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J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 21 Jun 2017

Just Accepted

ACS Publications

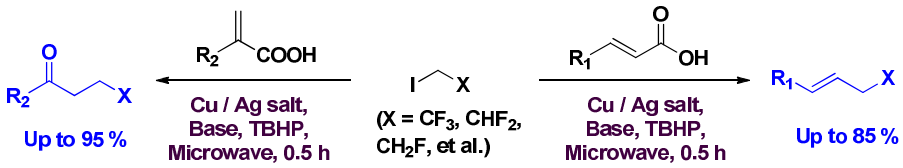
The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

A Free Radical Promoted Copper-Catalyzed Decarboxylative Alkylation of α,β-Unsaturated Carboxylic Acids with ICH_2CF_3 and its Analogues

Yan Zhu, Juwen Gong and Yonghui Wang*

School of Pharmacy, Fudan University, 826 Zhangheng Road, Pudong, Shanghai 201203, China

yonghuiwang@fudan.edu.cn

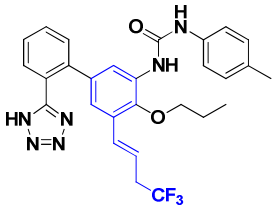


ABSTRACT: A novel and efficient free radical promoted copper-catalyzed decarboxylative alkylation of α,β-unsaturated carboxylic acids with ICH_2CF_3 and its analogues has been developed. This methodology provides with a convenient access to the synthesis of allylic trifluoromethyl and β-CF_3 ketone containing compounds as well as other biologically useful fluorinated molecules and materials.

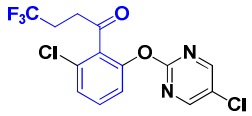
Introduction

Due to its unique properties such as high electronegativity and acting as a bioisostere of the hydrogen atom, fluorine is frequently found in some medicines and agrochemicals. About 20% of all marketed drugs, including a few blockbuster drugs, contain fluorine.[1] In particular, the trifluoromethyl group (CF_3) has attracted substantial attention in recent years and frequently found in certain pharmaceuticals and fluorocarbon-based compounds due to its unique chemical and physiological stability and lipophilicity.[2,3] For example, compound **A** (Figure 1) containing allylic trifluoromethyl moiety is a potential indoleamine 2,3-dioxygenase (IDO) inhibitor for cancer immunotherapy,[4] while compound **B** containing β-CF_3 ketone moiety is a potential herbicide which is extremely important in achieving high crop efficiency.[5] So far, tremendous progress has been acquired toward the incorporation of CF_3 groups into aromatic compounds.[6] However, direct trifluoroethylation especially for synthesizing allylic trifluoromethanes and β-CF_3 ketones using inexpensive ICH_2CF_3[7] was seldom reported.

Figure 1. Biologically active compounds containing allylic trifluoromethane and β-CF_3 ketone core structure



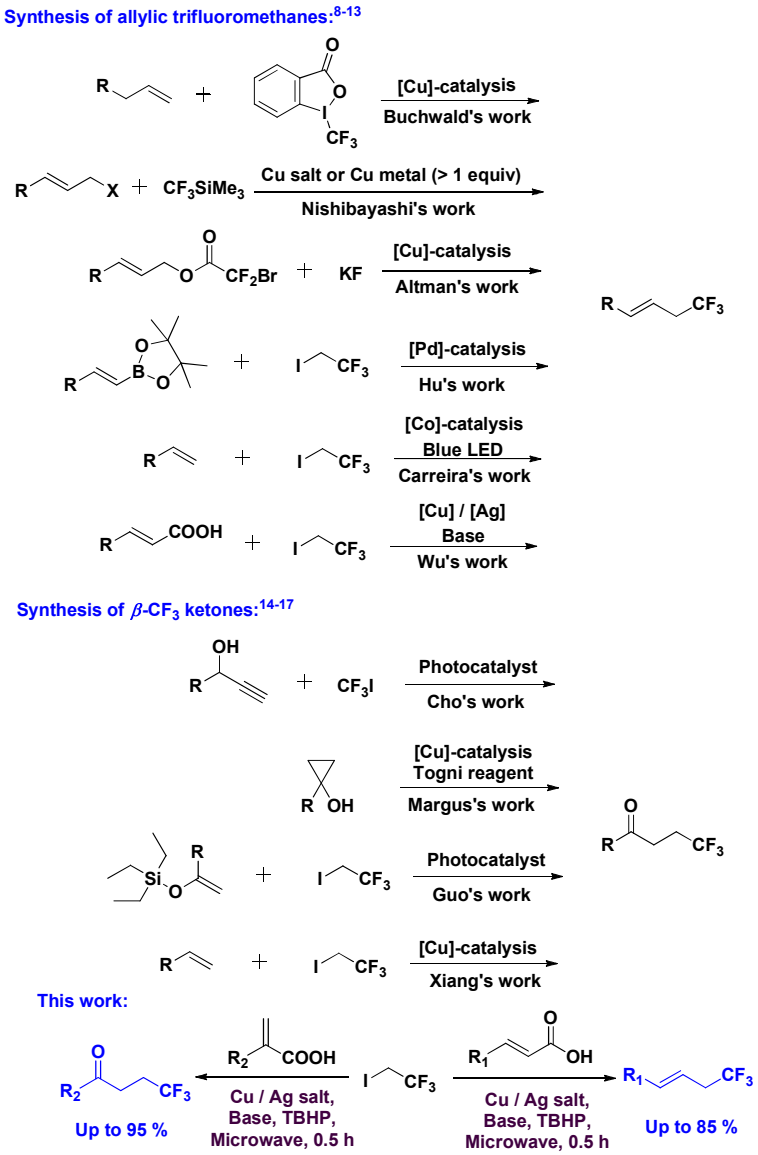
A



B

Recently, there have been some reports for synthesizing allylic trifluoromethanes using copper-catalyzed electrophilic allylic trifluoromethylation of terminal alkenes,[8] nucleophilic allylic trifluoroethylation of allylic halides,[9] and decarboxylative trifluoromethylation of allylic bromodifluoroacetate (Scheme 1).[10] In 2012, Hu and his co-workers reported palladium-catalyzed 2,2,2-trifluoroethylation of alkenyl boronic esters to synthesize allylic trifluoromethanes.[11] Later, Carreira reported the first example of cobalt-catalyzed Heck-type coupling reaction to synthesize allylic trifluoromethanes using ICH_2CF_3 in a novel photochemical flow reactor.[12] Very recently, Wu group reported a copper-catalyzed decarboxylative trifluoroethylation of cinnamic acids.[13] In 2015, Cho group reported synthesis of *β*-trifluoromethlated ketones from propargylic alcohols by visible light photoredox catalysis.[14] Later, Margus and Xu reported an access to *β*-trifluoromethyl-substituted ketones via copper-catalyzed ring-opening trifluoromethylation of substituted cyclopropanols.[15] In the same year, a method of visible-light-induced photocatalysis of 1,1,1-trifluoro-2-iodoethane with silyl enol ethers to prepare *β*-trifluoromethlated ketones was developed by Guo and his co-workers.[16] Xiang group recently reported copper/silver catalyzed oxidative coupling of vinylarenes with ICH_2CF_3 or ICH_2CHF_2, leading to *β*-CF_3/CHF_2 substituted ketones.[17] However, the reported methods of using vinylarenes and ICH_2CF_3 to synthesize allylic trifluoromethanes and *β*-trifluoromethlated ketones are still limited. We hope to develop a direct fluoroethylation method using inexpensive ICH_2CF_3 as well as its analogues such as ICH_2CHF_2, ICH_2CH_2F and $ICH_2CH_2CF_3$ to synthesize allylic trifluoromethanes, *β*-CF_3 ketones and other fluorinated compounds. We hypothesized that allylic trifluoromethanes and *β*-CF_3 ketones could be achieved by using cinnamic acids or 2-arylacrylic acids reacting with ICH_2CF_3 or its analogs through a free radical promoted process.

