JOC The Journal of Organic Chemistry
Cite This: J. Org. Chem. XXXX, XXX, XXX−XXX
Note
pubs.acs.org/joc

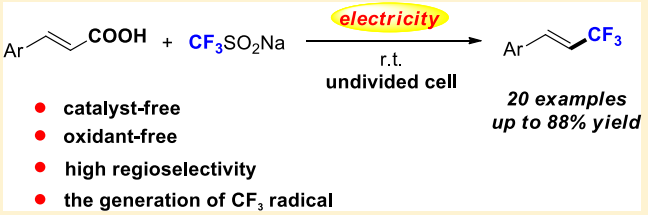
Electrochemical Synthesis Strategy for C_{vinyl}-CF_3 Compounds through Decarboxylative Trifluoromethylation

Huanliang Hong, Yibiao Li, Lu Chen, Bin Li, Zhongzhi Zhu, Xiuwen Chen, Ling Chen, and Yubing Huang*

School of Biotechnology and Health Sciences, Wuyi University, Jiangmen 529020, China

Supporting Information

ABSTRACT: An efficient decarboxylative trifluoromethylation of α,β-unsaturated carboxylic acids using the Langlois reagent as a trifluoromethyl precursor has been achieved by an electro-oxidative strategy. Under catalyst-free and external oxidant-free electrolysis conditions, a series of C_{vinyl}-CF_3 compounds are obtained with a high regioselectivity in good yields. The successful trapping of the CF_3 radical by a scavenger has confirmed that radical processes are involved in this system.



The development of efficient and sustainable trifluoromethylation reactions to introduce a CF_3 group into various organic molecules has important research value in drug development,[1] new material synthesis, and life sciences, as a CF_3 group can dramatically change molecular characteristics, such as stability, lipophilicity, bioavailability, etc.[2] C_{vinyl}-CF_3 has always been considered as an important moiety (Figure 1)

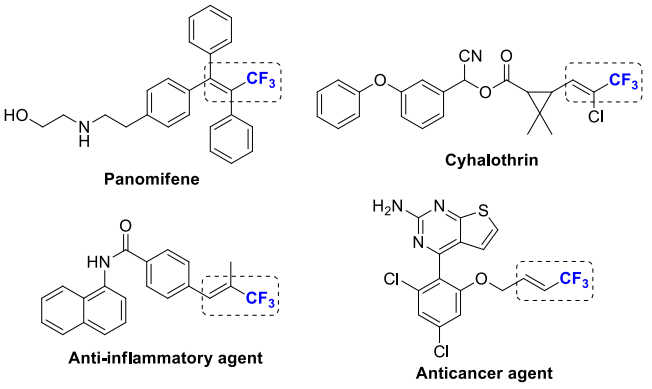
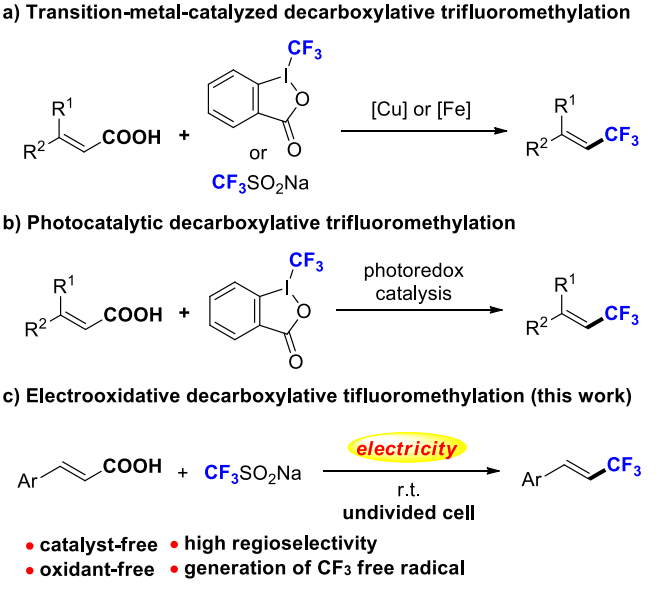


Figure 1. Drugs and agents containing a C_{vinyl}-CF_3 moiety.

in pharmaceutical reagents;[3] among them, compounds containing the C_{vinyl}-CF_3 moiety are basically non-natural and need to be constructed through a variety of organic synthesis methodologies. Some effective strategies have been reported to construct a C_{vinyl}-CF_3 moiety by using prefunctionalized olefins, such as vinyl boronic acids,[4] vinyl borates,[5] vinyl halides,[6] nitro olefins,[7] and vinyl carboxylic acids, which allow the reaction to exhibit a good reactivity and specific regioselectivity. Among them, carboxylic acids are ubiquitous compounds that are inexpensive and commercially available in large quantities,[8] Currently, α,β-unsaturated carboxylic acids have been used to synthesize C_{vinyl}-CF_3 compounds through transition-metal-catalyzed or photocatalytic decarboxylation trifluoromethylations. For example, the groups of Hu[9] and Liu[10] have shown the transition-metal-catalyzed decarboxylative trifluoromethylations of α,β-unsaturated carboxylic acids by using Togni's reagent and the cheaper Langlois reagent, respectively (Scheme 1a). Then, the group of Zhu[11] achieved a visible-light-induced decarboxylative trifluoromethylation at room temperature by using Togni's reagent as

Scheme 1. Synthesis of C_{vinyl}-CF_3 Compounds via Decarboxylative Trifluoromethylations



Received: March 18, 2019

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX−XXX

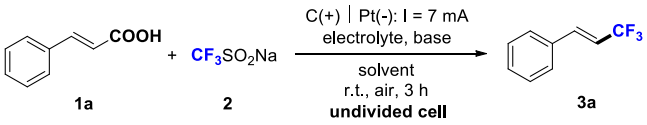
a trifluoromethyl source (Scheme 1b). In order to improve the methodology for decarboxylative trifluoromethylation, we have been seeking milder conditions without the addition of a metal catalyst to prepare C_{vinyl}-CF_3 compounds by using a cheaper trifluoromethylation reagent.

Electrochemical synthesis has emerged as an environmentally friendly synthesis tool with the prospect of avoiding the extensive use of chemical oxidants and reducing agents.[12] Electrosynthesis provides an efficient alternative to conventional chemical methods for redox transformations, through the loss or acquisition of electrons at the electrode surface to form highly reactive organic molecule intermediates, and is applied to the reactions of radicals.[13] As an easily available and inexpensive trifluoromethylation reagent, the Langlois reagent (CF_3SO_2Na), which releases a CF_3 radical by a single-electron oxidation process on the anode, has been shown to be useful as a trifluoromethyl precursor for the electro-oxidation trifluoromethylation reactions.[14] In order to develop convenient and efficient trifluoromethylation reactions using the Langlois reagent as a trifluoromethyl precursor and to further expand the synthetic application of electrochemical oxidation, herein, we propose an efficient electro-oxidative decarboxylative trifluoromethylation between α,β-unsaturated carboxylic acids and CF_3SO_2Na for the synthesis of diverse C_{vinyl}-CF_3 compounds (Scheme 1c).

