal olefinic C–H bonds.[18, 19] However, an olefin can be tuned to become highly polarized, exhibiting enhanced reactivity by attaching both an electron-do-



panomifene[1]

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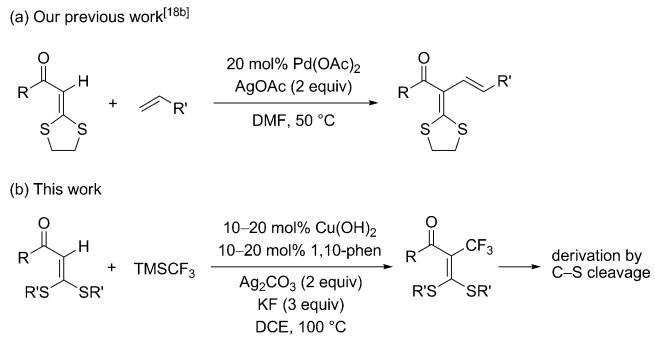


Scheme 1. Functionalization of internal olefinic C–H bonds.

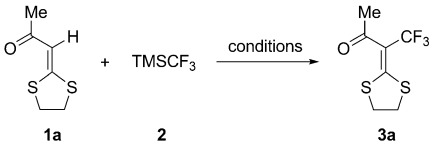
nating functionality, for example, a dithioalkyl moiety, and an electron-withdrawing moiety, such as a carbonyl group, to the two ends of the C=C bond (Scheme 1 a).[18b] Under metal-free conditions, some α-oxoketene dithioacetals were trifluoromethylated by PhI^+CF_3 species generated in situ.[20] Intrigued by the push–pull effect of the structural element in such an olefin, we envisioned that α-oxoketene dithioacetals, as internal olefins, may also be utilized as backbones to prepare multisubstituted trifluoromethylated olefins under transition-metal catalysis. Herein, we report Cu^{II}-catalyzed trifluoromethylation of α-oxoketene dithioacetals and transformation of the resultant CF_3 olefin products (Scheme 1 b).

Results and Discussion

Cu^{II}-catalyzed, Ag^{I}-mediated trifluoromethylation of α-oxoketene dithioacetals (1) with $TMSCF_3$ (2)

Although metal-free organic transformations of ketene dithioacetals have been well explored,[18c] only a few transition-metal-catalyzed reactions of these substrates are established, owing to the ease with which the dithioalkyl moiety can poison a transition-metal catalyst.[19] Thus, suitable metal catalysts and compatible reaction conditions need to be applied for the transformation of dithioacetal substrates. In our initial study, the reaction of internal olefin **1a** with Ruppert's reagent ($TMSCF_3$, **2**) was conducted to screen the reaction conditions. In the presence of CuI (10 mol%), 1,10-phenanthroline (1,10-phen, 10 mol%) as the ligand, Ag_2CO_3 (two equivalents) as the oxidant, and KF (three equivalents) as the base, in 1,2-dichloroethane (DCE) at 60 °C, the reaction afforded target product **3a** in 27% yield within 24 h (Table 1, entry 1). Elevating the temperature to 80 °C dramatically improved the reaction efficiency (Table 1, entry 2). Among the screened Cu^{I} and Cu^{II} sources, $Cu(OH)_2$ was found to provide **3a** in 96% yield (Table 1, entry 5). Without a copper catalyst, the reaction proceeded slowly (Table 1, entry 6). The bidentate ligand 1,10-phenanthroline (1,10-phen) was crucial for the reaction (Table 1, entry 7, also see the Supporting Information). KF was a suitable base to facilitate the reaction, but the strong base KO*t*Bu completely inhibited the reaction (Table 1, entries 5 and 8–11). Ag_2CO_3 behaved as the most efficient oxidant; in the absence of an oxidant the reaction did not proceed well (Table 1, entries 12–15). Increasing the temperature to 100 °C drove the reaction to completion, forming **3a** in 92% yield (Table 1, entry 16). It was noted that an air atmosphere slightly decreased the yield, and AgF and $Cu(OH)_2$ could not be solely used as the base/oxidant or catalyst/oxidant (Table 1, entries 17–19), respectively.