Scheme 1. Synthesis of allylic trifluoromethanes and *β*-CF_3 ketones

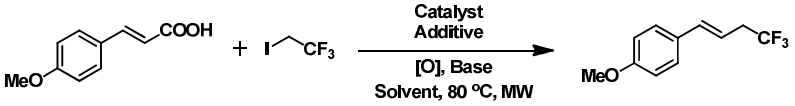


Results and Discussion

Initially, 4-methoxycinnamic acid (**1a**) and 2,2,2-trifluoroethyl iodide (**2a**) were taken as representative reactants to optimize the reaction conditions reported by Xiang.[17] As depicted in entry 1 of Table 1, only 5% yield of the desired product **3a** was obtained with the first attempt. The yield of the product **3a** rose to 29% when reaction was carried out with 20% of Ag_2SO_4 as additive (Table 1, entry 2). Further attempts in the control experiments showed that the reaction could hardly occur in absence of copper catalyst, base or oxidant (Table 1, entry 3-5). Next, different amounts of Ag_2SO_4 were examined, and the results indicated that 100% of Ag_2SO_4 was superior to the other amounts (Table 1,

entry 6-8), although the exact role of Ag_2SO_4 in promoting the reaction is not clear. However, to our great surprise and delight, explorations on the reactants ratio of **1a** and **2a** indicated that the yield of **3a** was able to be increased to 88% (85% yield) when a ratio of **1a** and **2a** being 2:1 was applied (Table 1, entry 9-13). The optimized reaction conditions (Table 1, entry 10) was then used for synthesizing allylic trifluoromethanes, *β*-trifluoromethlated ketones and other fluorinated compounds.

Table 1. Screening of the reaction conditions[a]



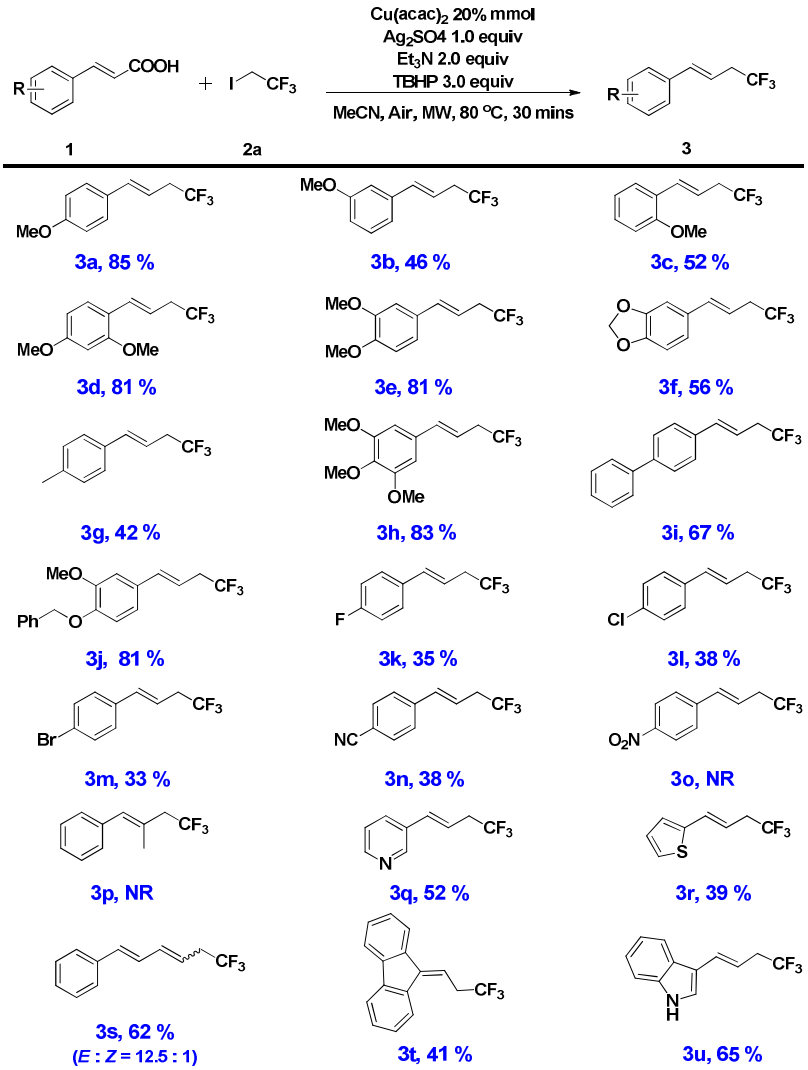
1a **2a** **3a**

Entry	Catalyst (mol%)	Additive (mol%)	Base/ Oxidant	Ratio (**1a** : **2a**)	Yield (%)[b]
1	$Cu(acac)_2$ (20)	-	Et_3N/ TBHP	1.25 : 1	5
2	$Cu(acac)_2$ (20)	Ag_2SO_4 (20)	Et_3N/ TBHP	1.25 : 1	29
3	-	Ag_2SO_4 (20)	Et_3N/ TBHP	1.25 : 1	trace
4	$Cu(acac)_2$ (20)	Ag_2SO_4 (20)	TBHP	1.25 : 1	NR
5	$Cu(acac)_2$ (20)	Ag_2SO_4 (20)	Et_3N	1.25 : 1	NR
6	$Cu(acac)_2$ (20)	Ag_2SO_4 (50)	Et_3N/ TBHP	1.25 : 1	38
7	$Cu(acac)_2$ (20)	Ag_2SO_4 (100)	Et_3N/ TBHP	1.25 : 1	47
8	$Cu(acac)_2$ (20)	Ag_2SO_4 (200)	Et_3N/ TBHP	1.25 : 1	43
9	$Cu(acac)_2$ (20)	Ag_2SO_4 (100)	Et_3N/ TBHP	1.5 : 1	64
10	**$Cu(acac)_2$ (20)**	**Ag_2SO_4 (100)**	**Et_3N/ TBHP**	**2 : 1**	**88 (85[c])**
11	$Cu(acac)_2$ (20)	Ag_2SO_4 (100)	Et_3N/ TBHP	2.5 : 1	60
12	$Cu(acac)_2$ (20)	Ag_2SO_4 (100)	Et_3N/ TBHP	1 : 2	51
13	$Cu(acac)_2$ (20)	Ag_2SO_4 (100)	Et_3N/ TBHP	1 : 3	30