Initially, we chose cinnamic acid (**1a**) as the model substrate to react with CF_3SO_2Na **2** for the optimization of conditions for electro-oxidative decarboxylative trifluoromethylation (Table 1). After different electrolytes were screened (Table 1, entries 1−5), $^nBu_4NBF_4$ was found to be suitable for the reaction under a constant current electrolysis at 7 mA in a solvent mixture DMSO/DCM (1.5:1) at room temperature, and the desired product **3a** was obtained in 59% yield (Table 1, entries 2). Subsequently, we explored the effect of solvent mixture types and found that other types of solvent mixtures would both lead to decreased reaction yields (Table 1, entries 6−8). Moreover, replacing the solvent mixture with a single solvent (DMSO) also hinders the progress of the reaction (Table 1, entry 9). A reduced yield was obtained when decreasing the amount of CF_3SO_2Na (Table 1, entry 10). We believed the addition of a base can further increase the reaction yield, so we investigated different types of bases, including organic bases and inorganic bases, and found that potassium salts are effective for this reaction. Then, we compared the effects of different potassium salts and found that the yield of **3a** reached a maximum of 76% when using 0.5 equiv of KO^tBu (Table 1, entry 12) but did not increase with the increase of the amount of KO^tBu (Table 1, entry 14). The reaction yield decreased when decreasing the constant current (Table 1, entry 15), and further, no expected product was detected when the reaction was conducted without electricity (Table 1, entry 16).

With the optimal reaction conditions in hand, we subsequently examined a series of α,β-unsaturated carboxylic acids for this electro-oxidative decarboxylative trifluoromethylation (Table 2). Both electron-rich substituents (methyl-, methoxy-, and benzyloxy-) and electron-poor substituents

Table 1. Optimization of the Reaction Conditions[a]

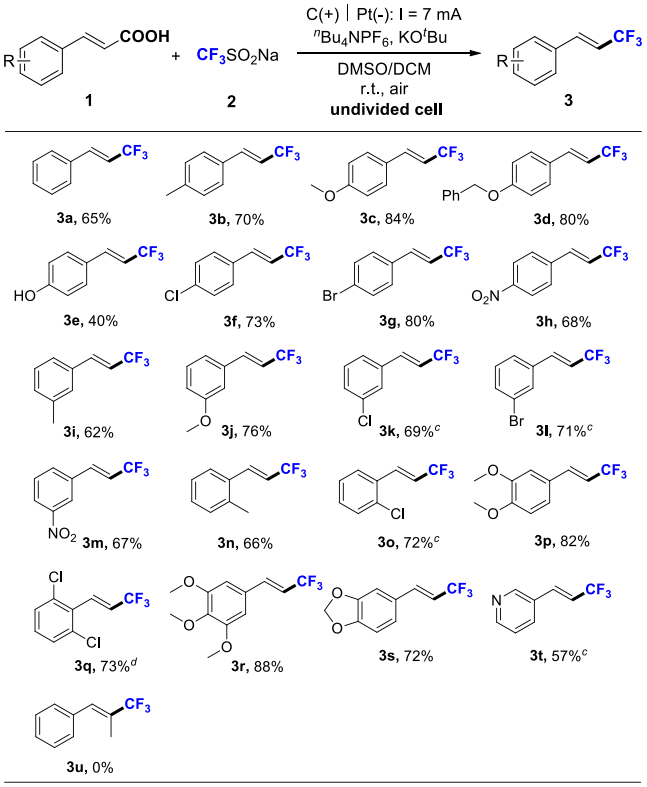


1a 2 3a

entry	electrolyte	base (equiv)	solvent	yield (%)[b]
1	$^nBu_4NBF_4$	none	DMSO/DCM	51
2	$^nBu_4NPF_6$	none	DMSO/DCM	59
3	$^nBu_4NOAc$	none	DMSO/DCM	46
4	$^nBu_4NHSO_4$	none	DMSO/DCM	22
5	Et_4NPF_6	none	DMSO/DCM	14
6	$^nBu_4NPF_6$	none	MeCN/DCM	trace
7	$^nBu_4NPF_6$	none	DMF/DCM	nd
8	$^nBu_4NPF_6$	none	DMSO/DCE	35
9	$^nBu_4NPF_6$	none	DMSO[c]	10
10[d]	$^nBu_4NPF_6$	none	DMSO/DCM	30
11	$^nBu_4NPF_6$	K_2CO_3 (0.5)	DMSO/DCM	65
12	$^nBu_4NPF_6$	KO^tBu (0.5)	DMSO/DCM	76
13	$^nBu_4NPF_6$	KOAc (0.5)	DMSO/DCM	70
14	$^nBu_4NPF_6$	KO^tBu (1)	DMSO/DCM	75
15[e]	$^nBu_4NPF_6$	KO^tBu (0.5)	DMSO/DCM	27
16[f]	$^nBu_4NPF_6$	KO^tBu (0.5)	DMSO/DCM	nd

[a]Reaction conditions: undivided cell, graphite rod (ϕ 6 mm) anode, Pt plate (10 mm × 10 mm) cathode, constant current = 7 mA, **1a** (0.1 mmol), CF_3SO_2Na **2** (0.3 mmol), electrolyte (0.5 equiv), base, solvent (1.5:1 v/v, 2.5 mL), air, 3 h. [b]Yield determined by GC analysis with *n*-dodecane as the internal standard. [c]DMSO (2 mL). [d]CF_3SO_2Na **2** (1 equiv). [e]*I* = 3 mA. [f]No electricity; nd = not detected.

Table 2. Substrate Scope of α,β-Unsaturated Carboxylic Acids[a,b]



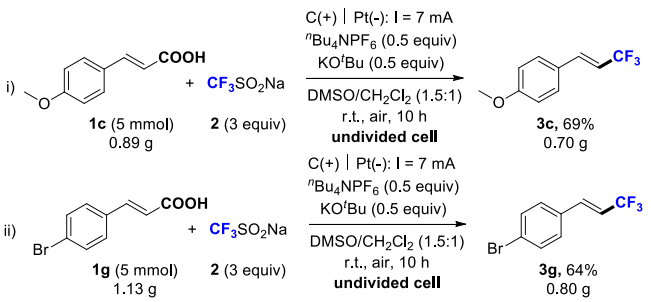
[a]Reaction conditions: graphite rod (ϕ 6 mm) anode, Pt plate (10 mm × 10 mm) cathode, constant current = 7 mA, **1a** (0.3 mmol), CF_3SO_2Na **2** (0.9 mmol), $^nBu_4NPF_6$ (0.5 equiv), KO^tBu (0.5 equiv), DMSO/DCM (1.5:1 v/v, 7.5 mL). The electrolysis was conducted in an undivided cell at room temperature under air for 3 h. [b]Yields refer to the isolated yields. [c]Electrolysis for 6 h. [d]Electrolysis for 7 h.

