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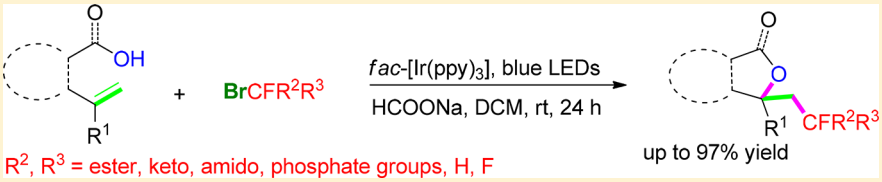
Photoredox-Catalyzed Cascade Difluoroalkylation and Intramolecular Cyclization for Construction of Fluorinated γ-Butyrolactones

Wanxing Sha,[†] Wenzhong Zhang,[†] Shengyang Ni,[†] Haibo Mei,[†,‡] Jianlin Han,*[,†,‡] and Yi Pan[†,‡]

[†]School of Chemistry and Chemical Engineering, State Key Laboratory of Coordination Chemistry, Jiangsu Key Laboratory of Advanced Organic Materials, Nanjing University, Nanjing 210093, China

[‡]MaAnShan High-Tech Research Institute of Nanjing University, MaAnShan 238200, China

Supporting Information

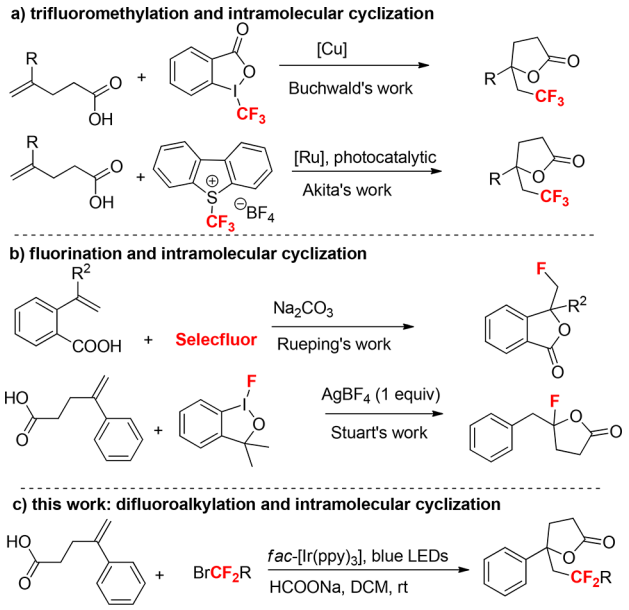


ABSTRACT: A cascade visible-light photocatalytic difluoroalkylation and intramolecular cyclization reaction has been developed for the synthesis of difluoroalkylated oxygen heterocycles. The reaction was carried out under very mild conditions, affording fluorinated isobenzofuran-1-ones, lactone, and cyclic ethers with up to 97% chemical yields. Furthermore, several types of bromofluoroalkane precursors bearing ester, keto, amido, and phosphate groups could all work very well in this reaction, which provides an easy method for the preparation of functionalized difluoroalkylated oxygen heterocycles.

The introduction of fluorine atoms into molecules has attracted much research interest in organic chemistry because the fluorine atom features unique electronic properties and fluorine-containing molecules show special bioactivities in pharmaceutical chemistry.[1,2] Thus, introducing fluorine into molecules continues as a hot topic in organic synthesis.[3] Among these research topics, fluorination and trifluoromethylation reactions have gained significant progress and have been well documented for inducing one or three fluorine atoms into organic molecules.[3b,4] However, difluoroalkylation still does not receive much attention[5] mainly because difluoroalkylation reagents are usually difficult to prepare, hard to handle, or incompatible with functional groups. To reverse this situation, halogenated difluoroacetate ($CF_2XCOOEt$) has been developed as a difluoroalkylation reagent in organic reactions,[6] which is low cost, convenient to hold, and easy to keep. Furthermore, the alkoxycarbonyldifluoromethyene (CF_2CO_2R) group is an interesting fluorinated motif due to its facile derivatization and high bioactivity.

Unsaturated carboxylic acids are an important type of organic intermediate and easily undergo the difunctionalization process to assemble lactone derivatives[7] as well as introduce an additional functional group in one reaction.[8] In recent years, several coupling partners have been developed to trigger intramolecular cyclization. In particular, fluorination or trifluoromethylation of C═C bond-initiated cyclization have been reported to construct the lactones and introduce fluoro and trifluoromethyl groups in the product at the same time. Buchwald[9] and Akita[10] have used different methods to synthesize trifluoromethyl lactone through trifluoromethylation lactonization of unsaturated carboxylic acids (Scheme 1a). In addition, Rueping[11] have developed fluorolactonization of unsaturated carboxylic acids by Selecfluor to give fluorinated isobenzofurans (Scheme 1b). Stuart[12] used hypervalent fluoroiodane reagent and unsaturated