Table 1. Screening of reaction conditions.[a]



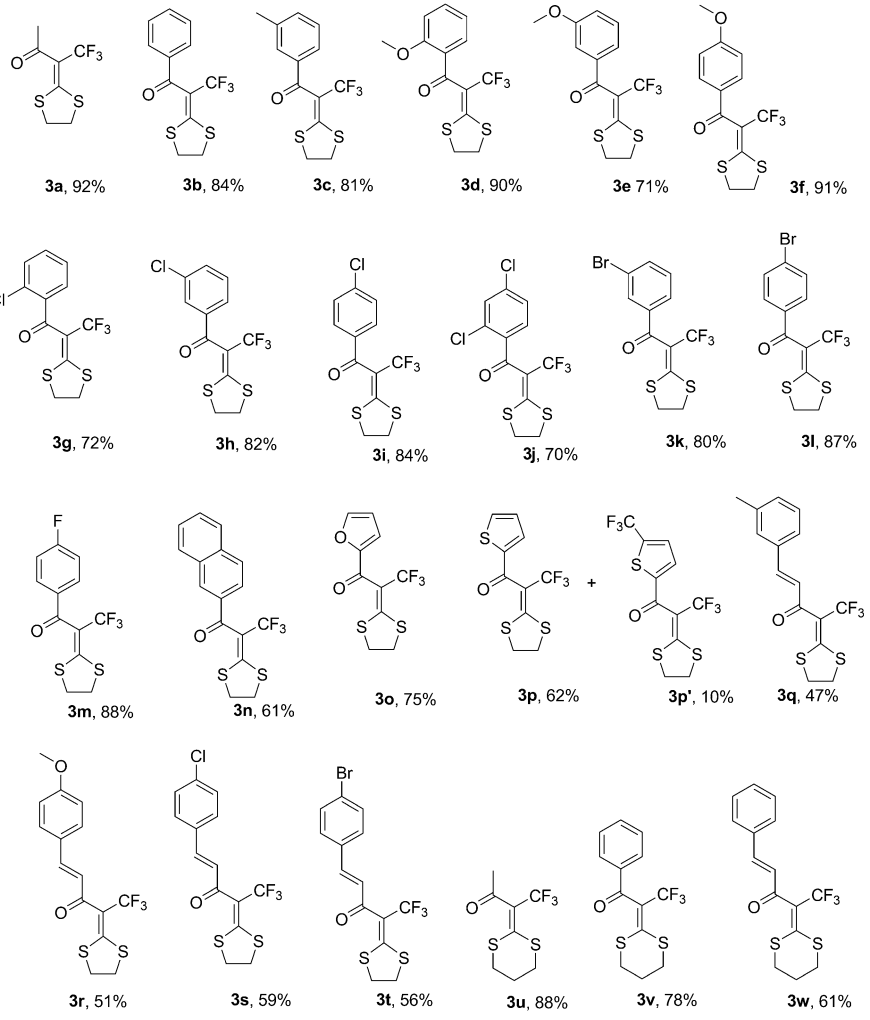
1a **2** **3a**

Entry	[Cu]	Base	Oxidant	Temperature [°C]	Yield[b] [%]
1	CuI	KF	Ag_2CO_3	60	27
2	CuI	KF	Ag_2CO_3	80	84
3	CuOAc	KF	Ag_2CO_3	80	83
4	$Cu(OAc)_2$	KF	Ag_2CO_3	80	66
5	$Cu(OH)_2$	KF	Ag_2CO_3	80	96
6	–	KF	Ag_2CO_3	80	29
7	$Cu(OH)_2$	KF	Ag_2CO_3	80	6[c]
8	$Cu(OH)_2$	CsF	Ag_2CO_3	80	3
9	$Cu(OH)_2$	K_2CO_3	Ag_2CO_3	80	54
10	$Cu(OH)_2$	NaOAc	Ag_2CO_3	80	36
11	$Cu(OH)_2$	KO*t*Bu	Ag_2CO_3	80	0
12	$Cu(OH)_2$	KF		80	4
13	$Cu(OH)_2$	KF	$PhI(OAc)_2$	80	34
14	$Cu(OH)_2$	KF	$Cu(OAc)_2$	80	3
15	$Cu(OH)_2$	KF	AgOAc	80	68
16	$Cu(OH)_2$	KF	Ag_2CO_3	100	>99 (92)[d]
17	$Cu(OH)_2$	KF	Ag_2CO_3	100	94[e]
18	$Cu(OH)_2$	–	AgF	100	21
19	$Cu(OH)_2$[f]	KF	–	100	0

[a] Conditions: **1a** (0.5 mmol), **2** (1.5 mmol), [Cu] (0.05 mmol), 1,10-phenanthroline (1,10-phen) (0.05 mmol), base (1.5 mmol), oxidant (1.0 mmol), 1,2-dichloroethane (DCE) (5 mL), 0.1 MPa Ar, 24 h. [b] Determined by GC analysis with $PhCF_3$ as an internal standard. [c] Without 1,10-phen. [d] Yield of isolated product given in parentheses. [e] In air. [f] $Cu(OH)_2$ (three equivalents).