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX−XXX

(halogen and nitro) at the *para*-position of the phenyl ring were tolerated in this conversion, and the corresponding C_{vinyl}-CF_3 products (**3b**–**3d** and **3f**–**3h**) were given in good to excellent yields. When the *para*-substituted group was hydroxyl, the reaction gave the desired product **3e** with a lower yield, 40% isolated yield. The position of the substituent on the aromatic ring had a slight effect on the reaction. Compared to the products containing a *para*-substituent, the isolated yields of products containing a *meta*- or *ortho*-substituent were slightly reduced (**3i**–**3o**); among them, unsaturated carboxylic acid substrates with methoxy and halogen were transformed into the corresponding products (**3j**–**3l** and **3o**) smoothly in good yields. The substrates containing multiple substituents, especially multiple methoxy groups, could be well applied to the reactions, and the corresponding products (**3p**–**3r**) were delivered in moderate to excellent yields. It should be noted that heterocyclic (benzo[*d*][1,3]dioxole and pyridine) substrates underwent the transformations smoothly, affording the desired products **3s** and **3t** in 72% and 57% yields, respectively. In addition, when (*E*)-2-methyl-3-phenylacrylic acid was used as a reaction substrate, no desired product (**3u**) was detected.

The practical utility of this electrochemical synthesis strategy was demonstrated by scale-up experiments (Scheme 2). When

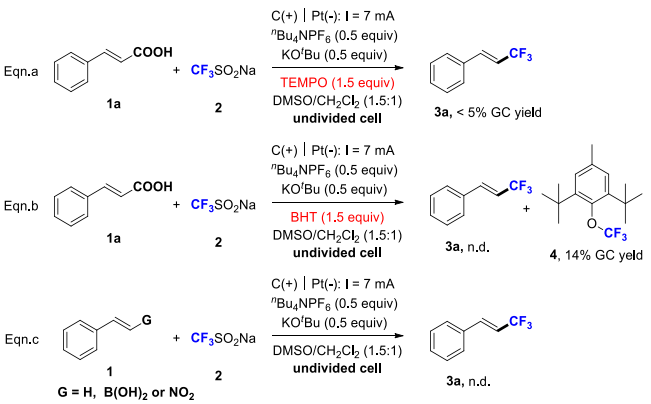
Scheme 2. Scale-Up Experiments



conducting the reactions at a 5 mmol scale, the desired products **3c** and **3g** were delivered smoothly in isolated yields of 69% and 64%, respectively. The experimental results exhibited the potential application of an electrochemical strategy in the actual synthesis.

To investigate the mechanism of the electro-oxidative decarboxylative trifluoromethylation, several control experiments were conducted (Scheme 3). By adding radical

Scheme 3. Control Experiments



scavengers[15] to the reaction and carefully analyzing the reaction results, we found that the addition of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and butylated hydroxytoluene (BHT) could both inhibit the reaction (eqs a and b). Meanwhile, the CF_3 radical formed in the reaction by BHT was trapped, a 14% yield of the trapping product **4** was detected (eq b), where trapping product **4** ($[M + H]^+$ = 289.1765) had been confirmed by HRMS. Subsequently, we also tested other olefin substrates, such as styrene, styrylboronic acid, and nitrovinylbenzene and found that they could not be applied to the reaction (eq c).

In order to analyze the reaction process in depth, we implemented cyclic voltammetry (CV) experiments and recorded cyclic voltammetry (CV) diagrams for different systems (Figure 2). With electrolyte solution as a test background, the oxidative peak of cinnamic acid (**1a**) was recorded at 1.01 V vs SCE in the presence of KO^tBu, and CF_3SO_2Na (**2**) had a close oxidative peak recorded at 0.95 V vs SCE (Figure 2a–c). As expected, the oxidative peak was recorded at 1.00 V vs SCE when KO^tBu was absent in the reaction system, while the recorded oxidative peak decreased to 0.77 vs SCE when KO^tBu was added in the reaction system, which indicated that KO^tBu played a key role in this transformation (Figure 2d,e).

On the basis of the above experimental results, a tentative mechanism for this electro-oxidative decarboxylative trifluoromethylation was proposed in Scheme 4. Initially, CF_3SO_2Na produced a CF_3 radical on the anode via the single-electron transfer (SET) oxidation process, while releasing SO_2.[14] Subsequently, the attack of the CF_3 radical onto α,β-unsaturated carboxylic acid **1** generated radical intermediate **B**, which would be further oxidized to release CO_2 and converted to the desired product **3**.

In summary, we have discovered an efficient electro-oxidative strategy using α,β-unsaturated carboxylic acids and CF_3SO_2Na for an operationally simple decarboxylative trifluoromethylation. The reaction is conducted under catalyst-free and external oxidant-free electrolysis conditions to deliver a series of C_{vinyl}-CF_3 compounds in good yields. Mechanistic studies have confirmed the formation of the CF_3 radical, which is provided by CF_3SO_2Na on the anode via the single-electron transfer (SET) oxidation process. Furthermore, simple and mild electrolysis conditions, inexpensive and readily available substrates, and a high regioselectivity provide a great advantage for the transformation. We anticipate that the protocol will not only enrich the content of the trifluoromethylations but also promote the innovation and development in sustainable chemistry. Further synthetic applications of this novel protocol are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all of the chemicals were purchased commercially and used without further purification. Technical grade petroleum ether (40–60 °C bp) and ethyl acetate were used for column chromatography. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Advance III 500 spectrometer using $CDCl_3$ as the solvent with TMS as the internal standard. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. Chemical shifts (δ) and coupling constants (J) are given in ppm and in hertz, respectively. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Electrolysis reactions were conducted using a Model MCH-K-300D (36 V) power supply purchased from Meichuang Instruments (Shenzhen) Co., Ltd. Cyclic voltammetry (CV) analysis was

