镍促进电化学还原交叉偶联合成偕二氟烯烃

常哲 王佳鑫 陆熹* 傅尧*

(中国科学技术大学应用化学系 合肥 230026)

摘要 偕二氟烯烃是一类重要的含氟有机化合物,在有机合成化学和药物化学研究领域展现出独特的结构优势。例如,偕二氟烯基可以便利地转化为单氟烯基、二氟烷基、三氟甲基以及其他多种含氟结构。偕二氟烯基结构作为羰基理想的电子等排体在药物设计研究中有广泛的应用。报道了一种镍促进的电化学还原交叉偶联反应合成功能化的偕二氟烯烃。该反应在非分隔电解槽中进行,在温和的电化学还原条件下,实现了三氟甲基烯烃烯丙基脱氟、氧化还原活性羧酸酯脱羧或者烷基卤化物脱卤素的有机结合。反应可有效避免使用化学计量的金属粉末或有机还原剂。该反应为含偕二氟烯基功能结构的生物活性分子提供了有效的合成途径。

关键词 偕二氟烯烃; 三氟甲基烯烃; 氧化还原活性羧酸酯; 烷基卤化物; 还原交叉偶联; 电化学

Synthesis of *gem*-Difluoroalkenes through Nickel-Promoted Electrochemical Reductive Cross-Coupling

Chang, Zhe Wang, Jiaxin Lu, Xi* Fu, Yao*

(Department of Applied Chemistry, University of Science and Technology of China, Hefei 230026)

Abstract *gem*-Difluoroalkenes are important fluorine-containing compounds with structural superiority in organic synthetic chemistry and medicinal chemistry. For instance, the *gem*-difluoroethylene moiety could be converted to monofluoroalkenyl, difluoroalkyl, trifluoromethyl moiety, and many other fluorine-containing structures conveniently. The *gem*-difluoroethylene moiety is also an ideal carbonyl group bioisostere and has already been widely used in drug design. Herein, a nickel-promoted electrochemical reductive cross-coupling to access functionalized and substituted *gem*-difluoroalkenes is reported. This reaction enables the combination of allylic defluorination of trifluoromethyl alkenes and decarboxylation of redox-active esters or dehalogenation of alkyl halides under mild electrochemical reduction conditions and in an undivided cell, therefore obviates the use of stoichiometric amount metal powder or organic reductants. Furthermore, this reaction provides efficient access to biologically interesting molecules containing *gem*-difluoroethylene moiety.

Keywords *gem*-difluoroalkene; trifluoromethyl alkene; redox-active ester; alkyl halide; reductive cross-coupling; electrochemistry

1 Introduction

gem-Difluoroalkenes are a kind of striking fluorine-containing compounds with structural superiority in organic synthetic chemistry and medicinal chemistry.^[1] The *gem*-difluoroethylene moiety could be converted to many other fluorine-containing structures conveniently (Figure 1a),^[2] such as defluorinative functionalization to access monofluoroalkenyl moiety,^[3] hydrogenation or hydrofunctionalization to access difluoroalkyl moiety,^[4] fluorination functionalization to produce trifluoromethyl moiety.^[5] The *gem*-difluoroethylene moiety is also an ideal carbonyl

group bioisostere and has already been widely used in drug design.^[6] Direct difluoroolefination of ketones or diazo compounds was an efficient strategy to deliver *gem*-difluoroalkenes (Figures 1b, i).^[7] Hu,^[8] Xiao,^[9] Wang,^[10] and others enjoyed outstanding achievements in this area. More recently, allylic defluorinative functionalization of trifluoromethyl alkenes with different nucleophiles has been developed as powerful tools to synthesize substituted *gem*-difluoroalkenes (Figures 1b, ii).^[11] For example, Cao,^[12] Shi,^[13] Murakami,^[14] Hayashi,^[15] Zhang,^[16] and others reported the defluorinative carbonation of trifluoro-

* Corresponding authors. E-mail: luxi@mail.ustc.edu.cn; fuyao@ustc.edu.cn

Received August 6, 2021; revised September 5, 2021; published online September 14, 2021.

Project supported by the National Natural Science Foundation of China (Nos. 21732006, 51821006, 51961135104), and the Research Funds of the Double First-Class Initiative of University of Science and Technology of China (No. YD3530002002).

国家自然科学基金(Nos. 21732006, 51821006, 51961135104)和中国科学技术大学双一流研究基金(No. YD3530002002)资助项目。

romethyl alkenes with Grignard, organozinc, organoboron, and other organometallic reagents. Molander,^[17] Zhou,^[18] and others^[19] achieved the defluorinative coupling of trifluoromethyl alkenes with radical precursors under photocatalysis conditions.

In 2017, our group^[20] proposed a concept of defluorinative reductive cross-coupling, which combined the C–F cleavage and alkyl electrophiles activation under mild reductive reaction conditions. Our group^[21] and Wang^[22] independently extended this concept to the allylic defluorinative reductive alkylation of trifluoromethyl alkenes and offered straightforward access to *gem*-difluoroalkenes (Figure 1c). Later, more attention has been paid to the nickel-catalyzed or transition-metal-free defluorinative reductive cross-couplings.^[23] A growing number of radical precursors generated under mild reductive conditions has been applied to the defluorinative functionalization reactions, such as epoxides, Katritzky salts, and cycloketone oxime esters.^[24] These reactions exhibited high efficiency and broad functional group compatibility. However, one of the limitations was using the stoichiometric amount of zinc or bis(pinacolato)diboron reductant.

Electrochemical synthesis has a unique attraction for organic synthetic chemists.^[25] The electrochemical reduction reaction has attracted substantial interest in organic synthesis.^[26] It avoids the surface activation and post-processing of excessive metal powder. Therefore, it is easy to be used in large-scale industries and significantly reduces the production cost in industrial production.^[27] Herein, we report a nickel-promoted electrochemical reductive cross-coupling of trifluoromethyl alkenes and alkyl halides or redox-active esters in an undivided cell (Figure 1d). This reaction enables the synthesis of functionalized and substituted *gem*-difluoroalkenes under mild electrochemical reduction conditions, therefore obviates the use of stoichiometric amount metal powder or organic reductants. Furthermore, this reaction provides efficient access to biologically interesting molecules containing *gem*-difluoroethylene moiety.

2 Results and discussion

Our investigation began with the synthesis of *gem*-difluoroalkene **4aa** through the nickel-promoted electrochemical reductive cross-coupling of trifluoromethyl alkene **1a** with primary alkyl iodide **2a**. The reaction parameters were screened systematically, and their impacts on the reaction conversion and coupling efficiency were summarized in Table 1. To our delight, the reaction underwent smoothly and provided 77% NMR yield and 73% isolated yield (Entry 1) using NiBr₂(diglyme) as the catalyst, Pybox as the ligand, ⁿBu₄NBr as the electrolyte, and dimethyl sulfoxide (DMSO) as the solvent in an undivided cell with Zn(+) and Ni foam(–) as electrodes under 5 mA current for 9 h at room temperature. NiCl₂ or Ni(acac)₂ could be used as catalysts, resulting in slightly diminished conversions and yields (Entries 2, 3). Bidentate N-ligands **L1** and **L2** and another tridentate N-ligand **L3** were tested, afford-

Figure 1 Synthetic routes to access *gem*-difluoroalkene

ing the desired product in moderate yields (Entries 4~6). Compared with the data shown in Entries 7~10, a satisfactory outcome was obtained when using 1.0 equiv. of ⁿBu₄NBr as the suitable electrolyte. *N,N*-Dimethylacetamide (DMAc), *N,N*-dimethylformamide (DMF), and CH₃CN were frequently-used solvents in electrochemical reactions; when using DMAc and DMF instead of DMSO (Entries 11, 12), the yields decreased to 57% and 53%, respectively; CH₃CN was inferior because of the low conversion of alkyl halide (Entry 13). Finally, the excessive amount of alkyl halides ensured the high yield of this reaction (Entries 14, 15).

Control experiments were carried out to clarify the importance of nickel catalyst and electrochemical reduction (Entries 16~22). When the nickel catalyst or electric current was removed, the coupling efficiency of this reaction decreased dramatically (Entries 16~18). When Fe(+) was used instead of Zn(+) as the sacrificial anode, a comparable 55% yield was obtained (Entry 19), while no product was observed when using Fe powder as the reductant (Entry 21). Therefore, these results indirectly explain the electrochemical reduction process rather than the reduction on the metal surface. Ni foam could be replaced with reticulated vitreous carbon (RVC) as cathode, and 73% NMR yield was obtained (Entry 23). The graphite or platinum plated as cathode provided much lower yields (Entries 25 and 27).

Furthermore, similar outcomes were also obtained when changing the alkyl electrophiles to redox-active esters. The reductive cross-coupling of trifluoromethyl alkenes and redox-active esters under standard conditions gave a grati-

Table 1 Optimization of reaction conditions^a

Entry	Variation from standard conditions	Conversion ^b / % of 1a	Yield ^b / % of 4aa
1	No	81	77 (73 ^c)
2	NiCl ₂ in lieu of NiBr ₂ (diglyme)	86	76
3	Ni(acac) ₂ in lieu of NiBr ₂ (diglyme)	76	52
4	L1 in lieu of Pybox	74	40
5	L2 in lieu of Pybox	62	41
6	L3 in lieu of Pybox	52	48
7	KBr in lieu of ⁿ Bu ₄ NBr	78	72
8	LiBr in lieu of ⁿ Bu ₄ NBr	77	62
9	0.5 equiv. ⁿ Bu ₄ NBr	76	75
10	2.0 equiv. ⁿ Bu ₄ NBr	74	70
11	DMAc in lieu of DMSO	66	57
12	DMF in lieu of DMSO	78	53
13	CH ₃ CN in lieu of DMSO	88	<2
14	<i>n</i> (1a) : <i>n</i> (2a) = 1 : 2	84	70
15	<i>n</i> (1a) : <i>n</i> (2a) = 2 : 1	66	53
16	No NiBr ₂ (diglyme)	79	44
17	No electric current	41	39
18	No NiBr ₂ (diglyme), no electric current	25	15
19	Fe(+) in lieu of Zn(+)	70	55
20	Al(+) in lieu of Zn(+)	95	<2
21	Fe powder in lieu of electric current	<2	<2
22	Al powder in lieu of electric current	<2	<2
23	RVC(—) in lieu of Ni foam(—)	87	73
24	RVC(—) in lieu of Ni foam(—), no NiBr ₂ (diglyme)	82	10
25	Graphite(—) in lieu of Ni foam(—)	69	48
26	Graphite(—) in lieu of Ni foam(—), no NiBr ₂ (diglyme)	60	13
27	Pt(—) in lieu of Ni foam(—)	81	35
28	3a in lieu of 2a	89	88 (84 ^c)
29	3a in lieu of 2a , no NiBr ₂ (diglyme)	83	64
30	3a in lieu of 2a , no electric current	70	69
31	3a in lieu of 2a , no NiBr ₂ (diglyme), no electric current	69	67
32	3a in lieu of 2a , Fe(+) in lieu of Zn(+)	60	42
33	3a in lieu of 2a , Al(+) in lieu of Zn(+)	>99	31
34	3a in lieu of 2a , Fe powder in lieu of electric current	<2	<2
35	3a in lieu of 2a , Al powder in lieu of electric current	<2	<2
36	3a in lieu of 2a , <i>n</i> (3a) = 1 : 1.5	50	50
37	3a in lieu of 2a , <i>n</i> (3a) = 1 : 2	77	52
38	3a in lieu of 2a , <i>n</i> (3a) = 1 : 2.5	82	76
39	3a in lieu of 2a , <i>n</i> (3a) = 2.5 : 1	70	37

^a Reaction was performed on a 0.2-mmol scale; ^b Determined by ¹⁹F NMR analysis. Benzotrifluoride was used as an internal standard; ^c Isolated yield. Diglyme = bis(2-methoxy ethyl) ether.

giving 88% NMR yield with 84% isolated yield (Entry 28). With the light of contrastive experiments, the nickel cata-

lyst and electric current have been proved to be of value for increasing the reaction yield (Entries 29~31). Moreo-

ver, Fe or Al powder can hardly be used in reductive cross-coupling; however, Fe(+) or Al(+) can be used in lieu of Zn(+) as the sacrificial anode (Entries 32~35), indicated the electrochemical reduction process in this reaction. Finally, the addition of nickel catalyst influences the coupling efficiency and may also alter the reaction mechanism. In Xiao's previous work, it has been demonstrated that both radical pathway and organozinc reagent pathway were possible for activating redox-active

esters.^[28] A radical path was more likely when nickel catalyst was added, and the generation of organozinc reagents was reliable under transition-metal-free conditions. The equivalents of the redox-active esters were tried to be reduced, while 3 equiv. of the redox-active esters were necessary for obtaining a satisfactory coupling efficiency (Entry 28 vs. Entries 36~39).