[a] Reaction conditions: **1a**, **2a**, catalyst, additive, Et_3N (0.8 mmol), TBHP (1.2 mmol, 70% in water), CH_3CN, microwave, 80 °C, 30 mins, air; [b] HPLC yield; [c] Yield based on ICH_2CF_3

With the optimized reaction conditions, a wide range of acrylic acids bearing either electron-donating or electron-withdrawing groups were subjected to the reactions with 2,2,2-trifluoroethyl iodide, as summarized in Table 2. The presence of electron-donating groups such as methoxy groups on the aromatic ring was found to be beneficial to the reaction and the formation of allylic trifluoromethanes **3** was in moderate to good yields (Table 2, **3b-j**). For the electron-withdrawing substituents such as flouro-(**3k**), chloro-(**3l**), bromo-(**3m**), cyano-(**3n**) on the para position of the aromatic ring, allylic trifluoromethanes were produced only in moderate yields. However, when *p*-nitrocinnamic acid with strong electron-withdrawing group was used, the reaction could hardly occur (Table 2, **3o**). It is noteworthy that α-methylcinnamic acid could not produce the desired product possibly due to a steric effect of the methyl group in α-position (Table 2, **3p**). Furthermore, heteroaryl-substituted acrylic acids were amenable to this reaction (Table 2, **3q** and **3r**). To our delight, 9-fluorenylideneacetic acid and (2*E*, 4*E*)-5-phenylpenta-2,4-dienoic acid could also gave the corresponding products in 62% (*E*:*Z* = 12.5:1) and 41% yields, respectively (Table 2, **3s** and **3t**). Most notably, indole moiety was found to be well tolerated in this type of reaction without any protection (Table 2, **3u**).

Table 2. Substrate scope for the reaction of cinnamic acids with ICH_2CF_3[a, b]

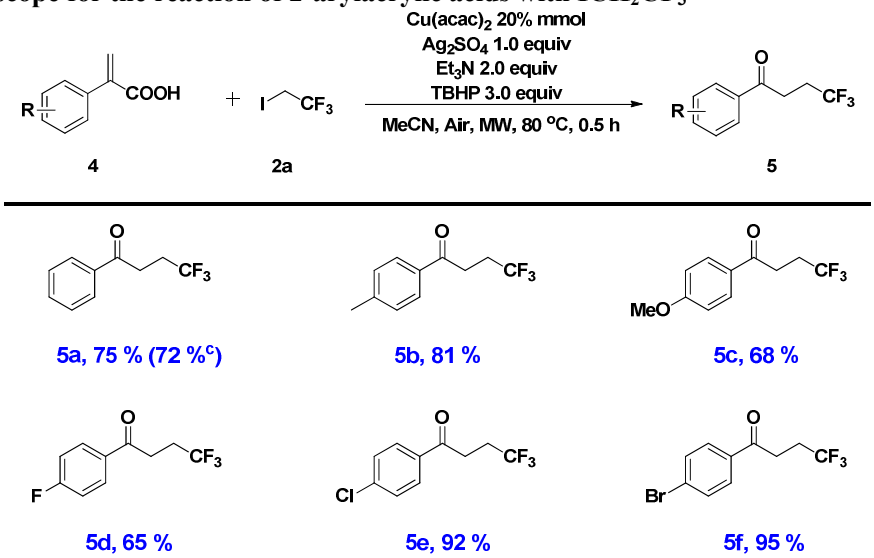


[a] Reaction conditions: **1** (0.8 mmol), **2a** (0.4 mmol), $Cu(acac)_2$ (0.08 mmol), Ag_2SO_4 (0.4 mmol), Et_3N (0.8 mmol), TBHP (1.2 mmol, 70% in water), CH_3CN, microwave, 80 °C, 30 mins, air; [b] Yield based on ICH_2CF_3

With the promising results obtained in our studies on cinnamic acids, we continued our efforts toward exploring the reactivity of various 2-arylacrylic acids with ICH_2CF_3 under the same optimized conditions (Table 3). It was shown that 2-arylacrylic acids with either electron-donating or electron-withdrawing groups were all well-tolerated in the reaction. The desired β-CF_3 ketones (Table 3. **5a-5c**) were isolated in yields of 68-81% with the electron-donating methyl or methoxy groups. For electron-withdrawing groups such as F, Cl and Br on the aromatic ring, moderate to excellent yields of the corresponding β-CF_3 ketones were obtained under the optimized conditions. (Table 3. **5d-5f**) Noting that 2-phenylacrylic acid gave rise to the corresponding β-CF_3 ketone in 72% yield under argon atmosphere (Table 3, **5a**[c]) which ruled out the possibility that the oxygen gas of air donating the oxygen atom to generate the

ketone.

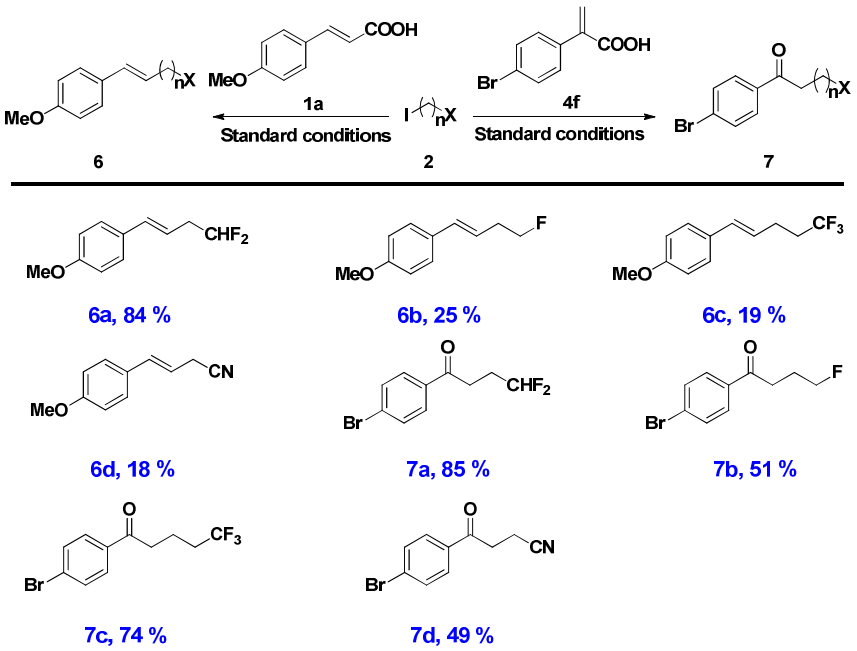
Table 3. Substrate scope for the reaction of 2-arylacrylic acids with ICH_2CF_3[a, b]



[a] Reaction conditions: **4** (0.8 mmol), **2a** (0.4 mmol), $Cu(acac)_2$ (0.08 mmol), Ag_2SO_4 (0.4 mmol), Et_3N (0.8 mmol), TBHP (1.2 mmol, 70% in water), CH_3CN, microwave, 80 °C, 30 mins, air.; [b] Yield based on ICH_2CF_3; [c] In Ar

Encouraged by the results of reactions using 2,2,2-trifluoroethyl iodide, the decarboxylative alkenylation strategy was subsequently applied to a variety of other fluorinated reagents. Like 2,2,2-trifluoroethyl iodide, 1,1-difluoro- 2-iodoethane performed well to give the corresponding allylic difluoromethane in 84% yield (Table 4, **6a**). When 1-fluoro-2- iodoethane, 1,1,1-trifluoro-3-iodopropane and 2-iodoacetonitrile were employed as substrates to react with **1a**, lower yields of the corresponding products were obtained (Table 4, **6b**, **6c** and **6d**). Gratefully, *β*-CHF_2 ketone, *γ*-F ketone, *γ*-CF_3 ketone and *β*-CN ketone core structures could be easily obtained under the optimized conditions (Table 4, **7a**-**7d**).