Under the optimized conditions, the protocol generality was explored by using various cyclic α-oxoketene dithioacetals **1** (Table 2). With benzoyl ketene dithioacetals as substrates, the target trifluoromethylation products **3b**–**m** were obtained in 70–91% yields. Substituents, such as methyl, methoxy, chloro, bromo, and fluoro groups were tolerated. A larger aryl group, that is, 2-naphthyl, inhibited formation of the target product **3n** (61%) owing to the increased steric hindrance. The furoyl analogue of **1a** also reacted with **2**, forming product **3o** (75%). Unexpectedly, the 2-thienoyl substrate underwent both mono- and di-trifluoromethylation to afford target product **3p** (62%) and the di-trifluoromethylation product, **3p′** (10%). With **3p** as the reactant, on a 1.5 mmol scale, **3p′** was prepared in 67% yield [Eq. (1)]. The reactions of cinnamoyl ketene dithioacetals gave products **3q**–**t** in 47–59% yields, revealing an obvious electronic effect from the cinnamoyl functionality. By extending the dithioalkyl moiety to $-S(CH_2)_3S-$, the corresponding ketene dithioacetals also exhibited good reactivity to form the target products **3u**–**w** (61–88%). The molecular structures of **3**

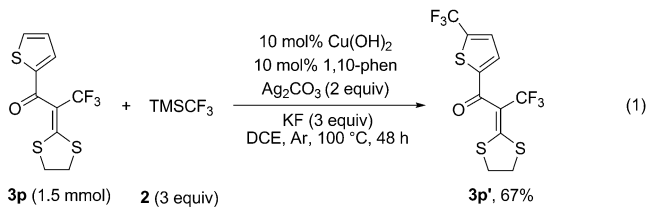
Table 2. Trifluoromethylation of cyclic α-oxoketene dithioacetals.[a,b]



[a] Conditions: **1** (1.0 mmol), **2** (3.0 mmol), $Cu(OH)_2$ (0.10 mmol), 1,10-phen (0.10 mmol), Ag_2CO_3 (2.0 mmol), KF (3.0 mmol), DCE (8 mL), 0.1 MPa Ar, 24 h. [b] Yields refer to the isolated products.

were further confirmed by the single-crystal X-ray structure determination of **3h** (Figure 1).

Next, the substrate scope was further extended to acyclic α-oxoketene dithioacetals **1′** (Table 3). The acyclic dimethylthio



(1)

analogue of **1a** reacted with **2** to afford target product **4a** in 80% yield, whereas the corresponding acyclic benzoyl substrates exhibited a lower reactivity. Thus, **4b** had to be prepared by using 20 mol% $Cu(OH)_2$ to reach 83% yield. Under similar conditions, over a period of 24–48 h, the target products **4c–j** were obtained in 62–83% yields. The acyclic diethylthio substrates also exhibited good reactivity, undergoing the Cu^{II}-catalyzed trifluoromethylation reaction to give products **4k** (82%) and **4l** (74%). Moreover, the ester ketene dithioacetal substrate underwent the reaction to afford **4m** in good yield (70%). On comparison with the recently documented metal-free electrophilic trifluoromethylation of α-oxoketene dithioacetals by PhI^+CF_3 generated in situ,[20] the present Cu^{II}-catalyzed protocol has demonstrated a much wider substrate scope and better efficiency. The molecular structure of **4j** was structurally characterized by single-crystal X-ray analysis (see the Supporting Information).

Cu^{II}-catalyzed, Ag^{I}-mediated versatile trifluoromethylation of internal olefins with $TMSCF_3$ (2)

To our delight, readily available ketene monomethylthio acetals **5**[21] underwent the same reaction to form products of type **6**, for example, **6a** (70%) and **6b** (65%), which were then conveniently transformed into tetrasubstituted CF_3 alkenes **8** by Liebeskind–Srogl cross-coupling reactions,[19,22] in good yields (74–81%; Scheme 2). This transformation suggests the potential application of the present trifluoromethylation methodology in the synthesis of multisubstituted CF_3 olefins.[1] Starting from internal olefin **9**,[21] the corresponding trifluoromethylation product **10** was also obtained in 68% yield [Eq. (2)].