The substrate scope of the electrochemical allylic defluorinative reductive alkylation reaction was shown in

Table 2 Scope of electrochemical allylic defluorinative reductive alkylation of trifluoromethyl alkenes^a

^a Reaction was performed on a 0.2 mmol scale. Reaction conditions are the same as those for Table 1, Entries 1 and 23. Isolated yield. ^b Reaction was performed on a 1 mmol scale under 25 mA current. Isolated yield. Bn=benzyl, Ts=tosyl, Bz=benzoyl, Bpin=pinacolato borate, Boc=tert-butoxycarbonyl, Ac=acetyl, Cy=cyclohexyl.

Table 2. A variety of alkyl radical precursors and trifluoromethyl alkenes with different synthetic useful functional groups could be readily transformed to the expected products, and modest to excellent yields (34%~98%) were obtained. Both alkyl iodides (e.g., **4aa**), alkyl bromides (e.g., **4bd**), and alkyl-substituted redox-active esters (e.g., **4cn**) were suitable substrates. Not only the primary (e.g., **4aa**) and secondary (e.g., **4cc**) but also the steric hindrance tertiary (e.g., **4bd**, **4bp**) alkyl electrophiles posed no problem. Both the cyclic (e.g., **4cc**) and the acyclic (e.g., **4be**) ones could be used. This electrochemical reduction reaction exhibited good compatibility to many functional groups, such as ether (**4bb**, **4fp**, **4bn**, and **4gd**), ester (**4be**), carbamate (**4bl**, **4bq**), and thioether (**4jd**). Heterocycles were well tolerated in the reaction, including thiophene (**4bf**), dibenzothiophene (**4cn**, **4co**), and pyridine (**4in**). This reaction could be conducted in the presence of base-sensitive groups. For instance, alkyl nitrile (**4bj**), aryl nitrile (**4bk**), and aryl boronate (**4bh**) groups posed no problem. More active functional groups, such as unprotected NH_2 group (**4kd**), terminal alkenyl group (**4bg**), aryl chloride (**4co**, **4hp**), and aryl bromide (**4bi**) were compatible. An interesting example is **4am**; alkyl bromide was proven to be less reactive than alkyl-substituted redox-active ester as the alkyl radical precursor. This chemoselectivity provided opportunities for further manipulations at the surviving alkyl carbon-halogen bonds. In another competition experiment, the standard reaction conditions were applied to a trifluoromethyl alkene substrate containing an acrylamide group (**1l**). The mono-alkylation (**4lna**, defluorinative alkylation) and di-alkylation (**4lnb**, defluorinative alkylation, and Giese addition) products were obtained. And the trifluoromethyl alkene site exhibited a much higher reactivity over the acrylamide site. The reaction of aliphatic substituted trifluoromethyl alkene (*E*)-((6,6,6-trifluorohex-4-en-1-yl)oxy)benzene with alkyl bromide **2p** was also tested under standard conditions. Unfortunately, the desired product was not observed; the aliphatic substituted trifluoromethyl alkene (*E*)-((6,6,6-trifluorohex-4-en-1-yl)oxy)benzene was recovered in 90% NMR yield. Finally, it should be pointed out that there were differences between the alkyl halides and alkyl-substituted redox-active esters when considering the laboratory synthesis methods and reagent sources; the two complement each other. In particular, many α -heteroatom alkyl halides may be very difficult and even chemically infeasible to prepare. But the corresponding alkyl-substituted redox-active esters (**4co** and **4bq**) were accomplished with extreme ease.

This reaction has been used as an efficient tool for the late-stage modification of natural products and drug molecules. As shown in Table 3, the derivatives of fructose (**4br**), amino acid (**4bs**), and dehydrocholic acid (**4bt**) performed well and delivered the desired products smoothly. With these efficient conversions as irresistible proof, it was assured that this electrochemical allylic defluorinative reductive alkylation reaction exhibited good compatibility to diverse functional groups and showed attraction in modifi-

cation of physiological activity molecules.

Table 3 Modification of biologically interesting molecules ^a

^a Reaction was performed on a 0.2 mmol scale. Reaction conditions are the same as those for Table 1, Entries 1 and 23. Isolated yield.

The possible mechanism of this electrochemical allylic defluorinative reductive alkylation reaction was studied (Scheme 1). (Bromomethyl)cyclopropane (**2u**) was used to participate in the coupling reaction, and only the ring-opening product **4bu** was obtained. For the substrate **2v** containing an intramolecular alkenyl group, under the standard conditions, a mixture of cyclized product **4bva** and linear acyclic product **4bvb** was received. The cyclized product **4bva** may be obtained through the radical cyclization process. Finally, by adding radical inhibitor 2,2,6,6-tetramethylpiperidinoxy (TEMPO) to the standard conditions, this reaction has been significantly inhibited in the presence of 0.5 equiv. of TEMPO. And R-TEMPO was isolated. Therefore, this reaction might undergo a radical pathway for activating alkyl electrophiles and was supported by the available evidence.

A proposed reaction mechanism was depicted for this electrochemical reductive coupling reaction (Figure 2). The $\text{NiBr}_2(\text{diglyme})$ catalyst was reduced to $\text{Ni}(0)$ active catalyst upon cathodic reduction at the reaction initiation step. Single-electron transfer (SET) from the $\text{Ni}(0)$ catalyst to alkyl halides or redox-active esters led to the generation of $\text{Ni}(\text{I})$ species and alkyl radicals. Next, the radical addition to trifluoromethyl alkenes afforded the α -trifluoromethyl benzylic radicals, which could be captured by $\text{Ni}(\text{I})$ (Pathway I) or reduced by cathodic reduction (Pathway II). The formed alkylnickel species or anions underwent β -fluoride elimination to deliver the desired products. The regeneration of $\text{Ni}(0)$ active catalyst was realized through cathodic reduction. However, other possible pathways in-

Reaction was performed on a 0.2 mmol scale. Reaction conditions are the same as those for Table 1, Entries 1 and 23. ^{19}F NMR yield

Scheme 1 Mechanistic probes involving Ni(I)/Ni(III) catalysis couldn't be ruled out at this stage.^[29]

Figure 2 Proposed reaction mechanism

3 Conclusions

A nickel-promoted electrochemical reductive cross-coupling reaction was developed to synthesize functionalized and substituted *gem*-difluoroalkenes. This reaction enables the combination of allylic defluorinative functionalization of trifluoromethyl alkenes, and radical pathway activation of alkyl halides or redox-active esters in an undivided cell obviates the use of stoichiometric amount metal powder or organic reductants. The mild reaction conditions led to high tolerance to many synthetically valuable functional groups and provided efficient access to biologically interesting molecules containing *gem*-difluoroethylene moiety.

4 Experimental section

4.1 General experimental information

^1H NMR (500 MHz), ^{13}C NMR (126 MHz), and ^{19}F NMR (471 MHz) spectra were recorded on a Bruker Avance 500 spectrometer in CDCl_3 . ^{19}F NMR spectra were recorded as ^{19}F experiment composite pulse decoupling (F19CPD) unless otherwise noted. High-resolution mass spectra (HRMS) were obtained with a Water XEVO G2 Q-ToF (Waters Corporation). Melting points were uncorrected and were recorded on a SG WRS-2A melting point apparatus. Column chromatographic purification of products was accomplished using forced-flow chromatography on Silica Gel (300~400 mesh). Commercially available reagents were purchased from Energy Chemical, J & K Scientific, Adamas-beta, and Sigma-Aldrich Co., Inc.

4.2 General procedure for Table 1

Nickel source (0.02 mmol, 10 mol%), ligand (0.03 mmol, 15 mol%), and electrolyte (0.2 mmol, 1.0 equiv.) were added to the electrochemical cell equipped with a stir bar. The tube was installed with a sacrificial anode and a Ni foam as the cathode and was evacuated and filled with argon (three cycles). Then, **1a** (0.2 mmol, 1.0 equiv.) and **2a** or **3a** (0.6 mmol, 3.0 equiv.) were added to 2.5 mL of solvent. Next, the solution was added to the tube and stirred at room temperature (*ca.* 25 °C) for 15 min. The reaction mixture was electrolyzed under a constant current of 5 mA for 9 h. After the reaction, benzotrifluoride was added to the solution as an internal standard, the yield was determined by ^{19}F NMR.

4.3 General procedure for Tables 2 and 3

$\text{NiBr}_2(\text{diglyme})$ (0.02 mmol, 10 mol%), Pybox (0.03 mmol, 15 mol%), and $n\text{-Bu}_4\text{NBr}$ (0.2 mmol, 1.0 equiv.) were added to the electrochemical cell equipped with a stir bar. The tube was installed with Zn as sacrificial anode and Ni foam as the cathode. Then, it was evacuated and filled with argon (three cycles). Then, **1** (0.2 mmol, 1.0 equiv.) and **2** or **3** (0.6 mmol, 3.0 equiv.) were added to 2.5 mL of DMSO. Next, the solution was added to the tube and stirred at room temperature (*ca.* 25 °C) for 15 min. The reaction mixture was electrolyzed under a constant current of 5 mA for 9 h. After the reaction, the mixture was puri-

fied by column chromatography to afford the desired product.