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX–XXX

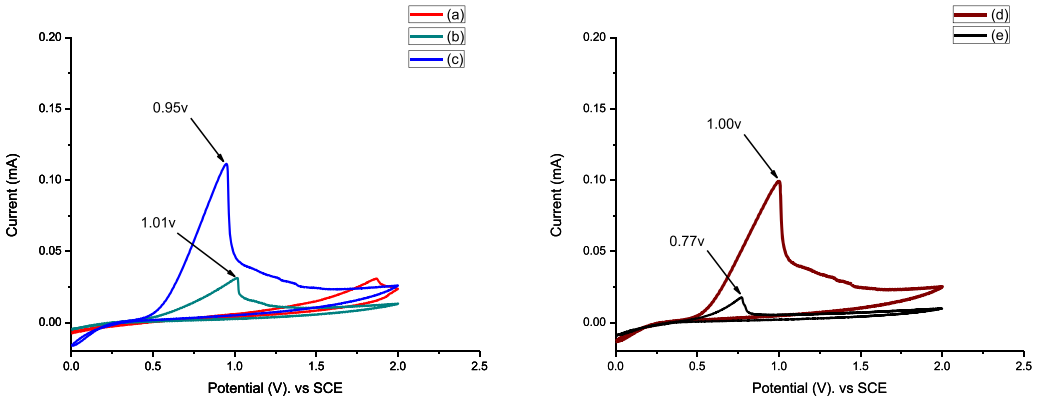
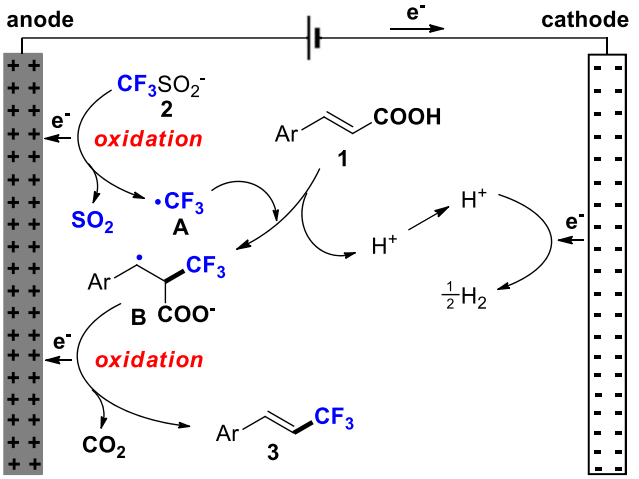


Figure 2. Cyclic voltammograms of 0.02 M $^{n}Bu_4NPF_6$ solution in DMSO/DCM (1.5:1) at room temperature: (a) none; (b) after the addition of cinnamic acid **1a** (0.04 M) and KO^{t}Bu(0.02 M); (c) after the addition of CF_3SO_2Na **2** (0.12 M); (d) after the addition of cinnamic acid **1a** (0.04 M) and CF_3SO_2Na **2** (0.12 M); (e) after the addition of cinnamic acid **1a** (0.04 M), CF_3SO_2Na **2** (0.12 M), and KO^{t}Bu(0.02 M). The voltammogram was obtained at a scan rate of 0.8 V/s with Pt electrode as an auxiliary electrode and a saturate calomel electrode (SCE) as a reference electrode.

Scheme 4. Proposed Mechanism



performed on a Princeton PARSTAT4000 electrochemical workstation, using a platinum electrode as a working electrode, a graphite rod as a counter electrode, and a saturated calomel electrode (SCE) as a reference electrode. Cyclic voltammograms were recorded at a scan rate of 0.8 V/s. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Bruker VERTEX 70 spectrometer. Mass spectra were recorded on a Shimadzu GCMS-QP2020 gas chromatograph−mass spectrometer. The high-resolution mass spectra were recorded by a Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap mass spectrometer (ESI-FTMS). TLC was performed by using commercially prepared 100−400 mesh silica gel plates, and visualization was affected at 254 nm.

General Procedure for the Synthesis of C_{vinyl}-CF_3 Compounds ***3.*** A mixture of **1a** (0.3 mmol), CF_3SO_2Na **2** (0.9 mmol), $^{n}Bu_4NPF_6$ (0.5 equiv), and KO^{t}Bu (0.5 equiv) in 7.5 mL of the solvent (DMSO/DCM = 1.5:1) was added to a round-bottomed flask (10 mL). The reaction flask was equipped with a graphite rod (ϕ 6 mm) as an anode and a Pt plate (10 mm × 10 mm) as a cathode. The solution was electrolyzed in an undivided cell at an ambient temperature under a constant current (7 mA) for 3−7 h. After electrolysis, the mixture was poured into water and extracted with ethyl acetate twice. The combined organic layer was washed with brine (10 mL) and dried over $MgSO_4$, filtered, and concentrated. The resulting mixture was purified by silica gel column chromatography to afford **3**.

*(E)-(3,3,3-Trifluoroprop-1-en-1-yl)benzene (**3a**):*[3b] 33 mg (65% yield), colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.49 (m, 2H), 7.42 (m, 3H), 7.18 (dd, J = 16.1, 2.1 Hz, 1H), 6.24 (dq, J = 16.1, 6.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 137.7 (q, J = 6.8 Hz), 133.4, 130.0, 129.0, 127.6, 123.6 (q, J = 269.6 Hz), 115.8 (q, J = 33.7 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.32; IR (KBr, cm^{-1}) ν 2928, 2861, 1731, 1459; HRMS (ESI) calcd for $C_9H_7F_3$ $[M + H]^+$ 173.0573, found 173.0568.

*(E)-1-Methyl-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3b**):*[3b] 39 mg (70% yield), colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.38 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.17−7.12 (m, 1H), 6.18 (dq, J = 16.1, 6.6 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 140.3, 137.5 (q, J = 6.6 Hz), 130.6, 129.6, 127.5, 123.8 (q, J = 269.6 Hz), 114.7 (q, J = 33.7 Hz), 29.7, 21.4; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.09; IR (KBr, cm^{-1}) ν 2921, 2854, 1728, 1460; HRMS (ESI) calcd for $C_{10}H_{10}F_3$ $[M + H]^+$ 187.0729, found 187.0724.

*(E)-1-Methoxy-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3c**):*[3b] 51 mg (84% yield), purple oil; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.42 (d, J = 8.7 Hz, 2H), 7.12 (dd, J = 16.1, 2.0 Hz, 1H), 6.94 (d, J = 8.7 Hz, 2H), 6.09 (dq, J = 16.0, 6.6 Hz, 1H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 161.0, 137.1 (q, J = 6.6 Hz), 129.1, 126.05, 124.0 (q, J = 268.4 Hz), 114.3, 113.4 (q, J = 33.6 Hz), 55.4; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −62.83; IR (KBr, cm^{-1}) ν 2924, 2850, 1663, 1514, 1259, 1119; HRMS (ESI) calcd for $C_{10}H_{10}F_3O$ $[M + H]^+$ 203.0678, found 203.0673.