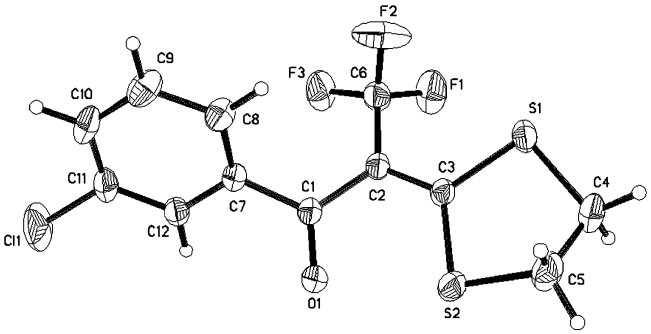
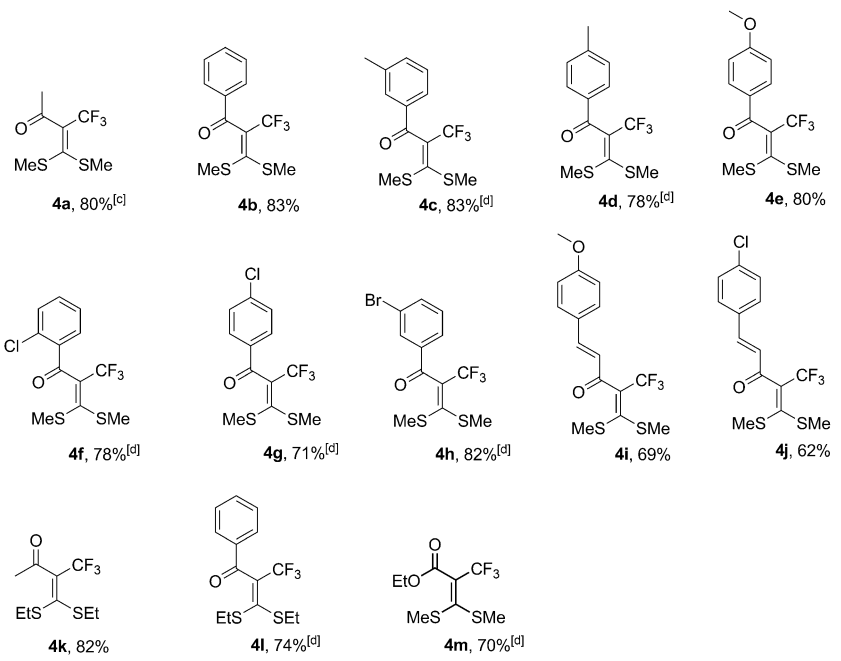
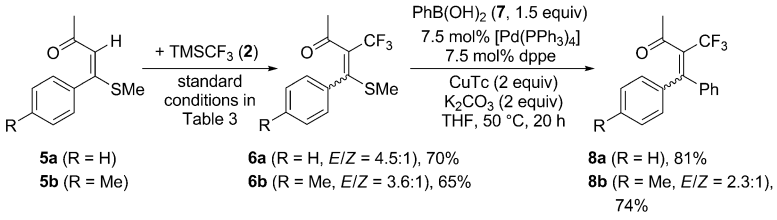


Figure 1. Molecular structure of compound **3h**.

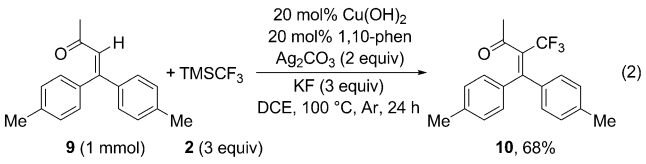
Table 3. Trifluoromethylation of acyclic α-oxoketene dithioacetals.[a,b]



[a] Conditions: **1** (1.0 mmol), **2** (3.0 mmol), $Cu(OH)_2$ (0.20 mmol), 1,10-phen (0.20 mmol), Ag_2CO_3 (2.0 mmol), KF (3.0 mmol), DCE (8 mL), 0.1 MPa Ar, 24 h. [b] Yields refer to the isolated products. [c] 10 mol% $Cu(OH)_2$ and 10 mol% 1,10-phen were used. [d] 48 h.