4.4 Nickel-promoted electrochemical reductive cross-coupling

2-((5-([1,1'-Biphenyl]-4-yl)-6,6-difluorohex-5-en-1-yl)oxy)naphthalene (**4aa**): Using 4-(3,3,3-trifluoroprop-1-en-2-yl)-1,1'-biphenyl (**1a**) and 2-(3-iodopropoxy)naphthalene (**2a**), the yield is 73% (60.4 mg as colorless oil) after column chromatography; using 4-(3,3,3-trifluoroprop-1-en-2-yl)-1,1'-biphenyl (**1a**) and 1,3-dioxoisindolin-2-yl 4-(naphthalen-2-yloxy)butanoate (**3a**), the yield is 84% (69.8 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.89~7.73 (m, 3H), 7.73~7.59 (m, 4H), 7.58~7.34 (m, 7H), 7.24~7.12 (m, 2H), 4.11 (t, $J=6.4$ Hz, 2H), 2.62 (tt, $J=7.6, 2.4$ Hz, 2H), 1.99~1.87 (m, 2H), 1.77~1.63 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ : 157.1, 153.9 (dd, $J=289.8, 288.0$ Hz), 140.6, 140.2, 134.7, 132.6, 129.5, 129.1, 128.9, 128.7 (dd, $J=3.4, 3.4$ Hz), 127.8, 127.5, 127.2, 127.1, 126.8, 126.4, 123.6, 119.1, 106.7, 92.0 (dd, $J=19.3, 15.2$ Hz), 67.5, 28.6, 27.3, 24.4 (dd, $J=2.5, 2.5$ Hz); ^{19}F NMR (471 MHz, CDCl_3) δ : -90.70 (d, $J=43.6$ Hz), -90.80 (d, $J=43.3$ Hz); ESI-HRMS calcd for $\text{C}_{28}\text{H}_{25}\text{F}_2\text{O}$ ($\text{M}+\text{H}$) $^+$ 415.1868, found 415.1872.

(4-(4-(Benzyloxy)phenyl)-5,5-difluoropent-4-ene-1,1-diyl)dibenzene (**4bb**): The yield is 36% (31.5 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.45~7.29 (m, 5H), 7.27~7.20 (m, 4H), 7.19~7.12 (m, 8H), 6.98~6.88 (m, 2H), 5.05 (s, 2H), 3.87 (t, $J=7.8$ Hz, 1H), 2.32 (tt, $J=8.1, 2.4$ Hz, 2H), 2.16~2.02 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.0, 153.5 (dd, $J=289.5, 286.5$ Hz), 144.6, 137.0, 129.5 (dd, $J=3.3, 3.3$ Hz), 128.8, 128.6, 128.2, 127.9, 127.6, 126.4, 126.0 (dd, $J=3.2, 3.2$ Hz), 115.0, 91.7 (dd, $J=21.7, 13.3$ Hz), 70.2, 51.0, 33.9 (dd, $J=2.1, 2.1$ Hz), 26.4; ^{19}F NMR (471 MHz, CDCl_3) δ : -91.96 (d, $J=45.2$ Hz), -92.27 (d, $J=45.5$ Hz); ESI-HRMS calcd for $\text{C}_{30}\text{H}_{27}\text{F}_2\text{O}$ ($\text{M}+\text{H}$) $^+$ 441.2024, found 441.2043.

4-(2-(Dibenzo[*b,d*]thiophen-4-yl)-3,3-difluoroallyl)-1-tosylpiperidine (**4cc**): The yield is 56% (56.2 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 8.16~8.05 (m, 2H), 7.87~7.82 (m, 1H), 7.60~7.54 (m, 2H), 7.48~7.42 (m, 3H), 7.28~7.20 (m, 3H), 3.77~3.67 (m, 2H), 2.48~2.40 (m, 2H), 2.36 (s, 3H), 2.06 (td, $J=12.0, 2.7$ Hz, 2H), 1.81~1.74 (m, 2H), 1.42~1.31 (m, 2H), 1.16~1.05 (m, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ : 153.7 (dd, $J=290.8, 289.8$ Hz), 143.4, 139.7 (dd, $J=2.0, 2.0$ Hz), 139.1, 136.2, 135.7, 133.2, 129.7, 128.6 (dd, $J=1.3, 1.3$ Hz), 127.8, 127.4 (dd, $J=1.3, 1.3$ Hz), 127.2, 124.9, 124.7, 122.8, 121.9, 121.2, 89.6 (dd, $J=23.4, 16.1$ Hz), 46.3, 34.8, 33.7 (dd, $J=2.5, 2.5$ Hz), 31.4, 21.6; ^{19}F NMR (471 MHz, CDCl_3) δ : -85.37 (d, $J=36.4$ Hz), -90.40 (d, $J=37.3$ Hz); ESI-HRMS calcd for $\text{C}_{27}\text{H}_{26}\text{F}_2\text{NO}_2\text{S}_2$ ($\text{M}+\text{H}$) $^+$ 498.1368, found 498.1373. The NMR data were consistent with those reported in previous literature.^[23c]

1-(Benzyloxy)-4-(1,1-difluoro-4,4-dimethyl-6-phenylhex-1-en-2-yl)benzene (**4bd**): The yield is 97% (78.5 mg as colorless oil) after column chromatography. ^1H NMR (400 MHz, CDCl_3) δ : 7.48~7.30 (m, 5H), 7.26~7.18 (m, 4H), 7.17~7.10 (m, 1H), 7.05~6.89 (m, 4H), 5.05 (s, 2H), 2.53~2.43 (m, 2H), 2.38 (t, $J=2.4$ Hz, 2H), 1.50~1.36 (m, 2H), 0.86 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ : 158.0, 154.5 (dd, $J=287.4, 286.5$ Hz), 143.2, 137.0, 129.8 (dd, $J=2.8, 2.8$ Hz), 128.7, 128.4, 128.4, 128.2, 128.1 (dd, $J=4.8, 2.6$ Hz), 127.6, 125.7, 114.9, 90.3 (dd, $J=21.3, 13.6$ Hz), 70.2, 44.5, 39.2, 35.5 (dd, $J=2.6, 2.6$ Hz), 30.8, 27.6; ^{19}F NMR (376 MHz, CDCl_3) δ : -90.17 (d, $J=42.5$ Hz), -92.56 (d, $J=42.9$ Hz); ESI-HRMS calcd for $\text{C}_{27}\text{H}_{28}\text{F}_2\text{ONa}$ ($\text{M}+\text{Na}$) $^+$ 429.2000, found 429.2012.

4-(4-(Benzyloxy)phenyl)-5,5-difluoro-2-methylpent-4-en-1-yl benzoate (**4be**): The yield is 85% (71.7 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 8.10~7.94 (m, 2H), 7.59~7.51 (m, 1H), 7.47~7.35 (m, 6H), 7.35~7.29 (m, 1H), 7.28~7.22 (m, 2H), 6.99~6.91 (m, 2H), 5.04 (s, 2H), 4.25~4.06 (m, 2H), 2.63~2.30 (m, 2H), 2.10~1.86 (m, 1H), 1.01 (d, $J=6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ : 166.6, 158.1, 154.1 (dd, $J=288.1, 288.1$ Hz), 137.0, 133.0, 130.4, 129.6, 129.5 (dd, $J=3.2, 3.2$ Hz), 128.7, 128.5, 128.1, 127.6, 125.8, 115.0, 90.2 (dd, $J=17.8, 17.8$ Hz), 70.1, 68.9, 31.6, 31.3 (dd, $J=2.5, 2.5$ Hz), 16.7; ^{19}F NMR (471 MHz, CDCl_3) δ : -91.48; ESI-HRMS calcd for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{O}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 445.1586, found 445.1591.

5-(4-(Benzyloxy)phenyl)-6,6-difluoro-3-methylhex-5-en-1-yl thiophene-2-carboxylate (**4bf**): The yield is 72% (63.9 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.75~7.65 (m, 1H), 7.56~7.48 (m, 1H), 7.47~7.29 (m, 5H), 7.25~7.18 (m, 2H), 7.10~7.03 (m, 1H), 6.96~6.87 (m, 2H), 5.04 (s, 2H), 4.39~4.21 (m, 2H), 2.48~2.23 (m, 1H), 1.86~1.77 (m, 1H), 1.72~1.63 (m, 1H), 1.61~1.52 (m, 1H), 0.95 (d, $J=6.7$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ : 162.3, 158.1, 154.1 (dd, $J=287.7, 287.7$ Hz), 137.0, 134.1, 133.4, 132.4, 129.5 (dd, $J=3.2, 3.2$ Hz), 128.7, 128.2, 127.8, 127.6, 126.0, 114.9, 90.7 (dd, $J=17.5, 17.5$ Hz), 70.1, 63.3, 35.1, 35.0, 28.2 (dd, $J=2.5, 2.5$ Hz), 19.3; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.03; ESI-HRMS calcd for $\text{C}_{25}\text{H}_{24}\text{F}_2\text{O}_3\text{SNa}$ ($\text{M}+\text{Na}$) $^+$ 465.1306, found 465.1307.

1-(Benzyloxy)-4-(1,1-difluoro-4,4-dimethyl-6-(4-(pent-4-en-1-yloxy)phenyl)hex-1-en-2-yl)benzene (**4bg**): The yield is 90% (88.1 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.50~7.35 (m, 5H), 7.30~7.25 (m, 2H), 7.01~6.96 (m, 2H), 6.93~6.87 (m, 2H), 6.83~6.77 (m, 2H), 5.95~5.82 (m, 1H), 5.13~4.99 (m, 4H), 3.95 (t, $J=6.5$ Hz, 2H), 2.48~2.36 (m, 4H), 2.30~2.22 (m, 2H), 1.93~1.84 (m, 2H), 1.47~1.40 (m, 2H), 0.88 (s, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.0, 157.2, 154.5 (dd, $J=287.8, 286.4$ Hz), 138.0, 137.0, 135.1, 129.8 (dd, $J=2.8, 2.8$ Hz), 129.5 (dd, $J=3.2, 3.2$ Hz), 129.2, 128.7, 128.1, 127.6, 115.2, 114.9, 114.4, 90.4 (dd, $J=21.4, 13.6$ Hz), 70.2, 67.3, 44.8, 39.2, 35.4 (dd, $J=2.5, 2.5$ Hz), 30.3, 29.8, 28.6, 27.6; ^{19}F NMR (471 MHz,

CDCl_3) δ : -90.22 (d, $J=43.4$ Hz), -92.60 (d, $J=43.3$ Hz); ESI-HRMS calcd for $\text{C}_{32}\text{H}_{37}\text{F}_2\text{O}_2$ ($\text{M} + \text{H}$) $^+$ 491.2756, found 491.2757.

8-(4-(Benzyloxy)phenyl)-9,9-difluoronon-8-en-1-yl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**4bh**): The yield is 60% (70.7 mg as colorless oil) after column chromatography. ^1H NMR (400 MHz, CDCl_3) δ : 8.07~7.95 (m, 2H), 7.92~7.80 (m, 2H), 7.50~7.30 (m, 5H), 7.25~7.17 (m, 2H), 7.03~6.89 (m, 2H), 5.06 (s, 2H), 4.30 (t, $J=6.7$ Hz, 2H), 2.45~2.27 (m, 2H), 1.80~1.69 (m, 2H), 1.42~1.29 (m, 20H); ^{13}C NMR (101 MHz, CDCl_3) δ : 166.8, 158.0, 153.6 (dd, $J=287.4$, 287.4 Hz), 137.0, 134.8, 132.8, 129.5 (dd, $J=3.3$, 3.3 Hz), 128.7, 128.7, 128.1, 127.6, 126.3, 114.9, 91.9 (dd, $J=17.4$, 17.4 Hz), 84.3, 70.1, 65.3, 29.1, 29.0, 28.7, 27.7, 27.7, 26.1, 25.0; ^{19}F NMR (376 MHz, CDCl_3) δ : -92.75 ; ^{11}B NMR (160 MHz, CDCl_3) δ : 30.46; ESI-HRMS calcd for $\text{C}_{35}\text{H}_{42}\text{BF}_2\text{O}_5$ ($\text{M} + \text{H}$) $^+$ 591.3088, found 591.3098.