*(E)-1-(Benzyloxy)-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3d**):*[16] 67 mg (80% yield), colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.45 (m, 6H), 7.38 (t, J = 7.0 Hz, 1H), 7.12 (dd, J = 16.1, 2.0 Hz, 1H), 7.02 (d, J = 8.7 Hz, 2H), 6.10 (dq, J = 16.0, 6.6 Hz, 1H), 5.13 (s, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 160.2, 137.1 (q, J = 6.8 Hz), 136.5, 129.1, 128.7, 128.2, 127.5, 126.3, 123.9 (q, J = 268.6 Hz), 115.2, 113.6 (q, J = 33.6 Hz), 70.1; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −62.82; IR (KBr, cm^{-1}) ν 2922, 2856, 1662, 1275, 1105; HRMS (ESI) calcd for $C_{16}H_{13}F_3O$ $[M + H]^+$ 279.0991, found 279.0988.

*(E)-4-(3,3,3-Trifluoroprop-1-en-1-yl)phenol (**3e**):*[3b] 22 mg (40% yield), yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.38 (d, J = 8.6 Hz, 2H), 7.09 (dd, J = 16.1, 2.1 Hz, 1H), 6.87 (m, 2H), 6.08 (dq, J = 16.1, 6.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 157.6, 137.1 (q, J = 7.0 Hz), 129.3, 125.9, 124.0 (q, J = 268.6 Hz), 115.9, 113.2 (q, J = 33.5 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −62.85; IR (KBr, cm^{-1}) ν 3370, 2930, 2860, 1604, 1265, 1117; HRMS (ESI) calcd for $C_9H_7F_3O$ $[M + H]^+$ 189.0522, found 189.0521.

*(E)-1-Chloro-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3f**):*[3b] 45 mg (73% yield), yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.30 (t, J = 6.4 Hz, 4H), 7.03 (dd, J = 16.1, 2.1 Hz, 1H), 6.11 (dq, J = 16.1,

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX−XXX

6.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 136.4 (q, J = 6.8 Hz), 136.0, 131.9, 129.2, 128.8, 123.4 (q, J = 269.0 Hz), 116.4 (q, J = 34.0 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.43; IR (KBr, cm^{-1}) ν 2922, 2854, 2354, 1726, 1266, 1030; HRMS (ESI) calcd for $C_9H_7ClF_3$ $[M + H]^+$ 207.0182, found 207.0179.

*(E)-1-Bromo-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3g**):*[3b] 65 mg (80% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.58−7.51 (m, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.12 (dd, J = 16.1, 2.1 Hz, 1H), 6.23 (dq, J = 16.1, 6.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 136.5 (q, J = 6.6 Hz), 132.3, 132.2, 129.0, 124.3, 123.4 (q, J = 269.6 Hz), 116.5 (q, J = 34.0 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.46; IR (KBr, cm^{-1}) ν 2921, 2854, 2356, 1657, 1275, 1126; HRMS (ESI) calcd for $C_9H_6BrF_3Na$ $[M + Na]^+$ 272.9497, found 272.9500.

*(E)-1-Nitro-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3h**):*[3b] 44 mg (68% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 8.29 (d, J = 8.7 Hz, 2H), 7.66 (d, J = 8.7 Hz, 2H), 7.25 (dd, J = 16.2, 2.0 Hz, 1H), 6.39 (dq, J = 16.2, 6.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 148.5, 139.5, 135.4 (q, J = 6.8 Hz), 128.4, 124.3, 122.9 (q, J = 269.7 Hz), 120.0 (q, J = 34.5 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.95; IR (KBr, cm^{-1}) ν 2924, 2357, 1521, 1344, 1121; HRMS (ESI) calcd for $C_9H_7F_3NO_2$ $[M + H]^+$ 218.0423, found 218.0420.

*(E)-1-Methyl-3-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3i**):*[3b] 34 mg (62% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.29 (m, 3H), 7.23 (m, 1H), 7.14 (m, 1H), 6.22 (dq, J = 16.1, 6.6 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 138.6, 137.8 (q, J = 6.7 Hz), 133.3, 130.8, 128.8, 128.2, 124.7, 121.6 (q, J = 269.6 Hz), 115.6 (q, J = 33.8 Hz), 21.3; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.26; IR (KBr, cm^{-1}) ν 2925, 2359, 1737, 1520, 1263; HRMS (ESI) calcd for $C_{10}H_9F_3$ $[M + H]^+$ 187.0729, found 187.0724.

*(E)-1-Methoxy-3-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3j**):*[3b] 46 mg (76% yield), purple oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.33 (t, J = 7.9 Hz, 1H), 7.16−7.12 (m, 1H), 7.07 (d, J = 7.6 Hz, 1H), 7.00−6.99 (m, 1H), 6.96 (dd, J = 8.2, 2.4 Hz, 1H), 6.22 (dq, J = 16.1, 6.5 Hz, 1H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 159.9, 137.6 (q, J = 6.5 Hz), 134.8, 130.0, 123.6 (q, J = 269.0 Hz), 120.1, 116.1 (q, J = 34.02 Hz), 115.7, 112.7, 55.3; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.32; IR (KBr, cm^{-1}) ν 2952, 2855, 2356, 1594, 1267, 1120; HRMS (ESI) calcd for $C_{10}H_{10}F_3O$ $[M + H]^+$ 203.0678, found 203.0674.

*(E)-1-Chloro-3-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3k**):*[3b] 43 mg (69% yield), colorless oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.48 (s, 1H), 7.39−7.35 (m, 3H), 7.12 (dd, J = 16.1, 2.1 Hz, 1H), 6.25 (dq, J = 16.1, 6.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 136.3 (q, J = 6.7 Hz), 135.2, 135.0, 130.2, 130.0, 127.4, 125.8, 123.3 (q, J = 269.6 Hz), 117.3 (q, J = 34.0 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.58; IR (KBr, cm^{-1}) ν 2921, 2854, 2360, 1726, 1530, 1269, 1126; HRMS (ESI) calcd for $C_9H_7ClF_3$ $[M + H]^+$ 207.0182, found 207.0181.

*(E)-1-Bromo-3-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3l**).* 58 mg (71% yield), purple oil; ^1H NMR (500 MHz, $CDCl_3$, ppm)) δ 7.63 (t, J = 1.7 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.29 (t, J = 3.9 Hz, 1H), 7.14−7.08 (m, 1H), 6.27−6.20 (m, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 136.2 (q, J = 6.7 Hz), 135.4, 132.9, 130.5, 130.3, 126.2, 123.3 (q, J = 269.2 Hz), 123.1, 117.3 (q, J = 34.1 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.60; IR (KBr, cm^{-1}) ν 2926, 2854, 2361, 1734, 1524; HRMS (ESI) calcd for $C_9H_6BrF_3Na$ $[M + Na]^+$ 272.9497, found 272.9498.