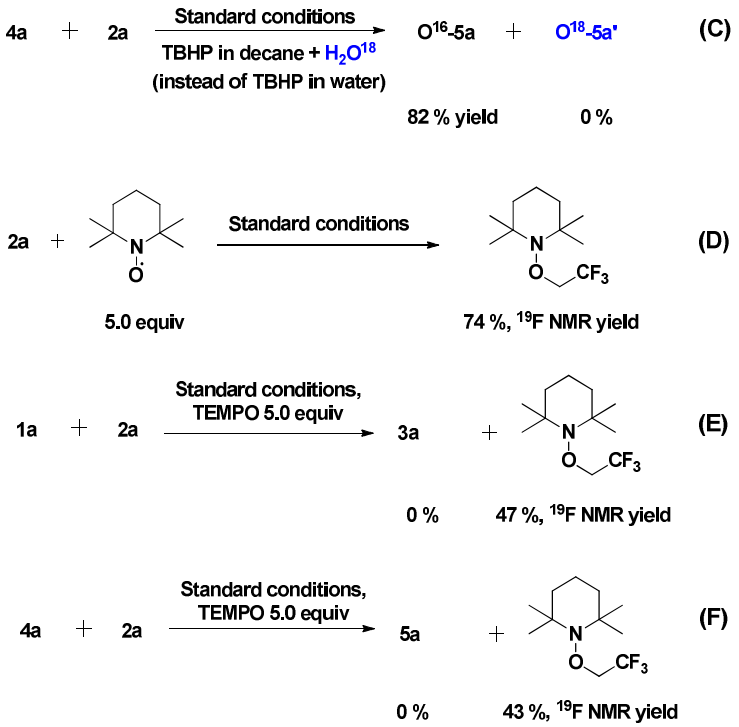
Table 4. Substrate scope for the reactions of *α, β*-unsaturated acids with analogues of ICH_2CF_3 [a, b]



[a] Reaction conditions: **1a** or **4f** (0.8 mmol), **2** (0.4 mmol), $Cu(acac)_2$ (0.08 mmol), Ag_2SO_4 (0.4 mmol), Et_3N (0.8 mmol), TBHP (1.2 mmol, 70% in water), CH_3CN, microwave, 80 °C, 30 mins, air; [b] Yield based on **2**

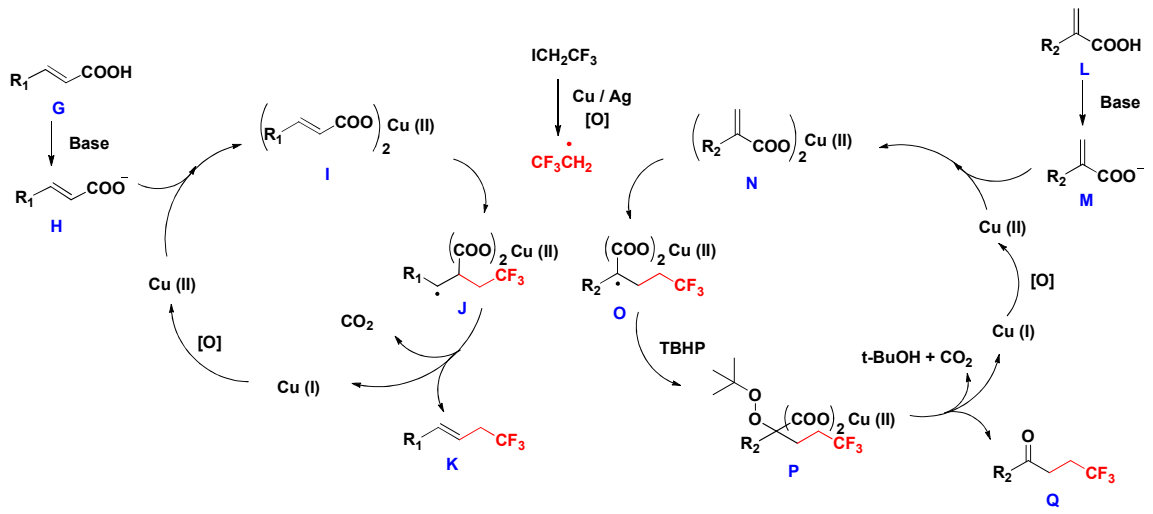
To study the reaction mechanism, some experiments were designed and performed. Firstly, isotope labelling experiment (TBHP in decane and H_2O^{18}, instead of TBHP in water) was performed, and the product **5a** was detected by HRMS and then isolated in 82% yield. No isotope product **O^{18}-5a'** was identified (Scheme 2, **C**). This indicates that the oxygen atom in product **5a** was not originally from water. Then the reaction of ICH_2CF_3 and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was attempted under the optimized conditions, and the expected product TEMPO-CH_2CF_3 was detected by HRMS, and the yield was 74% based on ^{19}F NMR data (Scheme 2, **D**). When TEMPO was added to the reaction of 4-methoxycinnamic acid with ICH_2CF_3 or 2-arylacrylic acid with ICH_2CF_3 under the optimized conditions, the corresponding products **3a** and **5a** were not detected by LC-MS and ^{19}F NMR, but TEMPO−CH_2CF_3 were formed in 47% and 43% yield, respectively (Scheme 2, **E** and **F**). These experimental results indicated that the reaction proceeded through a free radical process.

Scheme 2. Mechanism study



A proposed mechanism based on the literature precedent and experimental data is shown in Scheme 3. Initially, reaction of cinnamic acid with copper catalyst would produce a salt of Cu (II) carboxylate (**I**) in the presence of base and TBHP. A free radical $\cdot CH_2CF_3$ was generated under copper/silver catalyst and TBHP. Addition of $\cdot CH_2CF_3$ to the α-position of double bond in cupric cinnamate gave radical **J**. An elimination of Cu (I) carbon dioxide then occurred, generating product **K**.[18] Oxidation of Cu (I) by the oxidant in the presence of cinnamic acid would regenerate the cupric cinnamate. However, there is also a possibility that the decarboxylation occurred first and then α–CF_3 alkylcopper species formed.[19] Similarly, radical **N** was generated after addition of $\cdot CH_2CF_3$ to Cu (II) carboxylate (**N**), which then combined with *t*BuOO $\cdot$ to afford intermediate **P**. Finally **P**was converted into product β-CF_3 ketone in the presence of base by releasing Cu (I), carbon dioxide and one molecule of *tert*-butanol.[20]

Scheme 3. Proposed mechanism



Conclusions

In conclusion, we have developed a simple approach to the synthesis of allylic trifluoromethyl and β-CF_3 ketone compounds by a free radical promoted copper-catalyzed decarboxylative alkylation. This strategy provides an efficient and convenient access to the synthesis of fluorinated biologically active molecules and materials. Further investigations toward detailed mechanistic studies and synthetic applications are currently underway.