1-(Benzyloxy)-4-(6-(4-bromophenyl)-1,1-difluorohex-1-en-2-yl)benzene (**4bi**): The yield is 52% (47.7 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.49~7.31 (m, 7H), 7.23~7.18 (m, 2H), 7.03~6.92 (m, 4H), 5.08 (s, 2H), 2.58~2.48 (m, 2H), 2.45~2.32 (m, 2H), 1.66~1.53 (m, 2H), 1.45~1.33 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.0, 153.6 (dd, $J=286.4$, 285.9 Hz), 141.4, 137.0, 131.4, 130.3, 129.5 (dd, $J=3.3$, 3.3 Hz), 128.8, 128.2, 127.6, 126.1 (dd, $J=2.1$, 2.1 Hz), 119.5, 114.9, 91.7 (dd, $J=20.9$, 13.7 Hz), 70.2, 35.0, 30.6, 27.5, 27.1; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.42 (d, $J=46.6$ Hz), -92.56 (d, $J=46.4$ Hz); ESI-HRMS calcd for $\text{C}_{25}\text{H}_{23}\text{BrF}_2\text{ONa}$ ($\text{M} + \text{Na}$) $^+$ 479.0793, found 479.0791.

7-(4-(Benzyloxy)phenyl)-8,8-difluorooct-7-enenitrile (**4bj**): The yield is 45% (30.5 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.47~7.32 (m, 5H), 7.24~7.19 (m, 2H), 7.01~6.94 (m, 2H), 5.08 (s, 2H), 2.39 (tt, $J=7.2$, 2.4 Hz, 2H), 2.29 (t, $J=7.1$ Hz, 2H), 1.67~1.58 (m, 2H), 1.49~1.35 (m, 4H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.1, 153.6 (dd, $J=289.3$, 286.2 Hz), 137.0, 129.5 (dd, $J=3.3$, 3.3 Hz), 128.7, 128.2, 127.6, 125.9 (dd, $J=2.1$, 2.1 Hz), 119.7, 115.0, 91.5 (dd, $J=20.9$, 14.3 Hz), 70.2, 28.0, 27.4, 26.9 (dd, $J=2.5$, 2.5 Hz), 25.2, 17.2; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.26 (d, $J=45.9$ Hz), -92.42 (d, $J=46.0$ Hz); ESI-HRMS calcd for $\text{C}_{21}\text{H}_{21}\text{F}_2\text{NONa}$ ($\text{M} + \text{Na}$) $^+$ 364.1483, found 364.1485.

4-((8-(4-(Benzyloxy)phenyl)-9,9-difluoronon-8-en-1-yl)oxy)benzonitrile (**4bk**): The yield is 56% (51.6 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.61~7.53 (m, 2H), 7.48~7.29 (m, 5H), 7.25~7.19 (m, 2H), 7.00~6.88 (m, 4H), 5.07 (s, 2H), 3.97 (t, $J=6.5$ Hz, 2H), 2.45~2.26 (m, 2H), 1.82~1.73 (m, 2H), 1.45~1.31 (m, 8H); ^{13}C NMR (126 MHz, CDCl_3) δ : 162.5, 158.0, 153.6 (dd, $J=288.3$, 286.5 Hz), 137.0, 134.0, 129.5 (dd, $J=3.0$, 3.0 Hz), 128.7, 128.1, 127.6, 126.3 (dd, $J=2.4$, 2.4 Hz), 119.4, 115.3, 114.9, 103.7, 91.9 (dd, $J=19.7$, 14.9 Hz), 70.1, 68.4, 29.0, 29.0,

28.9, 27.7, 27.7 (dd, $J=2.2$, 2.2 Hz), 25.9; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.63 (d, $J=46.9$ Hz), -92.74 (d, $J=46.8$ Hz); ESI-HRMS calcd for $\text{C}_{29}\text{H}_{29}\text{F}_2\text{NO}_2\text{Na}$ ($\text{M} + \text{Na}$) $^+$ 484.2059, found 484.2064.

tert-Butyl 4-(4-(4-(benzyloxy)phenyl)-5,5-difluoropent-4-en-1-yl)phenyl carbamate (**4bl**): The yield is 84% (80.1 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.47~7.32 (m, 5H), 7.26~7.18 (m, 4H), 7.07~7.01 (m, 2H), 7.00~6.93 (m, 2H), 6.48 (s, 1H), 5.07 (s, 2H), 2.56 (t, $J=7.7$ Hz, 2H), 2.47~2.33 (m, 2H), 1.70~1.62 (m, 2H), 1.53 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.0, 153.4 (dd, $J=287.2$, 216.7 Hz), 137.0, 136.7, 136.3, 129.5 (dd, $J=3.2$, 3.2 Hz), 128.9, 128.7, 128.1, 127.6, 126.1, 118.8, 114.9, 91.7 (dd, $J=16.8$, 16.8 Hz), 80.4, 70.1, 34.6, 29.5 (dd, $J=2.7$, 2.7 Hz), 28.5, 27.3; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.34 ; ESI-HRMS calcd for $\text{C}_{29}\text{H}_{31}\text{F}_2\text{NO}_3\text{Na}$ ($\text{M} + \text{Na}$) $^+$ 502.2164, found 502.2165.

4-(8-Bromo-1,1-difluorooct-1-en-2-yl)-1,1'-biphenyl (**4am**): The yield is 61% (46.1 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.61 (td, $J=7.3$, 6.6, 1.8 Hz, 4H), 7.46 (t, $J=7.6$ Hz, 2H), 7.42~7.33 (m, 3H), 3.39 (t, $J=6.8$ Hz, 2H), 2.45 (tt, $J=7.8$, 2.4 Hz, 2H), 1.89~1.78 (m, 2H), 1.48~1.30 (m, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ : 153.8 (dd, $J=288.1$, 287.0 Hz), 140.7, 140.2, 132.8 (dd, $J=2.7$, 2.7 Hz), 128.9, 128.7 (dd, $J=3.4$, 3.4 Hz), 127.5, 127.3, 127.1, 92.1 (dd, $J=20.2$, 14.3 Hz), 34.0, 32.8, 28.2, 27.9, 27.7 (dd, $J=2.4$, 2.4 Hz), 27.5; ^{19}F NMR (471 MHz, CDCl_3) δ : -91.15 (d, $J=43.5$ Hz), -91.26 (d, $J=43.4$ Hz); ESI-HRMS calcd for $\text{C}_{20}\text{H}_{22}\text{BrF}_2$ ($\text{M} + \text{H}$) $^+$ 379.0867, found 379.0865.

4-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)dibenzo[b,d]thiophene (**4cn**): The yield is 98% (67.0 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 8.21~8.09 (m, 2H), 7.93~7.80 (m, 1H), 7.53~7.43 (m, 3H), 7.38~7.29 (m, 1H), 2.43 (dt, $J=7.2$, 2.3 Hz, 2H), 1.85~1.75 (m, 2H), 1.73~1.59 (m, 3H), 1.28~1.20 (m, 1H), 1.19~1.08 (m, 3H), 1.04~0.94 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ : 153.7 (dd, $J=289.3$, 289.3 Hz), 140.0, 139.4, 136.1, 135.9, 129.5 (dd, $J=1.5$, 1.5 Hz), 127.6 (dd, $J=1.4$, 1.4 Hz), 127.0, 124.8, 124.5, 122.9, 121.8, 121.0, 90.4 (dd, $J=23.9$, 15.2 Hz), 36.1 (dd, $J=2.6$, 2.6 Hz), 35.8, 33.2, 26.5, 26.2; ^{19}F NMR (471 MHz, CDCl_3) δ : -86.80 (d, $J=39.2$ Hz), -91.51 (d, $J=39.1$ Hz); ESI-HRMS calcd for $\text{C}_{21}\text{H}_{20}\text{F}_2\text{SNa}$ ($\text{M} + \text{Na}$) $^+$ 365.1146, found 365.1141.

4-(4-(2-Chlorophenoxy)-1,1-difluoropent-1-en-2-yl)dibenzo[b,d]thiophene (**4co**): The yield is 68% (56.6 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 8.19~8.07 (m, 2H), 7.88~7.77 (m, 1H), 7.51~7.41 (m, 3H), 7.37~7.31 (m, 1H), 7.31~7.27 (m, 1H), 7.05~6.98 (m, 1H), 6.86~6.80 (m, 1H), 6.64~6.57 (m, 1H), 4.39~4.23 (m, 1H), 3.14~2.78 (m, 2H), 1.39 (d, $J=6.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ : 154.4 (dd, $J=291.5$, 290.2 Hz), 153.4, 139.9, 139.2, 136.2, 135.8, 130.5, 128.3 (dd, $J=4.9$, 1.3 Hz), 127.9 (dd, $J=1.3$, 1.3 Hz), 127.5, 127.1, 124.9, 124.6, 124.1, 122.9, 121.9, 121.5,

121.3, 115.1, 88.5 (dd, $J=23.2$, 18.1 Hz), 73.2 (dd, $J=3.1$, 3.1 Hz), 35.0, 19.7; ^{19}F NMR (471 MHz, CDCl_3) δ : -84.91 (d, $J=33.6$ Hz), -89.52 (d, $J=34.1$ Hz); ESI-HRMS calcd for $\text{C}_{23}\text{H}_{17}\text{ClF}_2\text{OSNa}$ ($\text{M}+\text{Na}$) $^+$ 437.0549, found 437.0534.

1-(Benzyloxy)-4-(1,1-difluoro-4,4-dimethylpent-1-en-2-yl)benzene (**4bp**): The yield is 86% (54.2 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.48~7.32 (m, 5H), 7.27~7.22 (m, 2H), 7.00~6.92 (m, 2H), 5.07 (s, 2H), 2.38~2.28 (m, 2H), 0.83 (s, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ : 157.9, 154.5 (dd, $J=287.4$, 286.4 Hz), 137.1, 129.7 (dd, $J=3.2$, 2.6 Hz), 128.7, 128.1, 127.7, 114.8, 90.7 (dd, $J=21.6$, 12.9 Hz), 70.2, 41.3, 32.8 (dd, $J=2.1$, 2.1 Hz), 29.9; ^{19}F NMR (471 MHz, CDCl_3) δ : -90.64 (d, $J=43.3$ Hz), -93.17 (d, $J=43.3$ Hz); ESI-HRMS calcd for $\text{C}_{20}\text{H}_{22}\text{F}_2\text{ONa}$ ($\text{M}+\text{Na}$) $^+$ 339.1531, found 339.1561.

N-(4-(4-(Benzyloxy)phenyl)-5,5-difluoro-1-phenylpent-4-en-2-yl)acetamide (**4bq**): The yield is 60% (50.2 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.45~7.26 (m, 7H), 7.24~7.16 (m, 3H), 7.12~7.07 (m, 2H), 6.98~6.92 (m, 2H), 5.13~5.07 (m, 1H), 5.06 (s, 2H), 4.26~4.14 (m, 1H), 2.84~2.70 (m, 2H), 2.59~2.48 (m, 2H), 1.76 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ : 169.7, 158.2, 154.3 (dd, $J=285.9$, 285.9 Hz), 137.6, 137.0, 129.6 (dd, $J=3.2$, 3.2 Hz), 129.3, 128.8, 128.6, 128.2, 127.6, 126.7, 125.5 (dd, $J=3.7$, 3.7 Hz), 115.1, 89.4 (dd, $J=21.4$, 14.9 Hz), 70.1, 49.3 (dd, $J=2.4$, 2.4 Hz), 40.3, 32.5, 23.4; ^{19}F NMR (471 MHz, CDCl_3) δ : -90.82 (d, $J=43.4$ Hz), -91.25 (d, $J=43.4$ Hz); ESI-HRMS calcd for $\text{C}_{26}\text{H}_{25}\text{F}_2\text{NO}_2\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 444.1746, found 444.1754.