*(E)-1-Nitro-3-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3m**):* 44 mg (67% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 8.36 (t, J = 1.8 Hz, 1H), 8.27 (dd, J = 8.2, 1.4 Hz, 1H), 7.81 (d, J = 7.7 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.25 (ddd, J = 16.1, 4.1, 2.0 Hz, 1H), 6.39 (dq, J = 16.1, 6.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 148.7, 135.1, 135.4 (q, J = 6.8 Hz), 133.2, 130.1, 124.5, 123.0 (q, J = 269.2 Hz), 122.2, 119.1 (q, J = 34.6 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.86; IR (KBr, cm^{-1}) ν 3088, 2926, 2858, 1671, 1538, 1127; HRMS (ESI) calcd for $C_9H_6F_3NO_2$ $[M + H]^+$ 218.0423, found 218.0418.

*(E)-1-Methyl-2-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3n**):* 37 mg (66% yield), colorless oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.49 (d, J = 7.6 Hz, 1H), 7.44 (dd, J = 16.0, 2.1 Hz, 1H), 7.31 (d, J = 7.4 Hz, 1H), 7.25 (dd, J = 11.3, 7.5 Hz, 2H), 6.14 (dq, J = 15.9, 6.5 Hz, 1H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 137.0, 135.5 (q, J = 6.9 Hz), 132.6, 130.8, 129.8, 126.4, 126.2, 123.6 (q, J = 269.1 Hz), 117.0 (q, J = 33.6 Hz), 19.7; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.30; IR (KBr, cm^{-1}) ν 2923, 2857, 2356, 1732, 1263, 1094; HRMS (ESI) calcd for $C_{10}H_{10}F_3$ $[M + H]^+$ 187.0729, found 187.0725.

*(E)-1-Chloro-2-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3o**):* 44 mg (72% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.59 (m, 2H), 7.45 (dd, J = 7.7, 1.6 Hz, 1H), 7.34 (tt, J = 6.9, 3.5 Hz, 2H), 6.24 (dq, J = 16.1, 6.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 134.4, 134.0 (q, J = 6.8 Hz), 131.8, 131.0, 130.2, 127.4, 127.2, 123.2 (q, J = 269.6 Hz), 118.4 (q, J = 34.1 Hz, 1H); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.61; IR (KBr, cm^{-1}) ν 2924, 2855, 1662, 1319, 1130; HRMS (ESI) calcd for $C_9H_6ClF_3$ $[M + H]^+$ 207.0183, found 207.0185.

*(E)-1,2-Dimethoxy-4-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3p**):*[11] 57 mg (82% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.09 (dd, J = 16.1, 2.0 Hz, 1H), 7.04 (dd, J = 8.2, 1.7 Hz, 1H), 6.98 (d, J = 1.8 Hz, 1H), 6.88 (d, J = 8.3 Hz, 1H), 6.09 (dq, J = 16.0, 6.6 Hz, 1H), 3.93 (s, 3H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 150.7, 149.2, 137.4 (q, J = 6.9 Hz), 126.3, 123.9 (q, J = 268.6 Hz), 121.7, 113.6 (q, J = 33.6 Hz), 111.0, 109.2, 55.9, 55.9; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −62.80; IR (KBr, cm^{-1}) ν 2944, 2846, 1662, 1517, 1263, 1121; HRMS (ESI) calcd for $C_{11}H_{11}F_3O_2$ $[M + H]^+$ 233.0784, found 233.0778.

*(E)-1,3-Dichloro-2-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3q**):*[11] 52 mg (73% yield), colorless oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.39 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 2.6 Hz, 1H), 7.25−7.24 (m, 1H), 6.42 (dq, J = 16.4, 6.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 134.7, 131.5 (q, J = 7.3 Hz), 130.9, 130.0, 128.8, 124.5 (q, J = 33.9 Hz), 122.8 (q, J = 270.9 Hz,); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −64.71, −64.72; IR (KBr, cm^{-1}) ν 2926, 2856, 1673, 1434, 1310, 1131; HRMS (ESI) calcd for $C_9H_5Cl_2F_3$ $[M + H]^+$ 240.9793, found 240.9796.

*(E)-1,2,3-Trimethoxy-5-(3,3,3-trifluoroprop-1-en-1-yl)benzene (**3r**):* 69 mg (88% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.1 (m, 1H), 6.7 (s, 2H), 6.1 (dq, J = 16.0, 6.5 Hz, 1H), 3.9 (s, 6H), 3.9 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 153.5, 139.7, 137.6 (q, J = 6.9 Hz), 129.0, 123.6 (q, J = 269.6 Hz), 115.2 (q, J = 33.7 Hz), 104.6, 61.0, 56.2; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.07; IR (KBr, cm^{-1}) ν 2937, 2846, 1586, 1284, 1123; HRMS (ESI) calcd for $C_{12}H_{13}F_3O_3$ $[M + H]^+$ 263.0889, found 263.0885.

*(E)-5-(3,3,3-Trifluoroprop-1-en-1-yl)benzo[d][1,3]dioxole (**3s**):* 47 mg (72% yield), colorless oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.28 (s, 1H), 7.07 (dd, J = 16.1, 2.1 Hz, 1H), 6.98 (d, J = 1.6 Hz, 1H), 6.95−6.93 (m, 1H), 6.83 (d, J = 8.0 Hz, 1H), 6.03 (s, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 149.3, 148.4, 137.2 (q, J = 6.9 Hz), 127.7, 123.8 (q, J = 268.7 Hz), 123.5, 113.8 (q, J = 33.7 Hz), 108.5, 106.2, 101.6; ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −62.88; IR (KBr, cm^{-1}) ν 3830, 2922, 2356, 1501, 1258, 1114; HRMS (ESI) calcd for $C_{10}H_8F_3O_2$ $[M + H]^+$ 217.0470, found 217.0465.

*(E)-3-(3,3,3-Trifluoroprop-1-en-1-yl)pyridine (**3t**):*[5b] 29 mg (57% yield), yellow oil; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 8.72 (s, 1H), 8.65 (d, J = 3.3 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.38 (dd, J = 7.8, 4.9 Hz, 1H), 7.19 (dd, J = 16.2, 1.7 Hz, 1H), 6.32 (dq, J = 16.2, 6.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 150.8, 149.1, 134.3 (q, J = 6.5 Hz), 134.0, 129.3, 123.9, 123.1 (q, J = 269.3 Hz), 118.2 (q, J = 34.1 Hz); ^{19}F NMR (471 MHz, $CDCl_3$, ppm) δ −63.82; IR (KBr, cm^{-1}) ν 2925, 2858, 1732, 1424, 1126; HRMS (ESI) calcd for $C_8H_6F_3N$ $[M + H]^+$ 174.0525, found 174.0524.

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX−XXX

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge via the Internet at The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b00766.