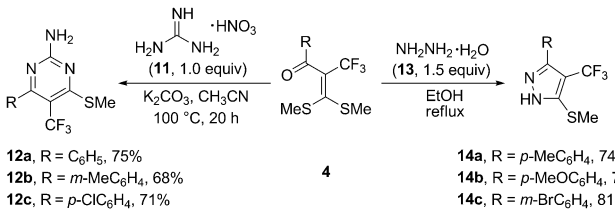


Scheme 2. Trifluoromethylation of monomethylthio acetals.



Reactions of Compound 4

Condensation of **4** with guanidine (**11**) and hydrazine (**13**) was carried out to synthesize fully substituted trifluoromethylated pyrimidines **12** (68–75%) and multifunctionalized 1*H*-pyrazoles **14** (74–81%), respectively (Scheme 3). Considering easy transformation of the SMe moiety in **12** and **14** into other functionalities,[19] the present trifluoromethylation method provides a potentially useful route to highly functionalized five- and six-membered N-heterocycles. The molecular structure of **12c** was determined by X-ray crystallographic analysis (Figure 2).



Scheme 3. Reactions of tetrasubstituted trifluoromethylated olefins.

Mechanism studies

To explore the reaction mechanism, kinetic isotope effect (KIE) experiments were performed by using deuterated benzoyl ketene dithioacetal, **1b[D]**, under the optimized conditions. No KIE ($k_H/k_D = 1.0$) was observed (Scheme 4), suggesting that cleavage of the internal olefinic C–H bond was not involved in the rate-determining step of the overall catalytic cycle.

The mechanistic details of this trifluoromethylation reaction remain unclear at the present stage, but the possibility of a radical pathway was explored. By using $TMSCF_3$, Ag_2CO_3, and KF base, CF_3 radicals from in situ generated $AgCF_3$ were found to be involved in the *ortho*-trifluoromethylation of aromatic triazenes.[7c] In our case, addition of two equivalents of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), a well-known radical scavenger, or BHT (2,6-*di*-tert-butyl-4-methylphenol), to the reaction mixture of **1a** and **2** completely inhibited formation of the target product **3a**, revealing the involvement of radical species during the reaction (Scheme 5). However, the radical-trapped adduct, TEMPO-CF_3,[6d,15b] was not detected by ^{19}F NMR analysis of the reaction mixture. Such a phenomenon was also observed by Qing et al.[23] Under the same conditions, addition of one or two equivalents of nitrobenzene, a known electron scavenger used to inhibit the single-electron-transfer (SET) reaction of perfluoroalkyl radicals,[24] had no effect on the reaction (see the Supporting Information). This finding is in agreement with the observation reported by Sanford et al. that

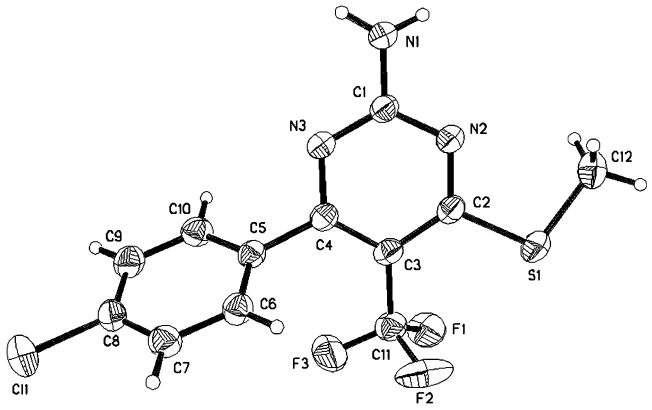
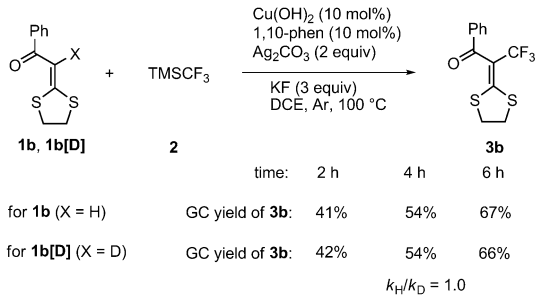
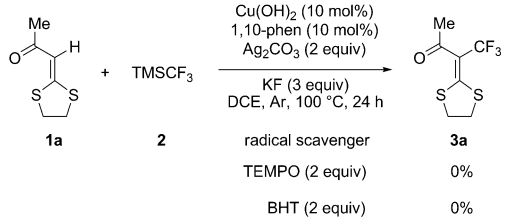


Figure 2. Molecular structure of compound **12c**.