1-(*tert*-Butyl)-4-(1,1-difluoro-4,4-dimethylpent-1-en-2-yl)benzene (**4dp**): The yield is 84% (44.5 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.38~7.28 (m, 2H), 7.25~7.19 (m, 2H), 2.36~2.27 (m, 2H), 1.31 (s, 9H), 0.80 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ : 154.5 (dd, $J=287.1$, 287.1 Hz), 150.0, 132.5 (dd, $J=2.8$, 2.4 Hz), 128.1 (dd, $J=2.7$, 2.7 Hz), 125.3, 90.9 (dd, $J=34.8$, 12.6 Hz), 41.2, 34.6, 32.8, 31.5, 29.9; ^{19}F NMR (471 MHz, CDCl_3) δ : -90.10 (dd, $J=42.6$, 4.0 Hz), -92.70 (dd, $J=41.9$, 4.6 Hz); ESI-HRMS calcd for $\text{C}_{17}\text{H}_{25}\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 267.1919, found 267.1931. The NMR data were consistent with those reported in previous literature.^[12]

2-(1,1-Difluoro-4,4-dimethylpent-1-en-2-yl)naphthalene (**4ep**): The yield is 60% (31.0 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.88~7.75 (m, 4H), 7.53~7.42 (m, 3H), 2.47 (t, $J=2.5$ Hz, 2H), 0.84 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ : 154.8 (dd, $J=290.6$, 287.8 Hz), 133.4, 133.2 (dd, $J=4.8$, 2.9 Hz), 132.5, 128.0, 127.8, 127.5 (dd, $J=3.0$, 3.0 Hz), 126.7 (dd, $J=2.8$, 2.8 Hz), 126.3, 126.1, 91.4 (dd, $J=21.7$, 12.7 Hz), 41.4, 33.0 (dd, $J=2.5$, 2.5 Hz), 29.9; ^{19}F NMR (471 MHz, CDCl_3) δ : -89.24 (d, $J=40.1$ Hz), -92.03 (d, $J=40.2$ Hz); ESI-HRMS calcd for $\text{C}_{17}\text{H}_{19}\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 261.1449, found 261.1453. The NMR data were consistent

with those reported in previous literature.^[30]

1-(1,1-Difluoro-4,4-dimethylpent-1-en-2-yl)-4-methoxybenzene (**4fp**): On a 0.2 mmol scale, the yield is 80% (38.4 mg as colorless oil) after column chromatography; on a 1 mmol scale, the yield is 78% (188 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.24~7.20 (m, 2H), 6.91~6.82 (m, 2H), 3.81 (s, 3H), 2.29 (t, $J=2.6$ Hz, 2H), 0.80 (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.6 (dd, $J=288.9$, 287.5 Hz), 129.7 (dd, $J=2.8$, 2.8 Hz), 127.9 (dd, $J=4.5$, 2.7 Hz), 123.6, 113.9, 90.8 (dd, $J=16.1$, 3.1 Hz), 55.4, 41.4, 32.8 (dd, $J=2.4$, 2.4 Hz), 29.9; ^{19}F NMR (471 MHz, CDCl_3) δ : -90.79 (d, $J=43.4$ Hz), -93.32 (d, $J=43.4$ Hz); ESI-HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{F}_2\text{O}$ ($\text{M}+\text{H}$) $^+$ 241.1398, found 241.1380. The NMR data were consistent with those reported in previous literature.^[12]

1-(Benzyloxy)-4-(3-cyclohexyl-1,1-difluoroprop-1-en-2-yl)benzene (**4bn**): The yield is 58% (39.9 mg as white solid) after column chromatography. m.p. 94~96 °C; ^1H NMR (400 MHz, CDCl_3) δ : 7.53~7.31 (m, 5H), 7.26~7.23 (m, 2H), 7.06~6.92 (m, 2H), 5.08 (s, 2H), 2.25 (dt, $J=7.3$, 2.5 Hz, 2H), 1.75~1.59 (m, 5H), 1.32~1.21 (m, 1H), 1.18~1.06 (m, 3H), 1.02~0.87 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ : 157.9, 154.0 (dd, $J=289.0$, 285.4 Hz), 137.1, 129.5 (dd, $J=3.2$, 3.2 Hz), 128.8, 128.2, 127.7, 126.7 (dd, $J=3.0$, 3.0 Hz), 114.8, 90.6 (dd, $J=22.0$, 12.9 Hz), 70.1, 35.8 (dd, $J=2.0$, 2.0 Hz), 35.4, 33.0, 26.6, 26.2; ^{19}F NMR (376 MHz, CDCl_3) δ : -92.18 (d, $J=46.3$ Hz), -92.61 (d, $J=46.4$ Hz); ESI-HRMS calcd for $\text{C}_{22}\text{H}_{24}\text{F}_2\text{O}$ ($\text{M}+\text{H}$) $^+$ 343.1868, found 343.1878. The NMR data were consistent with those reported in previous literature.^[21]

1-(1,1-Difluoro-4,4-dimethyl-6-phenylhex-1-en-2-yl)-4-phenoxybenzene (**4gd**): The yield is 98% (77.1 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.32~7.27 (m, 2H), 7.26~7.17 (m, 4H), 7.14~7.07 (m, 2H), 7.01~6.92 (m, 6H), 2.48~2.40 (m, 2H), 2.39~2.34 (m, 2H), 1.45~1.36 (m, 2H), 0.85 (s, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ : 157.0, 156.5, 154.5 (dd, $J=287.6$, 287.2 Hz), 143.1, 130.4 (dd, $J=4.8$, 2.5 Hz), 130.0 (dd, $J=2.7$, 2.7 Hz), 129.9, 128.4, 128.3, 125.7, 123.6, 119.3, 118.6, 90.3 (dd, $J=21.7$, 13.5 Hz), 44.5, 39.3, 35.5 (dd, $J=2.6$, 2.6 Hz), 30.8, 27.6; ^{19}F NMR (471 MHz, CDCl_3) δ : -89.61 (d, $J=41.6$ Hz), -92.00 (d, $J=41.7$ Hz); ESI-HRMS calcd for $\text{C}_{26}\text{H}_{26}\text{F}_2\text{O}$ (M) $^+$ 392.1952, found 392.1967.

1-Chloro-4-(1,1-difluoro-4,4-dimethylpent-1-en-2-yl)benzene (**4hp**): The yield is 66% (32.1 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.36~7.27 (m, 2H), 7.29~7.22 (m, 2H), 2.37~2.27 (m, 2H), 0.86~0.75 (m, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ : 154.5 (dd, $J=290.6$, 287.8 Hz), 134.3, 132.9, 129.9 (dd, $J=3.1$, 2.6 Hz), 128.7, 90.5 (dd, $J=22.4$, 12.7 Hz), 41.3, 32.9 (dd, $J=2.7$, 2.2 Hz), 29.9; ^{19}F NMR (471 MHz, CDCl_3) δ : -88.99 (dd, $J=39.5$, 9.0 Hz), -91.64 (dd, $J=39.5$, 9.0 Hz); ESI-HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{ClF}_2$ (M) $^+$ 244.0825, found 244.0851. The NMR data were consistent with those reported in previous literature.

ture.^[12]

5-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)-2-methoxy-pyridine (**4in**): The yield is 79% (42.0 mg as colorless oil) after column chromatography. ¹H NMR (500 MHz, CDCl₃) δ : 8.16~8.05 (m, 1H), 7.53~7.48 (m, 1H), 6.78~6.71 (m, 1H), 3.94 (s, 3H), 2.22 (dt, $J=7.2, 2.4$ Hz, 2H), 1.71~1.60 (m, 5H), 1.31~1.20 (m, 1H), 1.15~1.06 (m, 3H), 0.99~0.84 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ : 163.3, 154.2 (dd, $J=289.9, 286.7$ Hz), 146.4 (dd, $J=3.6, 3.6$ Hz), 138.6 (dd, $J=3.3, 3.3$ Hz), 123.0 (dd, $J=3.6, 3.6$ Hz), 110.8, 88.2 (dd, $J=23.7, 12.9$ Hz), 53.6, 35.8 (dd, $J=2.4, 2.4$ Hz), 35.1, 33.0, 30.3, 27.0, 26.5, 26.2; ¹⁹F NMR (471 MHz, CDCl₃) δ : -90.73 (d, $J=44.2$ Hz), -91.50 (d, $J=43.9$ Hz); ESI-HRMS calcd for C₁₅H₂₀F₂NO (M+H)⁺ 268.1507, found 268.1513. The NMR data were consistent with those reported in previous literature.^[22]

(4-(1,1-Difluoro-4,4-dimethyl-6-phenylhex-1-en-2-yl)phenyl)(methyl)sulfane (**4jd**): The yield is 90% (62.6 mg as colorless oil) after column chromatography. ¹H NMR (500 MHz, CDCl₃) δ : 7.25~7.13 (m, 7H), 7.01~6.89 (m, 2H), 2.50 (s, 3H), 2.49~2.44 (m, 2H), 2.41 (t, $J=2.5$ Hz, 2H), 1.48~1.41 (m, 2H), 0.88 (s, 6H); ¹³C NMR (126 MHz, CDCl₃) δ : 154.5 (dd, $J=289.8, 287.9$ Hz), 143.1, 137.6, 132.3 (dd, $J=2.7, 2.7$ Hz), 129.1 (dd, $J=2.8, 2.8$ Hz), 128.4, 128.3, 126.6, 125.7, 90.4 (dd, $J=21.6, 13.4$ Hz), 44.5, 39.0, 35.5 (dd, $J=2.4, 2.4$ Hz), 30.7, 27.6, 15.8; ¹⁹F NMR (471 MHz, CDCl₃) δ : -89.22 (d, $J=40.7$ Hz), -91.65 (d, $J=40.7$ Hz); ESI-HRMS calcd for C₂₁H₂₅F₂S (M+H)⁺ 347.1640, found 347.1646.

2-(1,1-Difluoro-4,4-dimethyl-6-phenylhex-1-en-2-yl)-aniline (**4kd**): The yield is 34% (21.2 mg as brown oil) after column chromatography. ¹H NMR (500 MHz, CDCl₃) δ : 7.23~7.09 (m, 5H), 6.99~6.86 (m, 2H), 6.84~6.67 (m, 2H), 3.57 (brs, 2H), 2.55~2.23 (m, 4H), 1.48~1.41 (m, 2H), 0.93 (s, 6H); ¹³C NMR (126 MHz, CDCl₃) δ : 154.0 (dd, $J=288.6, 288.6$ Hz), 144.1, 143.5, 130.8 (dd, $J=1.0, 1.0$ Hz), 129.1, 128.7, 128.6, 125.9, 120.7, 119.0, 116.5, 87.7 (dd, $J=20.9, 16.3$ Hz), 44.6, 39.2, 35.7 (dd, $J=2.5, 2.5$ Hz), 31.1, 27.9; ¹⁹F NMR (471 MHz, CDCl₃) δ : -86.86 (d, $J=37.7$ Hz), -89.46 (d, $J=37.4$ Hz); ESI-HRMS calcd for C₂₀H₂₄F₂N (M+H)⁺ 316.1871, found 316.1879.

