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

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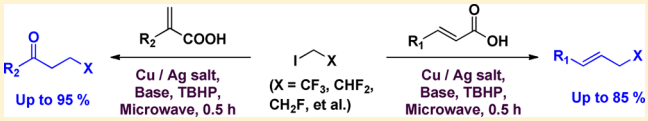
Supporting Information

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 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 ability to act 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 is 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 an allylic trifluoromethyl moiety is a potential

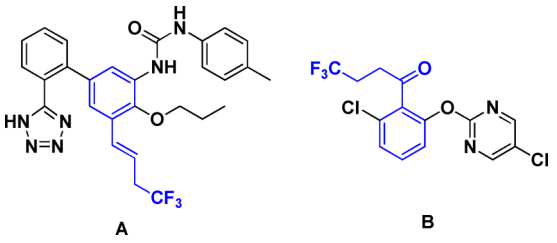


Figure 1. Biologically active compounds containing allylic trifluoromethane and β-CF_3 ketone core structure.

indoleamine 2,3-dioxygenase (IDO) inhibitor for cancer immunotherapy,[4] while compound **B** containing a 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 made 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] has seldem been reported.

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 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, the Wu group reported a copper-catalyzed decarboxylative trifluoroethylation of cinnamic acids.[13] In 2015, the Cho group reported the 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 co-workers.[16] The 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 analogues through a free-radical-promoted process.

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 the reaction was carried out with 20% of Ag_2SO_4 as the additive (Table 1, entry 2). Further attempts in the

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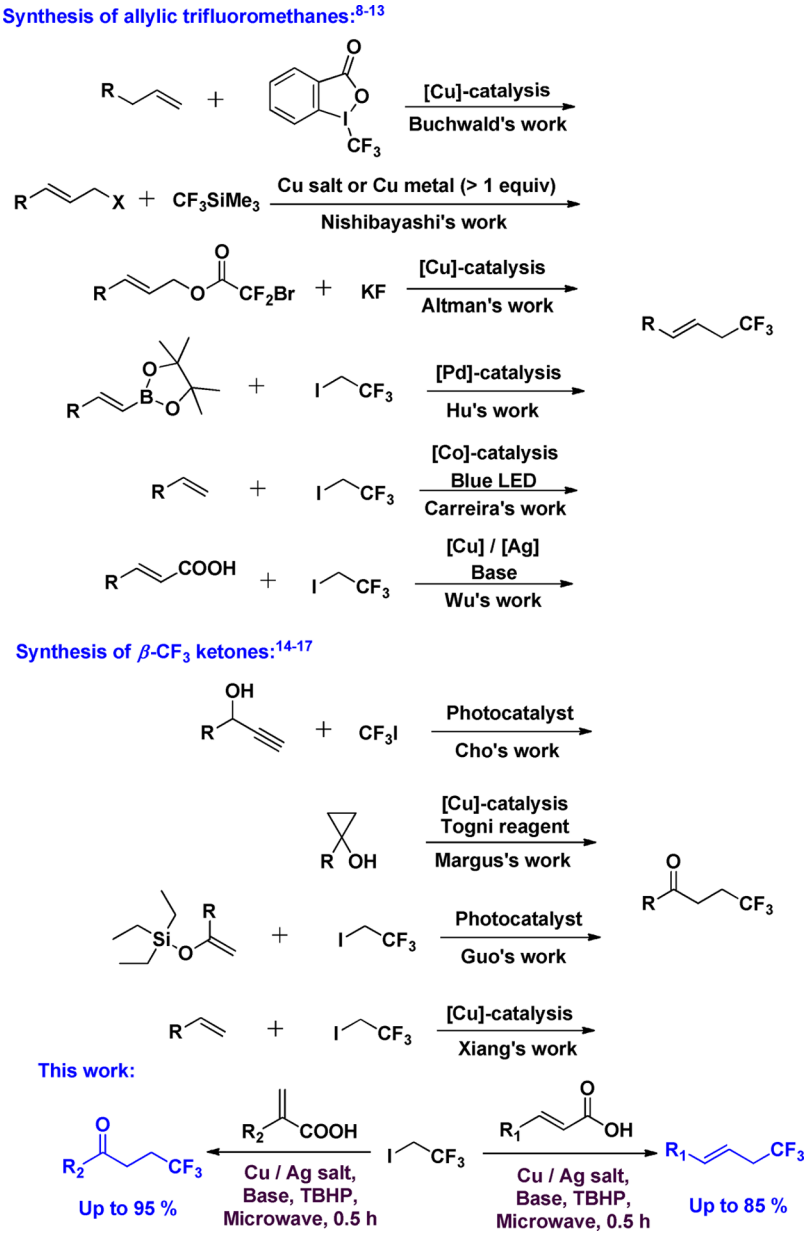
Scheme 1. Synthesis of Allylic Trifluoromethanes and β-CF_3 Ketones