Scheme 4. KIE experiments.

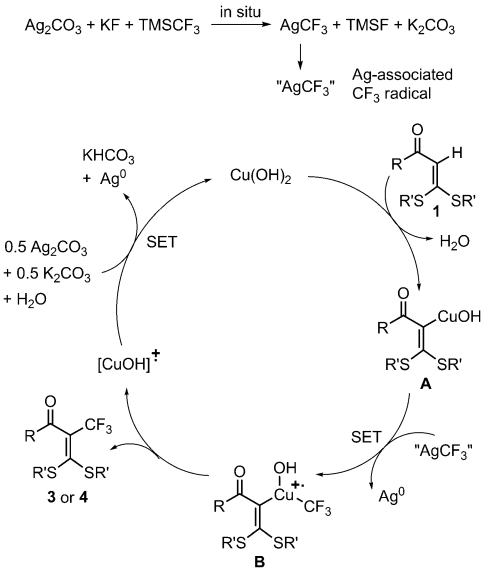


Scheme 5. Radical-trapping experiments.

caged and/or Ag-associated radicals may be involved in the AgOTf/KF-promoted reaction of benzene with $TMSCF_3$.[12f] These results suggest the absence of free $CF_3^{\bullet}$ intermediates during the reaction of **1a** with **2**. Thus, it is plausible to propose that the present trifluoromethylation reaction between **1** and **2** proceeds through a SET pathway[23,25] involving Ag-associated CF_3 radicals (Scheme 6). It is worth noting that a silver mirror was observed at the end of most of the trifluoromethylation reactions.

Conclusion

In conclusion, Cu^{II}-catalyzed trifluoromethylation of the internal olefinic C–H bond in α-oxoketene dithioacetals has been efficiently achieved by using $TMSCF_3$, Ag_2CO_3, and KF, exhibiting a wide substrate scope and substituent tolerance. Easy transformations of the monothioalkyl functionality in the resultant



Scheme 6. Proposed mechanism.

CF_3 olefins render the present synthetic methodology a potentially useful tool for the preparation of multifunctionalized tetrasubstituted CF_3olefins and trifluoromethylated N-heterocycles.

Experimental Section

General considerations

All the manipulations of air- and/or moisture-sensitive compounds were carried out under a nitrogen atmosphere by using the standard Schlenk techniques. Reaction solvents were dried and distilled prior to use by literature methods. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a Bruker DRX-400 spectrometer and all chemical shift values refer to $\delta_{TMS} = 0.00$ ppm or $CDCl_3$ ($\delta(^1H)$, 7.26 ppm; $\delta(^{13}C)$, 77.16 ppm). The HRMS analysis was achieved on a Waters GC-TOF CA156 mass spectrometer. All melting points are uncorrected. Analytical TLC plates, Sigma–Aldrich silica gel 60_{F200}, were viewed by UV light (254 nm). Chromatographic purifications were performed on SDZF silica gel 160. $FeCl_3{\cdot}6H_2O$ was purchased from Alfa Aesar Co. Known products were identified by comparison of their NMR features with the reported data of the authentic samples.

Typical procedure for the trifluoromethylation of α-oxoketene dithioacetals (1) with $TMSCF_3$ (2)

Synthesis of 3-(1,3-dithiolan-2-ylidene)-4,4,4-trifluorobutan-2-one (3a): Under an argon atmosphere, a mixture of α-oxoketene dithioacetal **1a** (160 mg, 1.0 mmol), $TMSCF_3$ (**2**) (426 mg, 3.0 mmol), $Cu(OH)_2$ (9.7 mg, 0.1 mmol), 1,10-phen (18.0 mg, 0.1 mmol), Ag_2CO_3 (547.6 mg, 2.0 mmol), and KF (174.0 mg, 3.0 mmol) in DCE (8 mL) was stirred at 100 °C for 24 h. After cooling to ambient temperature, the resulting mixture was filtered through a short pad of Celite and rinsed with CH_2Cl_2 (20 mL). The combined organic filtrate was evaporated under reduced pressure. The resultant residue was purified by silica-gel column chromato-

graphy (eluent: petroleum ether (60–90 °C)/CH_2Cl_2 = 10:1) to afford **3a** as a white crystalline solid (209.8 mg, 92%).