Experimental Section

General Information: All commercially available reagents were used without further purification unless otherwise stated. All of the microwave-assisted reactions were performed in an Initiator microwave system at the specified temperature which was monitored by external surface sensor using the standard mode of operation. The reactions were monitored by thin-layer chromatography (TLC analysis. Silica gel (200-300 mesh) was used for column chromatography. High-resolution MS (HRMS) were recorded on a commercial apparatus; the ion source is electrospray ionization (ESI). ^{1}H, ^{19}F NMR spectra were recorded on 400 MHz instrument and ^{13}C NMR spectra was recorded on 600 MHz instrument. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of $CDCl_3$ (7.26 ppm). Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in hertz (Hz), and integration. Chemical shifts of ^{13}C NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77.0 ppm) on the δ scale.

General procedure for the synthesis of arylacrylic acids [21]

Typical procedure (i): HCHO solution 37% (28 mmol, 2.8 equiv, 2.27 g), nBu$_4$NI (0.5 mmol, 0.05 equiv, 184.7 mg), and K_2CO_3 (30 mmol, 3 equiv, 4.15 g) were added to a solution of methyl 2-arylacetate (10 mmol, 1 equiv) in toluene (13 mL) at room temperature. The resulting mixture was stirred for 12 h at 50 °C. After cooling to room temperature, water (10 mL) was added and the aqueous phase was extracted with ethyl acetate (3x20 mL). The collected organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the corresponding methylene ester, which was purified by flash chromatography. (ii) An aqueous solution of 1 N sodium hydroxide (10 mL) was added to different ethyl acrylate (5 mmol), and then the reaction mixture was refluxed for 1 h. After cooling down to room temperature, the resulting mixture was extracted with diethyl ether three times (3x20 mL). The aqueous layer was then acidified with 3N aqueous HCl solutions (pH < 1.0 by litmus paper test), and extracted with ethyl ether (3x20 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated. The crude acrylic acids were separated on a silica gel column with petroleum ether (60-90 °C), ethyl acetate and HOAc (5‰) as eluent to afford the desired product (For detailed structure information please see Supporting Information Scheme S1 on page S2).

General procedure for the synthesis of 3, 5, 6 and 7. To a sealed microwave reaction vial were added acrylic acid (0.8 mmol), ICH_2CF_3 (0.4 mmol, 84.0 mg), $Cu(acac)_2$ (0.08 mmol, 20.9 mg), Ag_2SO_4 (0.4 mmol, 124.5 mg), Et_3N (0.8 mmol, 81.6 mg), TBHP (1.2 mmol, 154.4 mg, 70% in water) and MeCN (2 mL). Then the reaction mixture was stirred at 80 °C for 30 minutes in microwave reactor. After completion of the reaction, the resulting mixture was diluted with ethyl acetate (EA) and washed with water. The separated aqueous phase was washed with EA. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuo. The crude mixture was purified by column chromatography on silica gel (petroleum: ethyl acetate = 20:1~9:1) to afford the desired product **3a-3u**.

To a sealed microwave reaction vial were added 2-arylacrylic acid (0.8 mmol), ICH_2CF_3 (0.4 mmol, 84.0 mg), $Cu(acac)_2$ (0.08 mmol, 20.9 mg), Ag_2SO_4 (0.4 mmol, 124.5 mg), Et_3N (0.8 mmol, 81.6 mg), TBHP (1.2 mmol, 154.4 mg, 70% in water) and MeCN (2 mL). Then the reaction mixture was stirred at 80 °C for 30 minutes in microwave reactor. After completion of the reaction, the resulting mixture was diluted with ethyl acetate (EA) and washed with water. The separated aqueous phase was washed with EA. The combined organic layers were dried over $MgSO_4$,

filtered, and concentrated under vacuo. The crude mixture was purified by column chromatography on silica gel (petroleum: ethyl acetate = 10:1~5:1) to afford the desired product **5a-5f**.

To a sealed microwave reaction vial were added (*E*)-3-(4-methoxyphenyl)acrylic acid (0.8 mmol, 142.5 mg), **2** (0.4 mmol), $Cu(acac)_2$ (0.08 mmol, 20.9 mg), Ag_2SO_4 (0.4 mmol, 124.5 mg), Et_3N (0.8 mmol, 81.6 mg), TBHP (1.2 mmol, 154.4 mg, 70% in water) and MeCN (2 mL). Then the reaction mixture was stirred at 80 °C for 30 minutes in microwave reactor. After completion of the reaction, the resulting mixture was diluted with ethyl acetate (EA) and washed with water. The separated aqueous phase was washed with EA. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuo. The crude mixture was purified by column chromatography on silica gel (petroleum: ethyl acetate = 20:1~9:1) to afford the desired product **6a-6d**.

To a sealed microwave reaction vial were added 2-(4-bromophenyl)acrylic acid (0.8 mmol, 181.6 mg), **2** (0.4 mmol), $Cu(acac)_2$ (0.08 mmol, 20.9 mg), Ag_2SO_4 (0.4 mmol, 124.5 mg), Et_3N (0.8 mmol, 81.6 mg), TBHP (1.2 mmol, 154.4 mg, 70% in water) and MeCN (2 mL). Then the reaction mixture was stirred at 80 °C for 30 minutes in microwave reactor. After completion of the reaction, the resulting mixture was diluted with ethyl acetate (EA) and washed with water. The separated aqueous phase was washed with EA. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuo. The crude mixture was purified by column chromatography on silica gel (petroleum: ethyl acetate = 10:1~5:1) to afford the desired product **7a-7d**.

(E)-1-methoxy-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3a) [22] 73.5 mg, 85% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.57 (d, *J* = 15.8 Hz, 1H), 6.01 (dt, *J* = 14.8, 7.3 Hz, 1H), 3.83 (s, 3H), 3.06 – 2.93 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.6, 136.0, 129.0, 127.6, 126.1 (q, *J* = 276.0 Hz), 114.7, 114.0, 55.1, 37.5 (q, *J* = 29.8 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.40 (t, *J* = 10.6 Hz, 3F); MS (ESI) m/z 217.2 $[M + H]^+$.

(E)-1-methoxy-3-(4,4,4-trifluorobut-1-en-1-yl)benzene (3b) 39.8 mg, 46% yield; Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 9.5, 6.3 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.92 (s, 1H), 6.84 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.58 (d, *J* = 15.8 Hz, 1H), 6.18 – 6.04 (m, 1H), 3.82 (s, 3H), 3.06 – 2.91 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.9, 137.6, 136.6, 129.6, 125.9 (q, *J* = 274.5 Hz), 119.1, 117.5, 113.7, 111.8, 55.2, 37.6 (q, *J* = 29.9 Hz); ^{19}F {^{1}H} NMR

(376 MHz, $CDCl_3$) δ -66.19 (t, *J* = 10.7 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{12}F_3O$: 217.0835, found: 217.0836.