control experiments showed that the reaction could hardly occur in the absence of copper catalyst, base, or oxidant (Table 1, entries 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, entries 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** of 2:1 was applied (Table 1, entries 9–13). The optimized reaction conditions (Table 1, entry 10) were then used to synthesize allylic trifluoromethanes, β-trifluoromethlated ketones, and other fluorinated compounds.

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 fluoro- (**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 a 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 give 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**).

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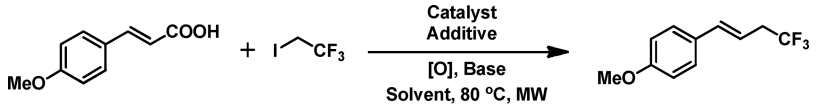
Table 1. Screening of the Reaction Conditions[a]



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 min, air. [b]HPLC yield. [c]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**−**c**) 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**−**f**). Note that 2-phenylacrylic acid gave rise to the corresponding β-CF_3 ketone in 72% yield under argon atmosphere (Table 3, **5a**), which ruled out the possibility that the oxygen gas of air donates the oxygen atom to generate the ketone.

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**−**d**).

To study the reaction mechanism, some experiments were designed and performed. First, an isotope-labeling experiment (TBHP in decane and $H_2{}^{18}O$, 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 with a yield of 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 was 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.

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 CH_2CF_3 was generated under copper/silver catalyst and TBHP. Addition of $^{\bullet}CH_2CF_3$ to the α-position of the 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 the α-CF_3 alkylcopper species formed.[19] Similarly, radical **N** was generated after addition of $^{\bullet}CH_2CF_3$ to Cu(II) carboxylate (**N**), which then combined with *t*BuOO$^{\bullet}$ 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*-butyl alcohol.[20]