NMR spectra of the products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wyuchemhyb@126.com.

ORCID

Yibiao Li: 0000-0001-8249-5630

Lu Chen: 0000-0002-9601-4241

Yubing Huang: 0000-0002-3025-8366

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Foundation of the Department of Education of Guangdong Province (2017KZDXM085), Chemical Industry Collaborative Innovation Center of Yueshan Town 2017 (368), and the Foundation for Young Talents (construction of *N*-biheteroarenes by the hydrogen transfer strategy and its antitumor activity).

■ REFERENCES

(1) (a) Müller, K.; Faeh, C.; Diederich, F. Fluorine in Pharmaceuticals: Looking Beyond Intuition. *Science* **2007**, *317*, 1881−1886. (b) Meanwell, N. A. Synopsis of Some Recent Tactical Application of Bioisosteres in Drug Design. *J. Med. Chem.* **2011**, *54*, 2529−2591. (c) Tang, X.; Huang, L.; Xu, Y.; Yang, J.; Wu, W.; Jiang, H. Copper-Catalyzed Coupling of Oxime Acetates with Sodium Sulfinates: An Efficient Synthesis of Sulfone Derivatives. *Angew. Chem., Int. Ed.* **2014**, *53*, 4205−4208. (d) Egami, H.; Sodeoka, M. Trifluoromethylation of Alkenes with Concomitant Introduction of Additional Functional Groups. *Angew. Chem., Int. Ed.* **2014**, *53*, 8294−8308. (e) Koike, T.; Akita, M. Fine Design of Photoredox Systems for Catalytic Fluoromethylation of Carbon-Carbon Multiple Bonds. *Acc. Chem. Res.* **2016**, *49*, 1937−1945. (f) Zhang, H.-Y.; Ge, C.; Zhao, J.; Zhang, Y. Cobalt-Catalyzed Trifluoromethylation-Peroxidation of Unactivated Alkenes with Sodium Trifluoromethanesulfinate and Hydroperoxide. *Org. Lett.* **2017**, *19*, 5260−5263. (g) Yang, X.; Tsui, G. C. Copper-Mediated Trifluoromethylation-Allylation of Arynes. *Org. Lett.* **2018**, *20*, 1179−1182.

(2) (a) Mu, X.; Wu, T.; Wang, H.-Y.; Guo, Y.-L.; Liu, G. Palladium-Catalyzed Oxidative Aryltrifluoromethylation of Activated Alkenes at Room Temperature. *J. Am. Chem. Soc.* **2012**, *134*, 878−881. (b) Feng, C.; Loh, T.-P. Copper-catalyzed olefinic trifluoromethylation of enamides at room temperature. *Chem. Sci.* **2012**, *3*, 3458−3462. (c) Carboni, A.; Dagousset, G.; Magnier, E.; Masson, G. One pot and selective intermolecular aryl- and heteroaryl-trifluoromethylation of alkenes by photoredox catalysis. *Chem. Commun.* **2014**, *50*, 14197−14200. (d) Liao, J.; Guo, W.; Zhang, Z.; Tang, X.; Wu, W.; Jiang, H. Metal-Free Catalyzed Regioselective Allylic Trifluoromethanesulfonylation of Aromatic Allylic Alcohols with Sodium Trifluoromethanesulfinate. *J. Org. Chem.* **2016**, *81*, 1304−1309. (e) Cheng, Y.-F.; Dong, X.-Y.; Gu, Q.-S.; Yu, Z.-L.; Liu, X.-Y. Achiral Pyridine Ligand-Enabled Enantioselective Radical Oxytrifluoromethylation of Alkenes with Alcohols. *Angew. Chem., Int. Ed.* **2017**, *56*, 8883−8886. (f) Zhao, Y.; Zhou, Y.; Zhang, C.; Wang, H.; Zhao, J.; Jin, K.; Liu, J.; Liu, J.; Qu, J. Palladium-catalyzed geometrically selective hydrogenation of (*Z*)-trifluoromethyl alkenyl triflate: an efficient approach to (*Z*) or (*E*)-3,3,3-trifluoropropenyl derivatives. *Org. Biomol. Chem.* **2017**, *15*, 5693−5700.

(3) (a) Hafner, A.; Bräse, S. Efficient Trifluoromethylation of Activated and Non-Activated Alkenyl Halides by Using (Trifluoromethyl)trimethylsilane. *Adv. Synth. Catal.* **2011**, *353*, 3044−3048. (b) Ma, J.-J.; Yi, W.-B.; Lu, G.-P.; Cai, C. Decarboxylative and Denitrative Trifluoromethylation for the Synthesis of C_{vinyl}-CF_3 Compounds with Togni (II) Reagent. *Adv. Synth. Catal.* **2015**, *357*, 3447−3452. (c) Straathof, N. J. W.; Cramer, S. E.; Hessel, V.; Noël, T. Practical Photocatalytic Trifluoromethylation and Hydrotrifluoromethylation of Styrenes in Batch and Flow. *Angew. Chem., Int. Ed.* **2016**, *55*, 15549−15553. (d) Wu, L.-H.; Zhao, K.; Shen, Z.-L.; Loh, T.-P. Copper-catalyzed trifluoromethylation of styrene derivatives with CF_3SO_2Na. *Org. Chem. Front.* **2017**, *4*, 1872−1875.

(4) Arimori, S.; Shibata, N. Catalytic Trifluoromethylation of Aryl- and Vinylboronic Acids by 2-Cyclopropyl-1-(trifluoromethyl)benzo[*b*]thiophenium Triflate. *Org. Lett.* **2015**, *17*, 1632−1635.

(5) (a) Parsons, A. T.; Senecal, T. D.; Buchwald, S. L. Iron(II)-Catalyzed Trifluoromethylation of Potassium Vinyltrifluoroborates. *Angew. Chem., Int. Ed.* **2012**, *51*, 2947−2950. (b) Yasu, Y.; Koike, T.; Akita, M. Visible-light-induced synthesis of a variety of trifluoromethylated alkenes from potassium vinyltrifluoroborates by photoredox catalysis. *Chem. Commun.* **2013**, *49*, 2037−2039.

(6) Cho, E. J.; Buchwald, S. L. The Palladium-Catalyzed Trifluoromethylation of Vinyl Sulfonates. *Org. Lett.* **2011**, *13*, 6552−6555.

(7) Huang, P.; Li, Y.; Fu, X.; Zhang, R.; Jin, K.; Wang, W.; Duan, C. Silver(I)-catalyzed denitrative trifluoromethylation of *β*-nitrostyrenes with CF_3SO_2Na. *Tetrahedron Lett.* **2016**, *57*, 4705−4708.