N-(3-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)phenyl)-methacrylamide (**4lna**): The yield is 70% (44.5 mg as white solid) after column chromatography. m.p. 88~90 °C; ¹H NMR (500 MHz, CDCl₃) δ : 7.59 (s, 1H), 7.55~7.47 (m, 2H), 7.36~7.26 (m, 1H), 7.08~7.03 (m, 1H), 5.80 (s, 1H), 5.46 (s, 1H), 2.26 (dt, $J=7.4, 2.5$ Hz, 2H), 2.06 (s, 3H), 1.71~1.60 (m, 5H), 1.31~1.20 (m, 1H), 1.17~1.05 (m, 3H), 0.96~0.85 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ : 166.8, 154.1 (dd, $J=290.1, 286.4$ Hz), 141.0, 138.0, 135.2 (dd, $J=4.6, 2.8$ Hz), 129.1, 124.5 (dd, $J=3.1, 3.1$ Hz), 120.0, 120.0 (dd, $J=3.4, 3.4$ Hz), 119.0, 91.1 (dd, $J=22.3, 12.6$ Hz), 35.8 (dd, $J=2.3, 2.3$ Hz), 35.3, 33.0, 26.5, 26.2, 18.9; ¹⁹F NMR (471 MHz, CDCl₃) δ : -90.98 (d, $J=42.8$ Hz), -91.24 (d, $J=43.1$ Hz);

ESI-HRMS calcd for C₁₉H₂₄F₂NO (M+H)⁺ 320.1820, found 320.1824.

3-Cyclohexyl-*N*-(3-(3-cyclohexyl-1,1-difluoroprop-1-en-2-yl)phenyl)-2-methylpropanamide (**4lnb**): The yield is 11% (8.7 mg as colorless oil) after column chromatography. ¹H NMR (500 MHz, CDCl₃) δ : 7.53~7.48 (m, 1H), 7.43 (s, 1H), 7.33~7.26 (m, 1H), 7.18~7.09 (m, 1H), 7.08~6.98 (m, 1H), 2.50~2.41 (m, 1H), 2.28~2.21 (m, 2H), 1.75~1.59 (m, 10H), 1.35~1.07 (m, 13H), 0.96~0.83 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ : 175.3, 154.1 (dd, $J=286.8, 286.2$ Hz), 138.3, 135.2, 129.1, 124.3, 119.7, 118.9, 91.1 (dd, $J=12.3, 9.1$ Hz), 42.1, 40.0, 35.8 (dd, $J=2.2, 1.5$ Hz), 35.5, 35.3, 33.7, 33.5, 33.0, 26.7, 26.5, 26.4, 26.3, 26.2, 18.5; ¹⁹F NMR (471 MHz, CDCl₃) δ : -91.02 (d, $J=43.3$ Hz), -91.24 (d, $J=43.3$ Hz); ESI-HRMS calcd for C₂₅H₃₆F₂NO (M+H)⁺ 404.2759, found 404.2763.

(3*aS*,5*aR*,8*aR*,8*bS*)-3*a*-(3-(4-(Benzyloxy)phenyl)-4,4-difluorobut-3-en-1-yl)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran (**4br**): The yield is 71% (71.3 mg as colorless oil) after column chromatography. ¹H NMR (500 MHz, CDCl₃) δ : 7.46~7.29 (m, 5H), 7.30~7.25 (m, 2H), 6.99~6.89 (m, 2H), 5.06 (s, 2H), 4.54 (dd, $J=8.0, 2.5$ Hz, 1H), 4.24~4.17 (m, 1H), 4.03 (d, $J=2.5$ Hz, 1H), 3.88~3.79 (m, 1H), 3.73 (d, $J=12.9$ Hz, 1H), 2.80~2.56 (m, 2H), 1.93 (td, $J=13.0, 4.7$ Hz, 1H), 1.73 (td, $J=13.0, 4.7$ Hz, 1H), 1.52 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ : 157.9, 153.4 (dd, $J=287.5, 287.1$ Hz), 137.0, 129.3 (dd, $J=3.7, 3.7$ Hz), 128.7, 128.1, 127.5, 125.9 (dd, $J=2.1, 1.7$ Hz), 114.9, 109.1, 107.7, 103.7, 91.5 (dd, $J=19.8, 14.8$ Hz), 73.9, 70.9, 70.7, 70.1, 61.1, 39.4 (dd, $J=2.6, 2.6$ Hz), 26.5, 25.9, 25.1, 24.3, 21.4; ¹⁹F NMR (471 MHz, CDCl₃) δ : -91.77 (d, $J=46.0$ Hz), -91.89 (d, $J=45.0$ Hz); ESI-HRMS calcd for C₂₈H₃₂F₂O₆Na (M+Na)⁺ 525.2059, found 525.2059.

Methyl (*S*)-5-(4-(benzyloxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)-6,6-difluorohex-5-enoate (**4bs**): The yield is 63% (58.5 mg as colorless oil) after column chromatography. ¹H NMR (500 MHz, CDCl₃) δ : 7.46~7.29 (m, 5H), 7.23~7.17 (m, 2H), 7.00~6.90 (m, 2H), 5.06 (s, 2H), 5.04~4.93 (m, 1H), 4.39~4.20 (m, 1H), 3.70 (s, 3H), 2.52~2.35 (m, 2H), 1.99~1.79 (m, 1H), 1.69~1.60 (m, 1H), 1.45 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ : 173.1, 158.2, 155.5, 153.6 (dd, $J=288.6, 288.6$ Hz), 136.9, 129.4 (dd, $J=3.2, 3.2$ Hz), 128.7, 128.2, 127.6, 125.4, 115.0, 90.8 (dd, $J=17.9, 17.9$ Hz), 80.1, 70.2, 53.1, 52.4, 30.9, 28.4, 24.0; ¹⁹F NMR (471 MHz, CDCl₃) δ : -91.43; ESI-HRMS calcd for C₂₅H₂₉F₂NO₅Na (M+Na)⁺ 484.1906, found 484.1906.

(8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-6-(4-(Benzyloxy)phenyl)-7,7-difluorohept-6-en-2-yl)-10,13-dimethyldodecahydro-3*H*-cyclopenta[*a*]phenanthrene-3,7,12(2*H*,4*H*)-trione (**4bt**): The yield is 36% (44.2 mg as white solid) after column chromatography. m.p. 174~176 °C; ¹H NMR (500 MHz, CDCl₃) δ : 7.46~7.30 (m, 5H), 7.24~7.16 (m, 2H), 7.02~6.89 (m, 2H), 5.07 (s,

2H), 2.95~2.78 (m, 3H), 2.37~1.92 (m, 15H), 1.87~1.75 (m, 1H), 1.67~1.55 (m, 2H), 1.39 (s, 3H), 1.28~1.18 (m, 5H), 1.04 (s, 3H), 0.77 (d, $J=6.6$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ : 212.2, 209.2, 208.9, 158.0, 155.9 (dd, $J=286.5$, 266.7 Hz), 137.1, 129.5 (dd, $J=3.2$, 3.2 Hz), 128.8, 128.2, 127.7, 126.4 (dd, $J=2.4$, 2.4 Hz), 114.9, 92.0 (dd, $J=19.7$, 15.8 Hz), 70.2, 57.0, 51.9, 49.2, 47.0, 45.9, 45.7, 45.1, 42.9, 38.8, 36.6, 36.2, 35.9, 35.4, 34.8, 28.1, 27.9, 25.3, 24.7, 22.1, 19.1, 12.0; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.71 (d, $J=46.3$ Hz), -92.83 (d, $J=46.8$ Hz); ESI-HRMS calcd for $\text{C}_{39}\text{H}_{46}\text{F}_2\text{O}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 639.3256, found 639.3262.

4.5 Mechanism experiments

Using the general procedure for Tables 2 and 3, (bromomethyl)cyclopropane (**2u**) and 6-iodohex-1-ene (**2v**) were used to participate in the coupling reaction. After the reaction, the mixture was purified by flash column chromatography to afford the crude product. In the case of (bromomethyl)cyclopropane (**2u**), the crude NMR spectra showed that a large amount of recovered **1b** (54% NMR yield determined by ^{19}F NMR analysis, benzotrifluoride was used as an internal standard) and the ring-opening product **4bu** were obtained (25% NMR yield determined by ^{19}F NMR analysis, benzotrifluoride was used as an internal standard). Despite the complexity of the spectrum, the presence of new vinyl protons and their splitting patterns confirmed the formation of ring-opening products. In the case of 6-iodohex-1-ene (**2v**), a mixture of cyclized product **4bva** and linear acyclic product **4bvb** was obtained. Despite the complexity of the spectrum, the presence of vinyl protons and their splitting patterns confirmed the linear acyclic product **4bvb**. Using the general procedure for Tables 2 and 3, cyclized product **4bva** could be synthesized as **4bw** from **1b** and (iodomethyl)cyclopentane (**2w**). The obtained standard product was used in the gas chromatography confirmation. The total yield of mixture products **4bva** and **4bvb** is 61% (determined by ^{19}F NMR analysis, benzotrifluoride was used as an internal standard), $n(\text{4bva}) : n(\text{4bvb}) = 5 : 1$ (determined by ^{19}F NMR and GC). GC retention time of **4bva** is 9.98 min, while **4bvb** is 9.35 min.

1-(Benzyloxy)-4-(4-cyclopentyl-1,1-difluorobut-1-en-2-yl)benzene (**4bw**, standard product of **4bva**): The yield is 31% (21.3 mg as colorless oil) after column chromatography. ^1H NMR (500 MHz, CDCl_3) δ : 7.48~7.30 (m, 5H), 7.26~7.20 (m, 2H), 7.01~6.94 (m, 2H), 5.07 (s, 2H), 2.37 (tt, $J=8.1$, 2.5 Hz, 2H), 1.81~1.69 (m, 3H), 1.64~1.45 (m, 4H), 1.40~1.33 (m, 2H), 1.12~1.00 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ : 158.0, 153.5 (dd, $J=287.5$, 287.5 Hz), 137.1, 129.5 (dd, $J=3.4$, 3.4 Hz), 128.8, 128.2, 127.6, 126.5, 114.9, 92.2 (dd, $J=17.2$, 17.2 Hz), 70.2, 39.8, 34.4 (dd, $J=2.5$, 2.5 Hz), 32.6, 27.1, 25.3; ^{19}F NMR (471 MHz, CDCl_3) δ : -92.90; ESI-HRMS calcd for $\text{C}_{22}\text{H}_{24}\text{F}_2\text{O}$ ($\text{M}+\text{H}$) $^+$ 343.1868, found 343.1868.

Using the general procedure for Tables 2 and 3, a radical inhibitor TEMPO was added to the standard conditions;

this reaction has been significantly inhibited in the presence of 0.5 equiv. of TEMPO. After adding 3.0 equiv. of TEMPO, the reaction was completely shut down. And the R-TEMPO was also isolated.

2,2,6,6-Tetramethyl-1-(3-(naphthalen-2-yloxy)propoxy)-piperidine (R-TEMPO): The product was isolated by column chromatography (25.9 mg, 0.076 mmol, as colorless oil). ^1H NMR (500 MHz, CDCl_3) δ : 7.79~7.71 (m, 3H), 7.47~7.42 (m, 1H), 7.36~7.31 (m, 1H), 7.18~7.14 (m, 2H), 4.22 (t, $J=6.5$ Hz, 2H), 3.98 (t, $J=6.2$ Hz, 2H), 2.16~2.03 (m, 2H), 1.64~1.30 (m, 6H), 1.19 (s, 6H), 1.12 (s, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ : 157.1, 134.8, 129.4, 129.1, 127.8, 126.9, 126.4, 123.6, 119.2, 106.8, 72.9, 65.2, 59.9, 39.8, 33.2, 28.9, 20.3, 17.3; ESI-HRMS calcd for $\text{C}_{22}\text{H}_{32}\text{NO}_2$ ($\text{M}+\text{H}$) $^+$ 342.2428, found 342.2435.