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

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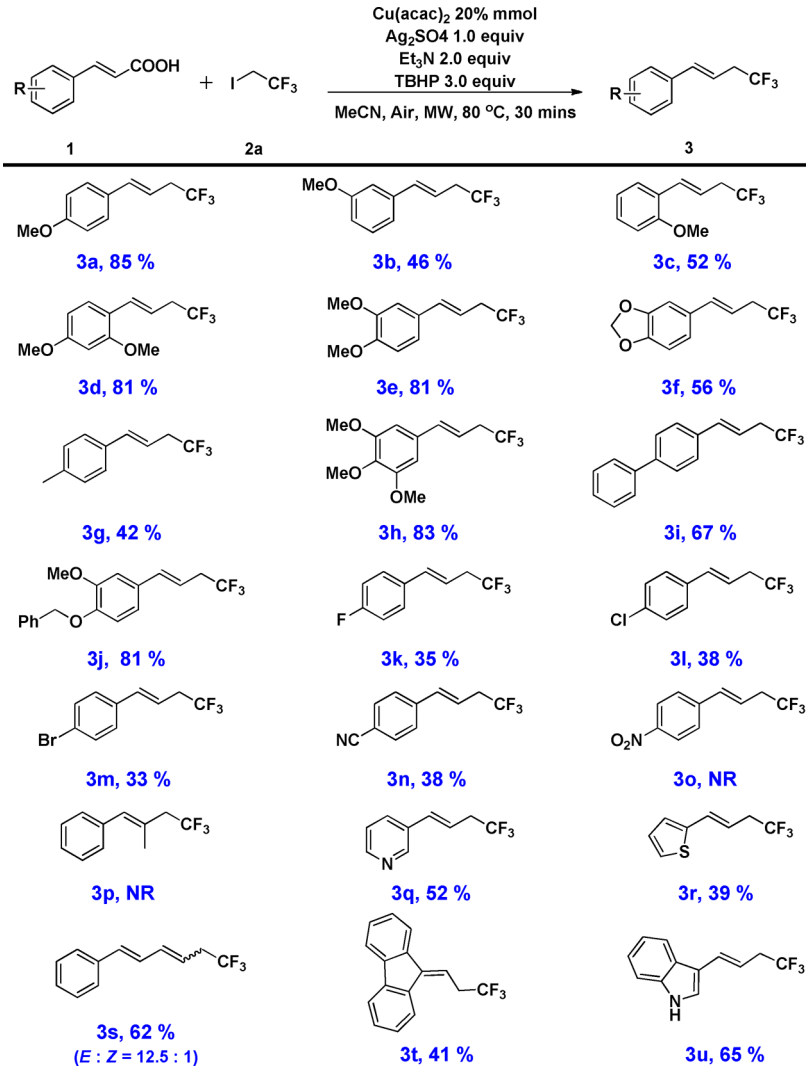
Table 2. Substrate Scope for the Reaction of Cinnamic Acids with ICH_2CF_3[a,b]



[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 min, air. [b]Yield based on ICH_2CF_3.

microwave-assisted reactions were performed in an Initiator microwave system at the specified temperature which was monitored by an 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) was recorded on a commercial apparatus; the ion source is electrospray ionization (ESI). ^1H, ^{19}F NMR spectra were recorded on a 400 MHz instrument, and ^{13}C NMR spectra were recorded on a 600 MHz instrument. Chemical shifts in ^1H 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 the mixture was cooled to room temperature, water (10 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 × 20 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 acrylates (5 mmol), and then the reaction mixture was refluxed for 1 h. After being cooled to room temperature, the resulting mixture was extracted with diethyl ether three times (3 × 20 mL). The aqueous layer was then acidified with 3 N aqueous HCl solutions (pH < 1.0 by litmus paper test) and extracted with ethyl ether (3 × 20 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, see Scheme S1).

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 min 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

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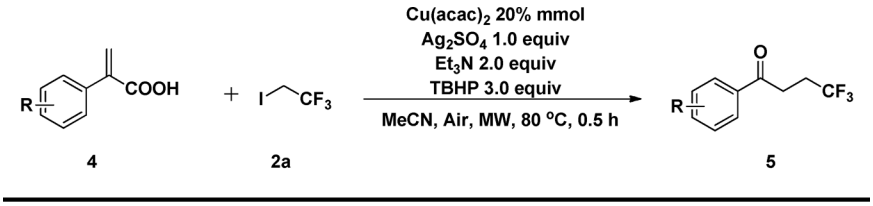
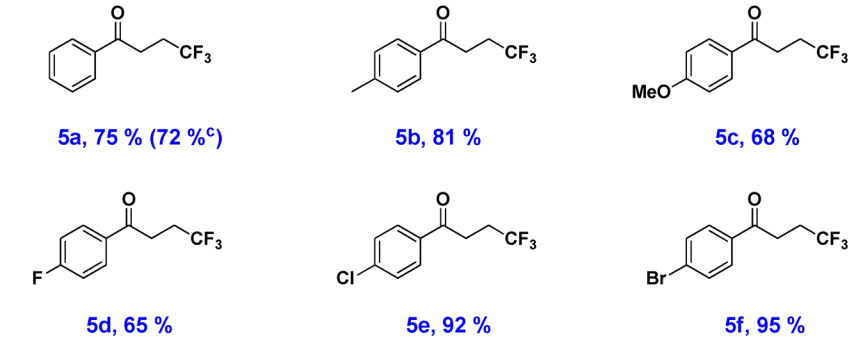
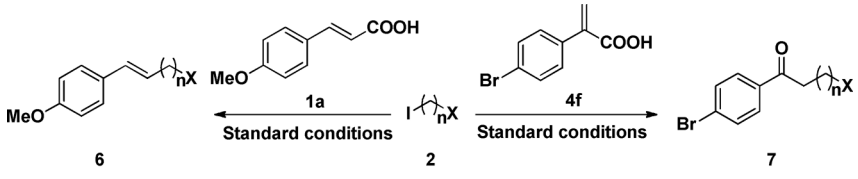
Table 3. Substrate Scope for the Reaction of 2-Arylacrylic Acids with ICH_2CF_3[a,b]