(E)-1-methoxy-2-(4,4,4-trifluorobut-1-en-1-yl)benzene (3c) [23] 45.0 mg, 52% yield; Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.6 Hz, 1H), 7.27 (dd, *J* = 13.2, 4.9 Hz, 1H), 7.02 – 6.93 (m, 2H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.16 (dt, *J* = 15.9, 7.2 Hz, 1H), 3.86 (s, 3H), 3.09 – 2.94 (m, 2H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 156.7, 131.6, 129.1, 128.8, 127.3, 126.0 (q, *J* = 274.5 Hz), 123.3, 120.7, 117.7, 110.9, 38.1 (q, *J* = 29.7 Hz); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -66.21 (t, *J* = 10.7 Hz, 3F); MS (ESI) m/z 217.2 $[M + H]^+$.

(E)-2,4-dimethoxy-1-(4,4,4-trifluorobut-1-en-1-yl)benzene (3d) 79.7 mg, 81% yield; Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 15.9 Hz, 1H), 6.54 – 6.42 (m, 2H), 6.03 (dt, *J* = 15.8, 7.2 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.08 – 2.90 (m, 2H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 160.8, 157.9, 131.2, 130.0, 126.1 (q, *J* = 274.5 Hz), 118.3, 115.3, 104.8, 98.4, 55.3, 55.2, 38.1 (q, *J* = 29.6 Hz); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -66.33 (t, *J* = 10.8 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{14}F_3O_2$: 247.0940, found: 247.0953.

(E)-1,2-dimethoxy-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3e) [24] 79.7 mg, 81% yield; Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, *J* = 9.5 Hz, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 15.8 Hz, 1H), 6.02 – 5.90 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.02 – 2.89 (m, 2H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 149.2, 149.0, 136.2, 129.2, 125.9 (q, *J* = 274.5 Hz), 119.7, 115.0, 111.0, 108.7, 55.8, 55.7, 37.5 (q, *J* = 29.8 Hz); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -66.76 (t, *J* = 10.7 Hz, 3F); MS (ESI) m/z 247.2 $[M + H]^+$.

(*E*)-5-(4,4,4-trifluorobut-1-en-1-yl)benzo[d][1,3]dioxole (3f) 51.5 mg, 56% yield; Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.93 (s, 1H), 6.79 (dd, *J* = 19.9, 8.0 Hz, 2H), 6.51 (d, *J* = 15.8 Hz, 1H), 5.98 – 5.90 (m, 1H), 5.96 (s, 2H), 3.03 – 2.89 (m, 2H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 148.1, 147.6, 136.2, 130. 7, 128.7, 125.9 (q, *J* = 274.5 Hz), 115.3, 108.3, 105.7, 101.1, 37.5 (q, *J* = 29.9 Hz); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -66.31 (t, *J* = 10.7 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{10}F_3O_2$: 231.0627, found: 231.0633.

(E)-1-methyl-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3g) [25] 33.4 mg, 42% yield; Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 13.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 6.60 (d, *J* = 15.8 Hz, 1H), 6.10 (dt, *J* = 14.9, 7.3 Hz, 1H), 3.10 – 2.89 (m, 2H), 2.38 (s, 3H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 138.0, 136.5, 133.5, 129.3, 126.3, 126.0 (q, *J* = 274.5 Hz), 116.1, 37.7 (q, *J* = 29.9 Hz), 21.1; ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -66.25 (t, *J* = 10.7 Hz, 3F); MS (ESI) m/z 200.1 $[M + H]^+$.

(E)-1,2,3-trimethoxy-5-(4,4,4-trifluorobut-1-en-1-yl)benzene (3h) 91.7 mg, 83% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 – 6.56 (m, 2H), 6.51 (d, *J* = 15.8 Hz, 1H), 6.08 – 5.90 (m, 1H), 3.86 (s, 6H), 3.83 (s, 3H), 3.04 – 2.89 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 153.3, 138.2, 136.5, 131.8, 125.8 (q, *J* = 274.5 Hz), 116.5, 103.5, 60.8, 56.0, 37.4 (q, *J* = 29.9 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -65.92 (t, *J* = 10.7 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_{16}F_3O_3$: 277.1046, found: 277.0973.

(E)-4-(4,4,4-trifluorobut-1-en-1-yl)-1,1'-biphenyl (3i) 70.2 mg, 67% yield; White solid, mp: 114.7-116.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 13.6, 5.0 Hz, 4H), 7.54 – 7.41 (m, 4H), 7.36 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 15.8 Hz, 1H), 6.16 (dt, *J* = 15.8, 7.3 Hz, 1H), 3.13 – 2.92 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 140.9, 140.6, 136.2, 135.2, 128.8, 128.7, 127.4, 127.3, 127.0, 125.9 (q, *J* = 283.5 Hz), 117.2, 37.7 (q, *J* = 30.0 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.15 (td, *J* = 10.6, 3.5 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{14}F_3$: 263.1042, found: 263.1049.

(E)-1-(benzyloxy)-2-methoxy-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3j) 104.4 mg, 81% yield; Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 6.98 (s, 1H), 6.93 – 6.81 (m, 2H), 6.54 (d, *J* = 15.8 Hz, 1H), 6.00 (dt, *J* = 14.8, 7.3 Hz, 1H), 5.18 (s, 2H), 3.93 (s, 3H), 3.06 – 2.89 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 149.7, 148.3, 136.9, 136.2, 129.7, 128.6, 128.5, 127.8, 125.9 (q, *J* = 274.5 Hz), 119.5, 115.2, 113.9, 109.4, 70.9, 55.9, 37.5 (q, *J* = 29.8 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.18 (t, *J* = 10.7 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{18}F_3O_2$: 323.1253, found: 323.1260.

(E)-1-fluoro-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3k) [25] 28.6 mg, 35% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 - 7.08 (m, 2 H), 6.83 (t, *J* = 8.4 Hz, 2 H), 6.37 (d, *J* = 15.8 Hz, 1 H), 5.92 – 5.75 (m, 1 H), 2.88 – 2.63 (m, 2 H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.6 (d, *J* = 247.5 Hz), 135.5, 132.4 (d, *J* = 2.7 Hz), 128.0 (d, *J* = 8.0 Hz), 125.9 (q, *J* = 274.5 Hz), 117.0, 115.6 (d, *J* = 21.7 Hz), 37.6 (q, *J* = 30.0 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.47 (t, *J* = 10.6 Hz, 3F), -113.91; MS (ESI) m/z 205.1 $[M + H]^+$.

(E)-1-chloro-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3l) [25] 33.5 mg, 38% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 4H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.10 (dt, *J* = 15.4, 7.2 Hz, 1H), 3.08 – 2.91 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 135.4, 134.7, 133.8, 128.8, 127.6, 125.8 (q, *J* = 276.0 Hz), 117.9, 37.6 (q, *J* = 30.0 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.17 (t, *J* = 10.6 Hz, 3F); MS (ESI) m/z 221.1 $[M + H]^+$.