Supporting Information The NMR spectra of reported new compounds are available free of charge via the Internet at <http://sioc-journal.cn/>.

References

- [1] (a) Zhang, X.; Cao, S. *Tetrahedron Lett.* **2017**, *58*, 375.
(b) Du, B.; Chan, C.-M.; Lee, P.-Y.; Cheung, L.-H.; Xu, X.; Lin, Z.; Yu, W.-Y. *Nat. Commun.* **2021**, *12*, 412.
(c) Zhang, X.-J.; Cheng, Y.-M.; Zhao, X.-W.; Cao, Z.-Y.; Xiao, X.; Xu, Y. *Org. Chem. Front.* **2021**, *8*, 2315.
(d) Zhuo, K.-F.; Xu, W.-Y.; Gong, T.-J.; Fu, Y. *Chem. Commun.* **2020**, *56*, 2340.
(e) Ma, X.; Song, Q. *Chem. Soc. Rev.* **2020**, *49*, 9197.
(f) Sheng, J.; Wu, N.; Liu, X.; Liu, F.; Liu, S.; Ding, W.; Liu, C.; Cheng, X. *Chin. J. Org. Chem.* **2020**, *40*, 3873 (in Chinese).
(盛杰, 吴娜, 刘旭, 刘峰, 刘帅, 丁伟杰, 刘畅, 程旭, 有机化学, **2020**, *40*, 3873.)
(g) Shen, X.; Liu, Q.; Ni, C.; Hu, J. *Chin. J. Chem.* **2014**, *32*, 703.
(h) Xiong, B.; Wang, T.; Sun, H.; Li, Y.; Kramer, S.; Cheng, G.-J.; Lian, Z. *ACS Catal.* **2020**, *10*, 13616.
- [2] (a) Fujita, T.; Fuchibe, K.; Ichikawa, J. *Angew. Chem., Int. Ed.* **2018**, *58*, 390.
(b) Cai, Y.; Tan, D.; Zhang, Q.; Lü, W.; Li, Q.; Wang, H. *Chin. Chem. Lett.* **2021**, *32*, 417.
- [3] (a) He, S.-J.; Pi, J.-J.; Li, Y.; Lu, X.; Fu, Y. *Acta Chim. Sinica* **2018**, *76*, 956 (in Chinese).
(何世江, 皮静静, 李炎, 陆熹, 傅尧, 化学学报, **2018**, *76*, 956.)
(b) Song, S.; Liu, H.; Wang, L.; Zhu, C.; Loh, T. P.; Feng, C. *Chin. J. Chem.* **2019**, *37*, 1036.
(c) Gao, P.; Wang, G.; Xi, L.; Wang, M.; Li, S.; Shi, Z. *Chin. J. Chem.* **2019**, *37*, 1009.
(d) Zhang, J.; Wang, B.; Liu, Y.; Cao, S. *Chin. J. Org. Chem.* **2019**, *39*, 249 (in Chinese).
(张娟, 王碧云, 刘熠森, 曹松, 有机化学, **2019**, *39*, 249.)
(e) He, S.-Y.; Zhang, X.-G. *Org. Chem. Front.* **2020**, *7*, 3174.
- [4] (a) Hu, X.-S.; Ding, P.-G.; Yu, J.-S.; Zhou, J. *Org. Chem. Front.* **2019**, *6*, 2500.
(b) Huang, X.; Zhao, W.; Liang, Y.; Wang, M.; Zhan, Y.; Zhang, Y.; Kong, L.; Wang, Z.-X.; Peng, B. *Org. Chem. Front.* **2021**, *8*, 1280.
- [5] (a) Lin, T.-Y.; Pan, Z.; Tu, Y.; Zhu, S.; Wu, H.-H.; Liu, Y.; Li, Z.; Zhang, J. *Angew. Chem., Int. Ed.* **2020**, *59*, 22957.
(b) Hu, J.; Yang, Y.; Lou, Z.; Ni, C.; Hu, J. *Chin. J. Chem.* **2018**, *36*, 1202.
- [6] Magueur, G.; Crousse, B.; Ourévitche, M.; Bonnet-Delpon, D.; Bégué, J.-P. *J. Fluorine Chem.* **2006**, *127*, 637.
- [7] (a) Qin, W.; Chen, J.; Xiong, W.; Liu, G. *Chin. J. Org. Chem.* **2020**, *40*, 3177 (in Chinese).

- (秦文兵, 陈嘉怡, 熊威, 刘国凯, 有机化学, **2020**, *40*, 3177.)
 (b) Jin, Y.; Wang, Y.; Bao, K.; Sheng, R.; Tao, X. *Chin. J. Org. Chem.* **2019**, *39*, 2726 (in Chinese).
 (陶雪芬, 盛荣, 鲍堃, 王玉新, 金银秀, 有机化学, **2019**, *39*, 2726.)
 (c) Xie, Q.; Hu, J. *Chin. J. Chem.* **2020**, *38*, 202.
- [8] (a) Zhao, Y.; Huang, W.; Zhu, L.; Hu, J. *Org. Lett.* **2010**, *12*, 1444.
 (b) Hu, M.; He, Z.; Gao, B.; Li, L.; Ni, C.; Hu, J. *J. Am. Chem. Soc.* **2013**, *135*, 17302.
 (c) Hu, M.; Ni, C.; Li, L.; Han, Y.; Hu, J. *J. Am. Chem. Soc.* **2015**, *137*, 14496.
- [9] (a) Zheng, J.; Cai, J.; Lin, J.-H.; Guo, Y.; Xiao, J.-C. *Chem. Commun.* **2013**, *49*, 7513.
 (b) Yu, J.; Lin, J.; Xiao, J. *Chin. J. Org. Chem.* **2019**, *39*, 265 (in Chinese).
 (于蛟, 林锦鸿, 肖吉昌, 有机化学, **2019**, *39*, 265.)
- [10] Zhang, Z.; Yu, W.; Wu, C.; Wang, C.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 273.
- [11] (a) Zeng, H.; Cai, Y.; Jiang, H.; Zhu, C. *Org. Lett.* **2021**, *23*, 66.
 (b) Liu, Y.; Zhou, Y.; Zhao, Y.; Qu, J. *Org. Lett.* **2017**, *19*, 946.
 (c) Zeng, H.; Zhu, C.; Jiang, H. *Org. Lett.* **2019**, *21*, 1130.
 (d) Cai, Y.; Zeng, H.; Zhu, C.; Liu, C.; Liu, G.; Jiang, H. *Org. Chem. Front.* **2020**, *7*, 1260.
 (e) Wu, X.; Xie, F.; Gridnev, I. D.; Zhang, W. *Org. Lett.* **2018**, *20*, 1638.
 (f) Gao, P.; Yuan, C.; Zhao, Y.; Shi, Z. *Chem* **2018**, *4*, 2201.
 (g) Gao, P.; Gao, L.; Xi, L.; Zhang, Z.; Li, S.; Shi, Z. *Org. Chem. Front.* **2020**, *7*, 2618.
 (h) Chen, G.; Wang, L.; Liu, X.; Liu, P. *Adv. Synth. Catal.* **2020**, *362*, 2990.
 (i) Yao, C.; Wang, S.; Norton, J.; Hammond, M. *J. Am. Chem. Soc.* **2020**, *142*, 4793.
 (j) Chen, F.; Xu, X.; He, Y.; Huang, G.; Zhu, S. *Angew. Chem., Int. Ed.* **2020**, *59*, 5398.
 (k) Fuchibe, K.; Hatta, H.; Oh, K.; Oki, R.; Ichikawa, J. *Angew. Chem., Int. Ed.* **2017**, *56*, 5890.
 (l) Fuchibe, K.; Takahashi, M.; Ichikawa, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 12059.
 (m) Ichitsuka, T.; Fujita, T.; Arita, T.; Ichikawa, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 7564.
 (n) Ichitsuka, T.; Fujita, T.; Ichikawa, J. *ACS Catal.* **2015**, *5*, 5947.
 (o) Jaroschik, F. *Chem. Eur. J.* **2018**, *24*, 14572.
 (p) Kojima, R.; Akiyama, S.; Ito, H. *Angew. Chem., Int. Ed.* **2018**, *57*, 7196.
 (q) Kojima, R.; Kubota, K.; Ito, H. *Chem. Commun.* **2017**, *53*, 10688.
 (r) Kojima, Y.; Takata, T.; Hirano, K.; Miura, M. *Chem. Lett.* **2020**, *49*, 637.
 (s) Liu, Y.; Li, C.; Liu, C.; He, J.; Zhao, X.; Cao, S. *Tetrahedron Lett.* **2020**, *61*, 151940.
 (t) Liu, Z.; Tu, X.-S.; Guo, L.-T.; Wang, X.-C. *Chem. Sci.* **2020**, *11*, 11548.
 (u) Yan, S.-S.; Wu, D.-S.; Ye, J.-H.; Gong, L.; Zeng, X.; Ran, C.-K.; Gui, Y.-Y.; Li, J.; Yu, D.-G. *ACS Catal.* **2019**, *9*, 6987.
 (v) Pan, Q.; Ping, Y.; Wang, Y.; Guo, Y.; Kong, W. *J. Am. Chem. Soc.* **2021**, *143*, 10282.
 (w) Tian, F.; Yan, G.; Yu, J. *Chem. Commun.* **2019**, *55*, 13486.
 (x) Xie, S.-L.; Cui, X.-Y.; Gao, X.-T.; Zhou, F.; Wu, H.-H.; Zhou, J. *Org. Chem. Front.* **2019**, *6*, 3678.
 (y) Li, Y.; Wang, Y.; Zhu, L.; Qu, L.; Lan, Y. *Chin. J. Org. Chem.* **2019**, *39*, 38 (in Chinese).
 (李园园, 王元鉴, 朱磊, 屈凌波, 蓝宇, 有机化学, **2019**, *39*, 38.)
- [12] Dai, W.; Lin, Y.; Wan, Y.; Cao, S. *Org. Chem. Front.* **2018**, *5*, 55.
- [13] Wang, M.; Pu, X.; Zhao, Y.; Wang, P.; Li, Z.; Zhu, C.; Shi, Z. *J. Am. Chem. Soc.* **2018**, *140*, 9061.
- [14] Miura, T.; Ito, Y.; Murakami, M. *Chem. Lett.* **2008**, *37*, 1006.
- [15] Huang, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2016**, *138*, 12340.
- [16] Cheng, R.; Xu, C.; Zhang, X. *Chin. J. Org. Chem.* **2020**, *40*, 3307 (in Chinese).
 (程然, 徐畅, 张新刚, 有机化学, **2020**, *40*, 3307.)
- [17] (a) Phelan, J. P.; Wiles, R. J.; Lang, S. B.; Kelly, C. B.; Molander, G. A. *Chem. Sci.* **2018**, *9*, 3215.
 (b) Lang, S. B.; Wiles, R. J.; Kelly, C. B.; Molander, G. A. *Angew. Chem., Int. Ed.* **2017**, *56*, 15073.
 (c) Wiles, R. J.; Phelan, J. P.; Molander, G. A. *Chem. Commun.* **2019**, *55*, 7599.
- [18] (a) Chen, H.; Anand, D.; Zhou, L. *Asian J. Org. Chem.* **2019**, *8*, 661.
 (b) Li, L.; Xiao, T.; Chen, H.; Zhou, L. *Chem. Eur. J.* **2017**, *23*, 2249.
 (c) Anand, D.; Sun, Z.; Zhou, L. *Org. Lett.* **2020**, *22*, 2371.
 (d) Chen, H.; Xiao, T.; Li, L.; Anand, D.; He, Y.; Zhou, L. *Adv. Synth. Catal.* **2017**, *359*, 3642.
 (e) He, Y.; Anand, D.; Sun, Z.; Zhou, L. *Org. Lett.* **2019**, *21*, 3769.
 (f) Xiao, T.; Li, L.; Zhou, L. *J. Org. Chem.* **2016**, *81*, 7908.
- [19] (a) Guo, Y.-Q.; Wang, R.; Song, H.; Liu, Y.; Wang, Q. *Org. Lett.* **2020**, *22*, 709.
 (b) Guo, Y.-Q.; Wu, Y.; Wang, R.; Song, H.; Liu, Y.; Wang, Q. *Org. Lett.* **2021**, *23*, 2353.
 (c) Xiang, P.; He, L.; Li, H.; Qi, Z.; Zhang, M.; Fu, Q.; Wei, J.; Du, X.; Yi, D.; Wei, S. *Tetrahedron Lett.* **2020**, *61*, 152369.
- [20] Lu, X.; Wang, Y.; Zhang, B.; Pi, J.-J.; Wang, X.-X.; Gong, T.-J.; Xiao, B.; Fu, Y. *J. Am. Chem. Soc.* **2017**, *139*, 12632.
- [21] Lu, X.; Wang, X.-X.; Gong, T.-J.; Pi, J.-J.; He, S.-J.; Fu, Y. *Chem. Sci.* **2019**, *10*, 809.
- [22] Lan, Y.; Yang, F.; Wang, C. *ACS Catal.* **2018**, *8*, 9245.
- [23] (a) Yu, L.; Tang, M.-L.; Si, C.-M.; Meng, Z.; Liang, Y.; Han, J.; Sun, X. *Org. Lett.* **2018**, *20*, 4579.
 (b) Du, H.-W.; Chen, Y.; Sun, J.; Gao, Q.-S.; Wang, H.; Zhou, M.-D. *S. Org. Lett.* **2020**, *22*, 9342.
 (c) Li, Z.; Wang, K.-F.; Zhao, X.; Ti, H.; Liu, X.-G.; Wang, H. *Nat. Commun.* **2020**, *11*, 5036.
 (d) Lin, Z.; Lan, Y.; Wang, C. *Org. Lett.* **2019**, *21*, 8316.
- [24] (a) Ding, D.; Lan, Y.; Lin, Z.; Wang, C. *Org. Lett.* **2019**, *21*, 2723.
 (b) Lin, Z.; Lan, Y.; Wang, C. *Org. Lett.* **2020**, *22*, 3509.
 (c) Lu, X.-Y.; Jiang, R.-C.; Li, J.-M.; Liu, C.-C.; Wang, Q.-Q.; Zhou, H.-P. *Org. Biomol. Chem.* **2020**, *18*, 3674.
 (d) Fan, P.; Zhang, C.; Lan, Y.; Lin, Z.; Zhang, L.; Wang, C. *Chem. Commun.* **2019**, *55*, 12691.
 (e) Jin, Y.; Wu, J.; Lin, Z.; Lan, Y.; Wang, C. *Org. Lett.* **2020**, *22*, 5347.
 (f) Zhu, C.; Liu, Z.-Y.; Tang, L.; Zhang, H.; Zhang, Y.-F.; Walsh, P. J.; Feng, C. *Nat. Commun.* **2020**, *11*, 4860.
- [25] (a) Kawamata, Y.; Vantourout, J. C.; Hickey, D. P.; Bai, P.; Chen, L.; Hou, Q.; Qiao, W.; Barman, K.; Edwards, M. A.; Garrido-Castro, A. F.; deGruyter, J. N.; Nakamura, H.; Knouse, K.; Qin, C.; Clay, K. J.; Bao, D.; Li, C.; Starr, J. T.; Garcia-Irizarry, C.; Sach, N.; White, H. S.; Neurock, M.; Minter, S. D.; Baran, P. S. *J. Am. Chem. Soc.* **2019**, *141*, 6392.
 (b) Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.
 (c) Li, C.; Kawamata, Y.; Nakamura, H.; Vantourout, J. C.; Liu, Z.; Hou, Q.; Bao, D.; Starr, J. T.; Chen, J.; Yan, M.; Baran, P. S. *Angew. Chem., Int. Ed.* **2017**, *56*, 13088.
 (d) Wang, P.; Yang, Z.; Wang, Z.; Xu, C.; Huang, L.; Wang, S.; Zhang, H.; Lei, A. *Angew. Chem., Int. Ed.* **2019**, *58*, 15747.
 (e) Liu, Q.; Sun, B.; Liu, Z.; Kao, Y.; Dong, B.-W.; Jiang, S.-D.; Li, F.; Liu, G.; Yang, Y.; Mo, F. *Chem. Sci.* **2018**, *9*, 8731.
 (f) Liu, D.; Ma, H.-X.; Fang, P.; Mei, T.-S. *Angew. Chem., Int. Ed.* **2019**, *58*, 5033.
 (g) Zou, Z.; Zhang, W.; Wang, Y.; Pan, Y. *Org. Chem. Front.* **2021**, *8*, 2786.
 (h) Lu, L.; Li, H.; Zheng, Y.; Bu, F.; Lei, A. *CCS Chem.* **2020**, *2*, 2669.
 (i) Dou, G.-Y.; Jiang, Y.-Y.; Xu, K.; Zeng, C.-C. *Org. Chem. Front.* **2019**, *6*, 2392.