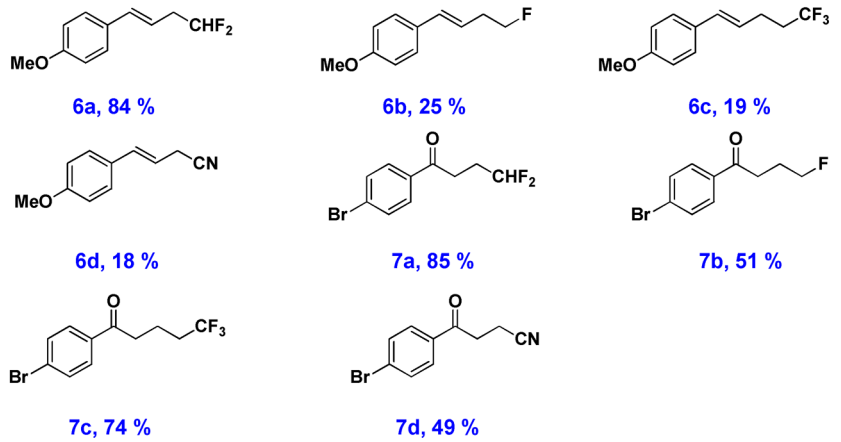




[a]Reaction conditions: **4** (0.8 mmol), **2a** (0.4 mmol), $Cu(acac)_2$ (0.08 mmol), Ag_2SO_4 (0.4 mmol), Et_3N (0.8 mmol), TBHP (1.2 mmol, 70% in water), CH_3CN, microwave, 80 °C, 30 min, air. [b]Yield based on ICH_2CF_3. [c]In Ar.

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 min, air. [b]Yield based on **2**.

mixture was purified by column chromatography on silica gel (petroleum/ethyl acetate = 20:1−9:1) to afford the desired products **3a−u**.

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 min in a 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 ether/ethyl acetate = 10:1−5:1) to afford the desired products **5a−f**.

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 min in a 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 in vacuo. The crude mixture was purified by column chromatography on silica gel (petroleum/ethyl acetate = 20:1−9:1) to afford the desired products **6a−d**.

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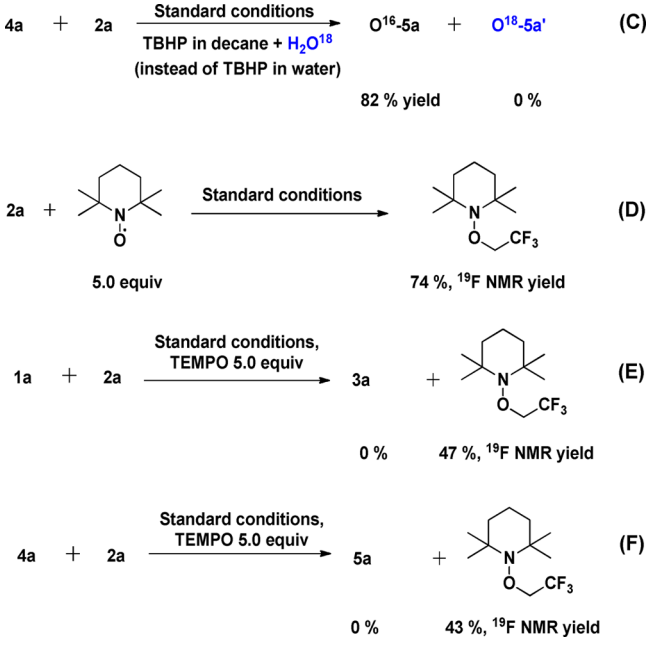
Scheme 2. Mechanism Study