(E)-1-bromo-4-(4,4,4-trifluorobut-1-en-1-yl)benzene (3m) [25] 35.0 mg, 33% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.18 – 6.01 (m, 1H), 3.07 – 2.84 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 135.5, 135.1, 131.8, 127.9, 125.7 (q, *J* = 274.1 5Hz), 122.0, 118.0, 37.6 (q, *J* = 30.0 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.14 (t, *J* = 10.6 Hz, 3F); MS (ESI) m/z 265.1 and 267.1 $[M + H]^+$.

(E)-4-(4,4,4-trifluorobut-1-en-1-yl)benzonitrile (3n) 32.1 mg, 38% yield; Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.18 (dt, *J* = 15.8, 7.2 Hz, 1H), 3.07 – 2.88 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 140.5, 135.0, 132.4, 126.9 125.6 (q, *J* = 274.5 Hz), 121.3, 118.7, 111.4, 37.6 (q, *J* = 30.2 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -65.96 (t, *J* = 10.5 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_9F_3N$: 212.0682, found: 212.0688.

(E)-3-(4,4,4-trifluorobut-1-en-1-yl)pyridine (3q) 38.9 mg, 52% yield; Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 37.1 Hz, 2H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.20 (s, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.21 – 6.00 (m, 1H), 3.06 – 2.83 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 149.1, 148.2, 133.2, 132.9, 131.8, 125.6 (q, *J* = 276.0 Hz), 123.5, 119.7, 37.7 (q, *J* = 30.2 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.25 (t, *J* = 10.6 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_9H_9F_3N$: 188.0682, found: 188.0695.

(E)-2-(4,4,4-trifluorobut-1-en-1-yl)thiophene (3r) 30.0 mg, 39% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 4.4 Hz, 1H), 6.98 (d, *J* = 4.6 Hz, 2H), 6.73 (d, *J* = 15.7 Hz, 1H), 5.94 (dt, *J* = 14.9, 7.3 Hz, 1H), 3.07 – 2.87 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.0, 129.6, 128.5, 127.4, 126.3,125.7 (q, *J* = 280.5 Hz), 116.6, 37.5 (q, *J* = 30.1 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.23 (t, *J* = 10.6 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_8H_8F_3S$: 193.0221, found:193.0220.

((1E, 3E)-6,6,6-trifluorohexa-1,3-dien-1-yl)benzene (3s) [23] (*E*:*Z* = 12.5:1): 52.6 mg, 62% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 14.8, 7.6 Hz, 2H), 7.31 (q, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 0.78H), 7.20 (d, *J* = 6.0 Hz, 0.16H), 6.91 (dd, *J* = 15.5, 11.2 Hz, 0.08H), 6.74 (dd, *J* = 15.7, 10.4 Hz, 0.95H), 6.63 (d, *J* = 15.5 Hz, 0.09H), 6.53 (d, *J* = 15.7 Hz, 0.94H), 6.42 – 6.30 (m, 1H), 5.67 (dt, *J* = 15.0, 7.4 Hz, 0.84H), 5.45 (q, *J* = 7.7 Hz, 0.04H), 3.14 – 2.98 (m, 0.16H), 2.96 – 2.79 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 136.9, 136.8, 135.4, 134.3, 133.5, 128.7, 128.6, 128.5, 127.8, 127.6, 126.6, 126.5, 125.9 (q, *J* = 274.5 Hz), 120.7 (q, *J* = 3.0 Hz), 37.4 (q, *J* = 29.9

Hz), 32.8 (q, J = 30.0 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -65.99 (t, J = 10.7 Hz), -66.24 (t, J = 10.6 Hz, 3F); MS (ESI) m/z 213.2 $[M + H]^+$.

9-(3,3,3-trifluoropropylidene)-9H-fluorene (3t) 42.7 mg, 41% yield; White solid; mp: 64.2-65.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.63 (m, 4H), 7.37 (dq, J = 23.5, 7.4 Hz, 4H), 6.60 (t, J = 6.9 Hz, 1H), 3.70 - 3.61 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.5, 139.8, 139.1, 138.5, 136.4, 128.9, 128.6, 127.3, 127.2, 125.9 (q, J = 273.0 Hz), 124.6, 120.2, 120.1, 119.6, 114.9, 34.3 (q, J = 30.1 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -65.92 (t, J = 10.6 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{12}F_3$: 261.0886, found: 261.0890.

(E)-3-(4,4,4-trifluorobut-1-en-1-yl)-1H-indole (3u) 58.5 mg, 65% yield; Yellow solid; mp: 91.8-93.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.84 (d, J = 7.7 Hz, 1H), 7.35 (d, J = 7.9 Hz, 1H), 7.21 (p, J = 7.1 Hz, 3H), 6.76 (d, J = 16.0 Hz, 1H), 6.20 – 5.96 (m, 1H), 3.12 – 2.88 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 136.7, 129.3, 126.2 (q, J = 274.5 Hz), 125.4, 123.7, 122.7, 120.5, 119.9, 114.4, 113.7, 111.4, 38.3 (q, J = 29.7 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.45 (t, J = 10.7 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{11}F_3N$: 226.0838, found: 226.0840.

4,4,4-trifluoro-1-phenylbutan-1-one (5a) [26] 60.6 mg, 75% yield; White solid; mp: 59.3-60.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.90 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 3.32 – 3.19 (m, 2H), 2.68 – 2.49 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 196.2, 136.1, 133.5, 129.9, 128.7, 127.2 (q, J = 273.0 Hz), 31.1 (d, J = 1.6 Hz), 28.3 (q, J = 29.7 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.85 (t, J = 10.9 Hz, 3F); MS (ESI) m/z 203.1 $[M + H]^+$.

4,4,4-trifluoro-1-(p-tolyl)butan-1-one (5b) [26] 70.0 mg, 81% yield; White solid; mp: 79.3-81.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.77 (m, 2H), 7.28 (d, J = 8.1 Hz, 2H), 3.23 (dd, J = 10.7, 4.8 Hz, 2H), 2.67 – 2.49 (m, 2H), 2.42 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 195.9, 144.5, 133.7, 129.4, 128.1, 125.4 (q, J = 274.5 Hz), 31.0, 28.4 (q, J = 29.7 Hz), 21.6; ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.42 (t, J = 12.0 Hz, 3F); MS (ESI) m/z 217.1 $[M + H]^+$.

4,4,4-trifluoro-1-(4-methoxyphenyl)butan-1-one (5c) [26] 63.1 mg, 68% yield; White solid; mp: 60.9-62.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 3.87 (s, 3H), 3.30 – 3.11 (m, 2H), 2.68 – 2.45 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 194.8, 163.8, 130.3, 129.2, 127.2 (q, J = 274.5 Hz), 113.9, 55.5, 30.8, 28.4 (q, J = 29.6 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.42 (t, J = 10.9 Hz, 3F); MS (ESI) m/z 233.1 $[M + H]^+$.