- (j) Liang, K.; Wang, S.; Cong, H.; Lu, L.; Lei, A. *CCS Chem.* **2021**, 3, 1727.
- (k) Huang, C.; Xu, H.-C. *Sci. China Chem.* **2019**, 62, 1501.
- (l) Feng, E.; Hou, Z.; Xu, H. *Chin. J. Org. Chem.* **2019**, 39, 1424 (in Chinese).
- (冯恩祺, 侯中伟, 徐海超, 有机化学, **2019**, 39, 1424.)
- (m) Zhang, C.; Bu, F.; Zeng, C.; Wang, D.; Lu, L.; Zhang, H.; Lei, A. *CCS Chem.* **2021**, 3, 1404.
- (n) Deng, Y.; Lu, F.; You, S.; Xia, T.; Zheng, Y.; Lu, C.; Yang, G.; Chen, Z.; Gao, M.; Lei, A. *Chin. J. Chem.* **2019**, 37, 817.
- (o) Hou, Z. W.; Xu, H. C. *Chin. J. Chem.* **2020**, 38, 394.
- (p) Liu, S.; Zhao, W.; Li, J.; Wu, N.; Liu, C.; Wang, X.; Li, S.; Zhu, Y.; Liang, Y.; Cheng, X. *CCS Chem.* **2021**, 3, 872.
- (q) Qiu, Y.; Zhu, C.; Stangier, M.; Struwe, J.; Ackermann, L. *CCS Chem.* **2020**, 2, 1529.
- (r) Xu, Y.; Lin, L.; Han, Y.; Liu, Y. *Chin. J. Org. Chem.* **2021**, 41, 934 (in Chinese).
- (许颖, 林立青, 韩莹徽, 刘颖杰, 有机化学, **2021**, 41, 934.)
- (s) Yang, Q.-L.; Wang, X.-Y.; Weng, X.-J.; Yang, X.; Xu, X.-T.; Tong, X.; Fang, P.; Wu, X.-Y.; Mei, T.-S. *Acta Chim. Sinica* **2019**, 77, 866 (in Chinese).
- (杨启亮, 王向阳, 翁信军, 杨祥, 徐学涛, 童晓峰, 方萍, 伍新燕, 梅天胜, 化学学报, **2019**, 77, 866.)
- (t) Zhang, Q.; Liang, K.; Guo, C. *CCS Chem.* **2021**, 3, 338.
- [26] (a) Li, H.; Breen, C. P.; Seo, H.; Jamison, T. F.; Fang, Y.-Q.; Bio, M. M. *Org. Lett.* **2018**, 20, 1338.
- (b) Jiao, K.-J.; Li, Z.-M.; Xu, X.-T.; Zhang, L.-P.; Li, Y.-Q.; Zhang, K.; Mei, T.-S. *Org. Chem. Front.* **2018**, 5, 2244.
- (c) Lai, Y.-L.; Huang, J.-M. *Org. Lett.* **2017**, 19, 2022.
- (d) Qiu, H.; Shuai, B.; Wang, Y.-Z.; Liu, D.; Chen, Y.-G.; Gao, P.-S.; Ma, H.-X.; Chen, S.; Mei, T.-S. *J. Am. Chem. Soc.* **2020**, 142, 9872.
- [27] (a) Chen, X.; Luo, X.; Peng, X.; Guo, J.; Zai, J.; Wang, P. *Chem. Eur. J.* **2020**, 26, 3226.
- (b) Gomes, P.; Gosmini, C.; Périchon, J. *J. Org. Chem.* **2003**, 68, 1142.
- (c) Gomes, P.; Gosmini, C.; Périchon, J. *Tetrahedron* **2003**, 59, 2999.
- (d) Jiao, K.-J.; Liu, D.; Ma, H.-X.; Qiu, H.; Fang, P.; Mei, T.-S. *Angew. Chem., Int. Ed.* **2020**, 59, 6520.
- (e) Kumar, G. S.; Peshkov, A.; Brzozowska, A.; Nikolaienko, P.; Zhu, C.; Rueping, M. *Angew. Chem., Int. Ed.* **2020**, 59, 6513.
- (f) Wang, X.-X.; Lu, X.; Li, Y.; Wang, J.-W.; Fu, Y. *Sci. China Chem.* **2020**, 63, 1586.
- (g) Truesdell, B. L.; Hamby, T. B.; Sevov, C. S. *J. Am. Chem. Soc.* **2020**, 142, 5884.
- (h) Perkins, R. J.; Pedro, D. J.; Hansen, E. C. *Org. Lett.* **2017**, 19, 3755.
- (i) Perkins, R. J.; Hughes, A. J.; Weix, D. J.; Hansen, E. C. *Org. Process Res. Dev.* **2019**, 23, 1746.
- [28] Jiang, W.-T.; Yang, S.; Xu, M.-Y.; Xie, X.-Y.; Xiao, B. *Chem. Sci.* **2020**, 11, 488.
- [29] (a) Wang, X.-X.; Yu, L.; Lu, X.; Zhang, Z.-L.; Liu, D.-G.; Tian, C.; Fu, Y. *CCS Chem.* **2021**, 3, 727.
- (b) Lu, X.; Xiao, B.; Zhang, Z.; Gong, T.; Su, W.; Yi, J.; Fu, Y.; Liu, L. *Nat. Commun.* **2016**, 7, 11129.
- (c) Wang, J.-W.; Li, Y.; Nie, W.; Chang, Z.; Yu, Z.-A.; Zhao, Y.-F.; Lu, X.; Fu, Y. *Nat. Commun.* **2021**, 12, 1313.
- [30] Supranovich, V. I.; Levin, V. V.; Kokorekin, V. A.; Dilman, A. D. *Adv. Synth. Catal.* **2021**, 363, 2888.

(Cheng, F.)