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 min in a 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 products **7a−d**.

(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; ^{1}H 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 {^{1}H} 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 {^{1}H} NMR (376 MHz, $CDCl_3$) δ −66.21 (t, J = 10.7 Hz, 3F); MS (ESI) m/z 217.2 $[M + H]^+$.

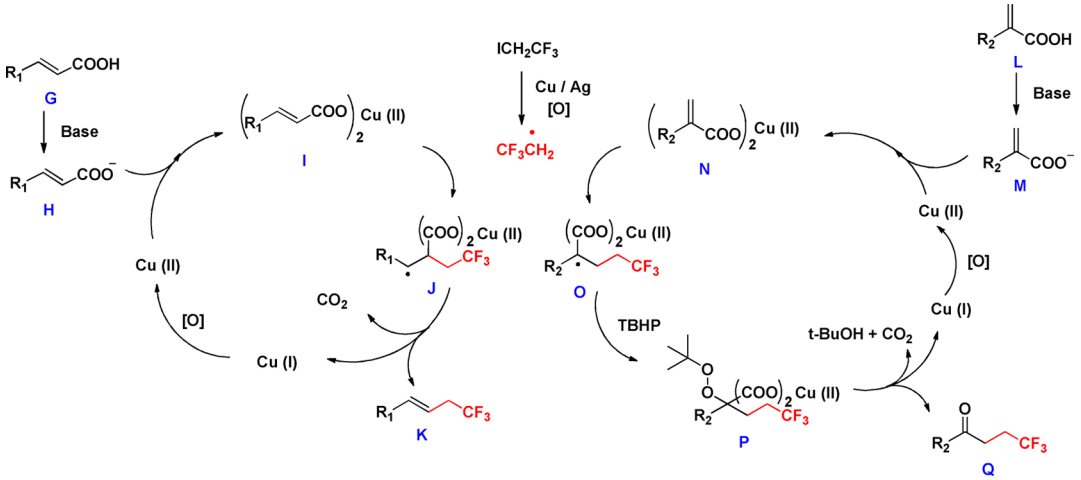
(E)-2,4-Dimethoxy-1-(4,4,4-trifluorobut-1-en-1-yl)benzene (***3d***): 79.7 mg, 81% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 15.9 Hz, 1H), 6.54−6.42 (m, 2H), 6.03 (dt, J = 15.8, 7.2 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.08−2.90 (m, 2H); ^{13}C {^{1}H} 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 {^{1}H} 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; ^{1}H 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 {^{1}H} 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 {^{1}H} 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; ^{1}H 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 {^{1}H} 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 {^{1}H} 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; ^{1}H 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 {^{1}H} 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 {^{1}H}

Scheme 3. Proposed Mechanism



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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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} NMR (150 MHz, $CDCl_3$) δ 135.5, 135.1, 131.8, 127.9, 125.7 (q, J = 274.1 5 Hz), 122.0, 118.0, 37.6 (q, J = 30.0 Hz); ^{19}F {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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 {^1H} 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; ^1H 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 {^1H} 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

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(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

Ⓢ Supporting Information

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Segmental experiment data, mechanism studies, and ^{1}H, ^{13}C, and ^{19}F NMR data for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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