4,4,4-trifluoro-1-(4-fluorophenyl)butan-1-one (5d) [26] 57.2 mg, 65% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.91 (m, 2H), 7.15 (t, *J* = 8.6 Hz, 2H), 3.23 (dd, *J* = 9.9, 5.6 Hz, 2H), 2.68 – 2.48 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 194.7, 166.0 (d, *J* = 255.6 Hz), 132.6, 130.7 (d, *J* = 9.4 Hz), 127.1 (q, *J* = 274.5 Hz), 115.9 (d, *J* = 22.0 Hz), 31.1, 28.3 (q, *J* = 29.8 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.49 (t, *J* = 10.8 Hz, 3F), -104.29 (ddd, *J* = 13.2, 6.6, 4.3 Hz, 1F); MS (ESI) m/z 221.1 $[M + H]^+$.

1-(4-chlorophenyl)-4,4,4-trifluorobutan-1-one (5e) [26] 86.9 mg, 92% yield; White solid; mp: 66.9-68.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.4 Hz, 2H), 7.43 (d, *J* = 7.4 Hz, 2H), 3.47 – 3.07 (m, 2H), 2.73 – 2.39 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 195.0, 140.1, 134.4, 129.4, 129.1, 127.0 (q, *J* = 274.5 Hz), 31.1, 28.2 (q, *J* = 29.8 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.58 (t, *J* = 10.8 Hz, 3F); MS (ESI) m/z 237.1 $[M + H]^+$.

1-(4-bromophenyl)-4,4,4trifluorobutan-1-one (5f) [26] 106.8 mg, 95% yield; White solid; mp: 78.6-80.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 3.27 – 3.13 (m, 2H), 2.67 – 2.45 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 195.2, 134.8, 132.0, 129.4, 128.7, 127.0 (q, *J* = 273.0 Hz), 31.1, 28.2 (q, *J* = 29.8 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.44 (t, *J* = 10.8 Hz, 3F); MS (ESI) m/z 281.1 and 283.1 $[M + H]^+$.

(E)-1-(4,4-difluorobut-1-en-1-yl)-4-methoxybenzene (6a) 66.6 mg, 84% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.00 (dt, *J* = 15.7, 7.3 Hz, 1H), 5.86 (t, *J* = 4.4 Hz, 0.41H), 5.72 (t, *J* = 4.4 Hz, 0.16H), 3.82 (s, 3H), 2.84 – 2.64 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.3, 134.6, 129.5, 127.4, 117.2 (t, *J* = 238.5 Hz), 117.1 (t, *J* = 6.6 Hz), 114.0, 55.2, 38.0 (t, *J* = 21.9 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -115.53 (dtd, *J* = 56.7, 17.3, 2.4 Hz, 2F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{13}F_2O$: 199.0929, found: 199.0935.

(E)-1-(4-fluorobut-1-en-1-yl)-4-methoxybenzene (6b) 18.0 mg, 25% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.15 – 5.98 (m, 1H), 4.53 (dt, *J* = 47.2, 6.3 Hz, 2H), 3.79 (s, 3H), 2.59 (dq, *J* = 23.7, 6.5 Hz, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.9, 132.1, 129.9, 127.1, 126.2, 113.8, 83.1 (d, *J* = 167.7 Hz), 55.0, 33.9 (d, *J* = 20.5 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -217.02 (ttd, *J* = 47.4, 23.7, 2.7 Hz, 1F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{14}FO$: 181.1023, found: 181.1022.

(E)-1-methoxy-4-(5,5,5-trifluoropent-1-en-1-yl)benzene (6c) 17.5 mg, 19% yield; Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.40 (d, *J* = 15.8 Hz, 1H), 6.10 – 5.95 (m, 1H), 3.80 (s, 3H), 2.46 (dd, *J* = 15.4, 7.1 Hz, 2H), 2.33 – 2.15 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, CDCl3) δ 159.1, 131.0, 130.3,

129.8, 126.9 (q, J = 276.0 Hz), 124.5, 123.4, 114.0, 55.1, 33.7 (q, J = 28.1 Hz), 25.4; ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.27 (t, J = 10.7 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{14}F_3O$: 231.0991, found: 231.0995.

(E)-4-(4-methoxyphenyl)but-3-enenitrile (6d) [27] 12.5 mg, 18% yield; Pale yellow solid; mp: 74.9-76.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 15.8 Hz, 1H), 5.91 (dt, J = 15.8, 5.7 Hz, 1H), 3.81 (s, 3H), 3.27 (d, J = 5.7 Hz, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.7, 134.1, 128.4, 127.7, 117.5, 114.4, 114.1, 55.3, 20.7; MS (ESI) m/z 174.2 $[M + H]^+$.

1-(4-bromophenyl)-4,4-difluorobutan-1-one (7a) [26] 89.5 mg, 85% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 6.00 (tt, J = 56.9, 4.1 Hz, 1H), 3.13 (t, J = 7.2 Hz, 2H), 2.38 – 2.18 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 196.6, 135.0, 131.9, 129.4, 128.5, 116.3 (t, J = 238.7 Hz), 30.7 (t, J = 4.9 Hz), 28.2 (t, J = 21.9 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -117.13 (dt, J = 56.8, 17.8 Hz, 2F); MS (ESI) m/z 263.1 and 265.1 $[M + H]^+$.

1-(4-bromophenyl)-4-fluorobutan-1-one (7b) [28] 50.0 mg, 51% yield; Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 4.56 (dt, J = 47.2, 5.7 Hz, 2H), 3.12 (t, J = 7.1 Hz, 2H), 2.25 – 2.06 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 198.0, 135.5, 131.9, 129.5, 128.3, 83.1 (d, J = 164.7 Hz), 33.9 (d, J = 3.8 Hz), 24.7 (d, J = 20.0 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ 45.44 (tt, J = 47.7, 27.5 Hz, 1F); MS (ESI) m/z 245.1 and 247.1 $[M + H]^+$.

1-(4-bromophenyl)-5,5,5-trifluoropentan-1-one (7c) 87.0 mg, 74% yield; Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 3.04 (t, J = 6.9 Hz, 2H), 2.34 – 2.12 (m, 2H), 2.12 – 1.92 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 197.5, 135.3, 132.0, 129.4, 128.4, 127.0 (q, J = 274.5 Hz), 36.7, 32.9 (q, J = 28.7 Hz), 16.3 (d, J = 2.4 Hz); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -66.11 (t, J = 10.8 Hz, 3F); HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{11}BrF_3O$: 294.9940, found: 294.9943.

4-(4-bromophenyl)-4-oxobutanenitrile (7d) [29] 46.7 mg, 49% yield; White solid; mp: 87.1-88.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H), 3.34 (d, J = 6.7 Hz, 2H), 2.76 (d, J = 6.7 Hz, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 194.3, 134.3, 132.2, 129.4, 129.2, 119.0, 34.2, 11.7; MS (ESI) m/z 238.1 and 240.1 $[M + H]^+$.

Associated Content

Author Information

Corresponding Author

*E-mail for Y. Wang: yonghuiwang@fudan.edu.cn

Notes

The authors declare no competing financial interest.

Acknowledgments

This work was supported by Grant 81573276 from the National Science Foundation of China and Grant 15431900300 from Shanghai Bio-pharmaceutical Science and Technology Supporting Plan.

Supporting Information

Segmental experiment data, mechanism studies, ^{1}H, ^{13}C and ^{19}F NMR data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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