(8) (a) Chen, Q.; Wang, C.; Zhou, J.; Wang, Y.; Xu, Z.; Wang, R. $CuSO_4$-Mediated Decarboxylative Difluoroacetamidation of *α*, *β*-Unsaturated Carboxylic Acids. *J. Org. Chem.* **2016**, *81*, 2639−2645. (b) Wei, X.-J.; Boon, W.; Hessel, V.; Noel, T. Visible-Light Photocatalytic Decarboxylation of *α*, *β*-Unsaturated Carboxylic Acids: Facile Access to Stereoselective Difluoromethylated Styrenes in Batch and Flow. *ACS Catal.* **2017**, *7*, 7136−7140. (c) Pimpasri, C.; Sumunnee, L.; Yotphan, S. Copper-catalyzed oxidative decarboxylative coupling of *α*-keto acids and sulfoximines. *Org. Biomol. Chem.* **2017**, *15*, 4320−4327. (d) Tan, X.; Liu, Z.; Shen, H.; Zhang, P.; Zhang, Z.; Li, C. Silver-Catalyzed Decarboxylative Trifluoromethylation of Aliphatic Carboxylic Acids. *J. Am. Chem. Soc.* **2017**, *139*, 12430−12433. (e) Schwarz, J.; König, B. Decarboxylative reactions with and without light-a comparison. *Green Chem.* **2018**, *20*, 323−361.

(9) He, Z.; Luo, T.; Hu, M.; Cao, Y.; Hu, J. Copper-Catalyzed Di- and Trifluoromethylation of *α*, *β*-Unsaturated Carboxylic Acids: A Protocol for Vinylic Fluoroalkylations. *Angew. Chem.* **2012**, *124*, 4010−4013.

(10) Li, Z.; Cui, Z.; Liu, Z.-Q. Copper- and Iron-Catalyzed Decarboxylative Tri- and Difluoromethylation of *α*, *β*-Unsaturated Carboxylic Acids with CF_3SO_2Na and $(CF_2HSO_2)_2Zn$ *via* a Radical Process. *Org. Lett.* **2013**, *15*, 406−409.

(11) Xu, P.; Abdukader, A.; Hu, K.; Cheng, Y.; Zhu, C. Room temperature decarboxylative trifluoromethylation of *α*, *β*-unsaturated carboxylic acids by photoredox catalysis. *Chem. Commun.* **2014**, *50*, 2308−2310.

(12) For selected reviews, see: (a) Francke, R.; Little, R. D. Redox catalysis in organic electrosynthesis: basic principles and recent developments. *Chem. Soc. Rev.* **2014**, *43*, 2492−2521. (b) Gütz, C.; Klöckner, B.; Waldvogel, S. R. Electrochemical Screening for Electroorganic Synthesis. *Org. Process Res. Dev.* **2016**, *20*, 26−32. (c) Jiang, Y.; Xu, K.; Zeng, C. Use of Electrochemistry in the Synthesis of Heterocyclic Structures. *Chem. Rev.* **2018**, *118*, 4485−4540. (d) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance. *Chem. Rev.* **2017**, *117*, 13230−13319. (e) Tang, S.; Liu, Y.; Lei, A. Electrochemical Oxidative Cross-coupling with Hydrogen Evolution: A Green and Sustainable Way for Bond Formation. *Chem.* **2018**, *4*,

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX−XXX

27−45. (f) Sauermann, N.; Meyer, T. H.; Qiu, Y.; Ackermann, L. Electrocatalytic C-H Activation. *ACS Catal.* **2018**, *8*, 7086−7103. (g) Ma, C.; Fang, P.; Mei, T.-S. Recent Advances in C-H Functionalization Using Electrochemical Transition Metal Catalysis. *ACS Catal.* **2018**, *8*, 7179−7189. (h) Parry, J. B.; Fu, N.; Lin, S. Electrocatalytic Difunctionalization of Olefins as a General Approach to the Synthesis of Vicinal Diamines. *Synlett* **2018**, *29*, 257−265.

(13) (a) O'Brien, A. G.; Maruyama, A.; Inokuma, Y.; Fujita, M.; Baran, P. S.; Blackmond, D. G. Radical C-H Functionalization of Heteroarenes under Electrochemical Control. *Angew. Chem.* **2014**, *126*, 12062−12065. (b) Xiong, P.; Xu, H.-H.; Xu, H.-C. Metal- and Reagent-Free Intramolecular Oxidative Amination of Triand Tetrasubstituted Alkenes. *J. Am. Chem. Soc.* **2017**, *139*, 2956−2959. (c) Siu, J. C.; Sauer, G. S.; Saha, A.; Macey, R. L.; Fu, N.; Chauviré, T.; Lancaster, K. M.; Lin, S. Electrochemical Azidooxygenation of Alkenes Mediated by a TEMPO-N_3 Charge-Transfer Complex. *J. Am. Chem. Soc.* **2018**, *140*, 12511−12520. (d) Huang, P.; Wang, P.; Tang, S.; Fu, Z.; Lei, A. Electro-oxidative Cross S-H/S-H Coupling with Hydrogen Evolution: A Facile Access to Unsymmetrical Disulfides. *Angew. Chem.* **2018**, *130*, 8247−8251.

(14) (a) Beatty, J. W.; Douglas, J. J.; Cole, K. P.; Stephenson, C. R. J. A scalable and operationally simple radical trifluoromethylation. *Nat. Commun.* **2015**, *6*, 7917. (b) Ye, K.-Y.; Pombar, G.; Fu, N.; Sauer, G. S.; Keresztes, I.; Lin, S. Anodically Coupled Electrolysis for the Heterodifunctionalization of Alkenes. *J. Am. Chem. Soc.* **2018**, *140*, 2438−2441. (c) Zhang, L.; Zhang, G.; Wang, P.; Li, Y.; Lei, A. Electrochemical Oxidation with Lewis-Acid Catalysis Leads to Trifluoromethylative Difunctionalization of Alkenes Using CF_3SO_2Na. *Org. Lett.* **2018**, *20*, 7396−7399.

(15) Yang, Q.-L.; Wang, X.-Y.; Lu, J.-Y.; Zhang, L.-P.; Fang, P.; Mei, T.-S. Copper-Catalyzed Electrochemical C-H Amination of Arenes with Secondary Amines. *J. Am. Chem. Soc.* **2018**, *140*, 11487−11494.

(16) Omote, M.; Tanaka, M.; Ikeda, A.; Nomura, S.; Tarui, A.; Sato, K.; Ando, A. Simple Synthesis of *β*-Trifluoromethylstyrenes Using (*E*)-Trimethyl-(3,3,3-trifluoroprop-1-enyl)silane. *Org. Lett.* **2012**, *14*, 2286−2289.

DOI: 10.1021/acs.joc.9b00766
J. Org. Chem. XXXX, XXX, XXX−XXX