Typical procedure for the direct trifluoromethylation of 1′ with $TMSCF_3$ (2)

Synthesis of 4,4-bis(methylthio)-3-(trifluoromethyl)but-3-en-2-one (4a): Under an argon atmosphere, a mixture of α-oxoketene dithioacetal **1a**′ (162 mg, 1.0 mmol), $TMSCF_3$ **2** (426 mg, 3.0 mmol), $Cu(OH)_2$ (19.4 mg, 0.2 mmol), phen (36.0 mg, 0.2 mmol), KF (174.0 mg, 3.0 mmol), and Ag_2CO_3 (547.6 mg, 2.0 mmol) in DCE (8 mL) was stirred at 100 °C for 24 h. After cooling to ambient temperature, the resulting mixture was filtered through a short pad of Celite and rinsed with CH_2Cl_2 (20 mL). The combined organic filtrate was evaporated under reduced pressure. The resultant residue was purified by silica-gel column chromatography (eluent: petroleum ether (60–90 °C)/CH_2Cl_2 = 10:1) to afford **4a** as a yellow oil (184.0 mg, 80%).

Typical procedure for the direct trifluoromethylation of 5 with $TMSCF_3$ (2)

Synthesis of 4-(methylthio)-4-phenyl-3-(trifluoromethyl)but-3-en-2-one (6a): Under an argon atmosphere, a mixture of **5a** (192.0 mg, 1.0 mmol), $TMSCF_3$ (**2**) (426 mg, 3.0 mmol), $Cu(OH)_2$ (19.4 mg, 0.2 mmol), phen (36.0 mg, 0.2 mmol), KF (174.0 mg, 3.0 mmol), and Ag_2CO_3 (547.6 mg, 2.0 mmol) in DCE (8 mL) was stirred at 100 °C for 24 h. After cooling to ambient temperature, the resulting mixture was filtered through a short pad of Celite and rinsed with CH_2Cl_2 (20 mL). The combined organic filtrate was evaporated under reduced pressure. The resultant residue was purified by silica-gel column chromatography (eluent: petroleum ether (60–90 °C)/CH_2Cl_2 = 10:1) to afford **6a** as a yellow oil (182.0 mg, 70%).

Typical procedure for the arylation of 6 with phenylboronic acid (7)

Synthesis of 4,4-diphenyl-3-(trifluoromethyl)but-3-en-2-one (8a): Under a nitrogen atmosphere, a mixture of **6a** (260 mg, 1.0 mmol), phenylboronic acid (**7**) (183 mg, 1.5 mmol), $Pd(PPh_3)_4$ (86 mg, 0.075 mmol), 1,2-bis(diphenylphosphino)ethane (dppe, 30 mg, 0.075 mmol), copper(I) thiophene-2-carboxylate (CuTC, 382 mg, 2.0 mmol), and K_2CO_3 (276 mg, 2.0 mmol) in THF (10 mL) was stirred at 50 °C for 13 h. After cooling to ambient temperature, the resulting mixture was filtered through a short pad of Celite and rinsed with CH_2Cl_2 (20 mL). The combined organic filtrate was evaporated under reduced pressure. The resultant residue was purified by silica-gel column chromatography (eluent: petroleum ether (60–90 °C)/CH_2Cl_2 = 10:1) to afford **8a** as a yellow solid (235 mg, 81%).

Trifluoromethylation of 9 with $TMSCF_3$ (2)

Synthesis of 4,4-dip-tolyl-3-(trifluoromethyl)but-3-en-2-one (10): Under an argon atmosphere, a mixture of **9** (250.0 mg, 1.0 mmol), $TMSCF_3$ (**2**) (426 mg, 3.0 mmol), $Cu(OH)_2$ (19.4 mg, 0.2 mmol), phen (36.0 mg, 0.2 mmol), KF (174.0 mg, 3.0 mmol), and Ag_2CO_3 (547.6 mg, 2.0 mmol) in DCE (8 mL) was stirred at 100 °C for 24 h. After cooling to ambient temperature, the resulting mixture was filtered through a short pad of Celite and rinsed with CH_2Cl_2 (20 mL). The combined organic filtrate was evaporated under reduced pressure. The resultant residue was purified by silica-gel column chromatography (eluent: petroleum ether (60–90 °C)/CH_2Cl_2 = 10:1) to afford **10** as a yellow oil (216.3 mg, 68%).

Typical procedure for the reactions of 4 with guanidine (11)

Synthesis of 4-(methylthio)-6-phenyl-5-(trifluoromethyl)pyrimidin-2-amine (12a): A mixture of **4b** (292.0 mg, 1.0 mmol), guanidine nitrate (122 mg, 1.0 mmol), and K_2CO_3 (275.8 mg, 2 mmol) was stirred in CH_3CN (10 mL) at 100 °C for 20 h. The resultant mixture was cooled to ambient temperature and poured into ice-cold water (20 mL), and extracted with ethyl acetate (3×25 mL), dried over anhydrous Na_2SO_4, and filtered. The combined orgainc filtrate was evaporated under reduced pressure. The resulting residue was purified by silica-gel column chromatography (eluent: petroleum ether (60–90 °C)/ethyl acetate = 4:1) to afford **12a** as a white solid (213.8 mg, 75%).

Typical procedure for the reactions of 4 with hydrazine (13)

Synthesis of 5-(methylthio)-3-p-tolyl-4-(trifluoromethyl)-1H-pyrazole (14a): To a stirred solution of **4d** (306.0 mg, 1.0 mmol) in ethanol (10 mL), hydrazine hydrate (85%, 88.3 mg, 1.5 mmol) was added, and the resultant mixture was refluxed for 8 h. After the reaction was complete (monitored by TLC), the volatiles were removed under reduced pressure. The resulting residue was dissolved in chloroform (20 mL), and washed with water (2×20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The organic filtrate was evaporated under reduced pressure. The resultant residue was purified by silica-gel column chromatography (eluent: petroleum ether (60–90 °C)/ethyl acetate = 10:1) to afford **14a** as a colorless crystalline solid (201.3 mg, 74%). m.p. 128–130 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ = 11.94 (br, 1H, NH), 7.30 (d, J = 8.0 Hz, 2H, aromatic CH) and 7.21 (d, J = 8.0 Hz, 2H, aromatic CH), 2.43 (s, 3H, SCH_3), 2.39 ppm (s, 3H, $CH_3C_6H_4$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 146.5 (br), 140.2 and 125.3 (Cq), 129.5 and 128.5 (aromatic CH), 123.1 (q, J = 266 Hz, CF_3), 108.6 (q, J = 36 Hz, C–CF_3), 21.4 ($CH_3C_6H_4$), 15.6 ppm (SCH_3); ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −53.99 ppm (s, 3 F); HRMS (ESI): *m/z* calcd for $C_{12}H_{12}F_3N_2S$: 273.0673 $[M+H]^+$; found: 273.0680.

Kinetic isotope effect (KIE) experiments

The trifluoromethylation reactions of **1b** and its deuterated form, **1b[D]**, were carried out in a parallel manner under the optimized conditions. The GC yields from the reactions were carefully checked by the signal integration of the target product **3b** with *n*-dodecane as the internal standard. The k_H/k_D (0.41/0.42 = 1.0) value was calculated according to the yields of **3b** from the reactions at 2 h.

TEMPO- or BHT-trapping radical experiment

Under an argon atmosphere, a mixture of α-oxoketene dithioacetal **1a** (160 mg, 1.0 mmol), $TMSCF_3$ (**2**) (426 mg, 3.0 mmol), $Cu(OH)_2$ (9.7 mg, 0.1 mmol), phen (18.0 mg, 0.1 mmol), KF (174.0 mg, 3.0 mmol), TEMPO or BHT (2.0 mmol), and Ag_2CO_3 (547.6 mg, 2.0 mmol) in DCE (8 mL) was stirred at 100 °C for 24 h. The resultant mixture was cooled to room temperature and subject to GC analysis by using $PhCF_3$ as the internal standard. No target product **3a** was found in the reaction mixture.

Inhibition of SET reaction experiment

In a fashion similar to the radical trapping experiment, one or two equivalents of nitrobenzene, instead of TEMPO or BHT, was added to the reaction mixture. At the end of the reaction, GC analysis of the reaction mixture revealed formation of the target product **3a** in >99% yield, suggesting that inhibition of the SET reaction in the overall catalytic cycle did not occur during the trifluoromethylation reaction.

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