Scheme 1. Fluorination of Unsaturated Carboxylic Acids



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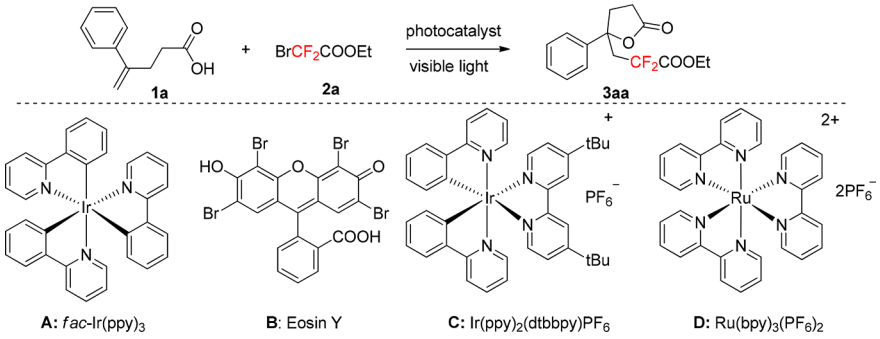
carboxylic acids to deliver novel fluoro lactones in the presence of $AgBF_4$ (Scheme 1b). To the best of our knowledge, the difluoroalkylation-triggered cyclization of unsaturated carboxylic acids in the presence of visible light has not been reported until now. Notably, the Wu group developed two-step methods on palladium-catalyzed reactions between polyfluoroalkyl iodides and 4-pentenoic acid to synthesize fluoroalkylated γ-lactones.[13] In our continuous work on the synthesis of fluorine-containing compounds and functionalized lactones,[14,15] we reported herein an efficient visible light photocatalytic method for the preparation of difluoroalkylated lactones via the reaction between bromofluoroalkanes and unsaturated acids/alcohols (Scheme 1c). This reaction was carried out under mild conditions, which provides a new strategy to difluoroalkylated oxygen heterocycles from readily available bromofluoroalkanes as starting materials.

Recently, dual catalysis by merging visible-light-induced photoredox catalysis with other catalytic modes has undergone signficant development.[16] Sanford[17] and Liu[18] have done elegant work on combining copper catalysis and photoredox as catalyst. Thus, we envision that a photocatalyst/copper system could be efficient for our reaction. We started the reaction conditions optimization by using unsaturated carboxylic acid **1a** as the model substrate to react with $BrCF_2COOEt$ **2a** in the presence of sodium carbonate, photocatalyst fac-$[Ir(ppy)_3]$, and CuI at room temperature. It was pleasing that expected product **3aa** was obtained in 45% yield (Table 1, entry 1) after 12 h of irradiation with visible light from blue LEDs (5 W, λ_{max} = 455 nm). With a contrast test, we carried out the reaction without the addition of CuI and found that dramatically increased yields were obtained (70%, entry 2). Next, we prolonged the reaction time to 24 h, and a slightly higher yield was found (entry 3). Photocatalyst screening showed that Eosin Y, $[Ru(bpy)_3]PF_6$, and $[Ir(ppy)_2(dtbbpy)_3]PF_6$ could not promote this reaction, as no reaction occurred at all (entries 4−6). The use of other regular solvents, such as DMF and 1,4-dioxane, did not provide any improvement in the yields (entries 7 and 8), and these results show that DCM is the best choice. Further reaction condition optimization found that bases have an obvious effect on this reaction. Inorganic bases such as $NaHCO_3$ and Na_2HPO_4 gave similar results (entries 9 and 10). However, an organic base, such as Et_3N, resulted in a dramatically decreased yield (entry 11). The highest yield was obtained when HCOONa was used as base for this reaction (entry 12). Strangely, increasing the amount of $BrCF_2COOEt$ **2a** diminished the reaction yields (entries 13 and 14). Finally, control experiments demonstrated that the photocatalyst *fac*-$[Ir(ppy)_3]$, visible light, and base were vital to this reaction (entries 15−17).

With the optimized conditions in hand, we then explored the scope of different unsaturated carboxylic acids, and the results are summarized in Scheme 2. This cascade catalytic strategy is compatible with a variety of alkenoic acids bearing either electron-donating or -withdrawing groups on the aryl substituent, affording the corresponding products in moderate to excellent yields (**3aa**−**3ha**). Specifically, the para-substituted methoxy alkenoic acid could furnish desired product **3ea** in 97% yield. Otherwise, unsaturated carboxylic acids containing a nonterminal

Table 1. Optimization of the Reaction Conditions[a]



entry	photocatalyst	base	solvent	time (h)	yield[b] (%)
1	**A**	Na_2CO_3	DCM	12	45[c]
2	**A**	Na_2CO_3	DCM	12	70
3	**A**	Na_2CO_3	DCM	24	73
4	**B**	Na_2CO_3	DCM	24	NR
5	**C**	Na_2CO_3	DCM	24	NR
6	**D**	Na_2CO_3	DCM	24	NR
7	**A**	Na_2CO_3	DMF	24	47
8	**A**	Na_2CO_3	dioxane	24	70
9	**A**	$NaHCO_3$	DCM	24	70
10	**A**	Na_2HPO_4	DCM	24	71
11	**A**	Et_3N	DCM	24	26
12	**A**	HCOONa	DCM	24	77
13[d]	**A**	HCOONa	DCM	24	69
14[e]	**A**	HCOONa	DCM	24	67
15	**A**		DCM	24	trace
16[f]	**A**	HCOONa	DCM	24	NR
17		HCOONa	DCM	24	NR

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol, 1.0 equiv), base (0.2 mmol, 2.0 equiv), photocatalyst (0.004 mmol, 2 mol %), solvent (2 mL), room temperature, 5 W LEDs, 24 h. [b]Isolated yield. [c]Using 0.1 equiv CuI. [d]Using 1.2 equiv of **2a**. [e]Using 1.5 equiv of **2a**. [f]In the dark.

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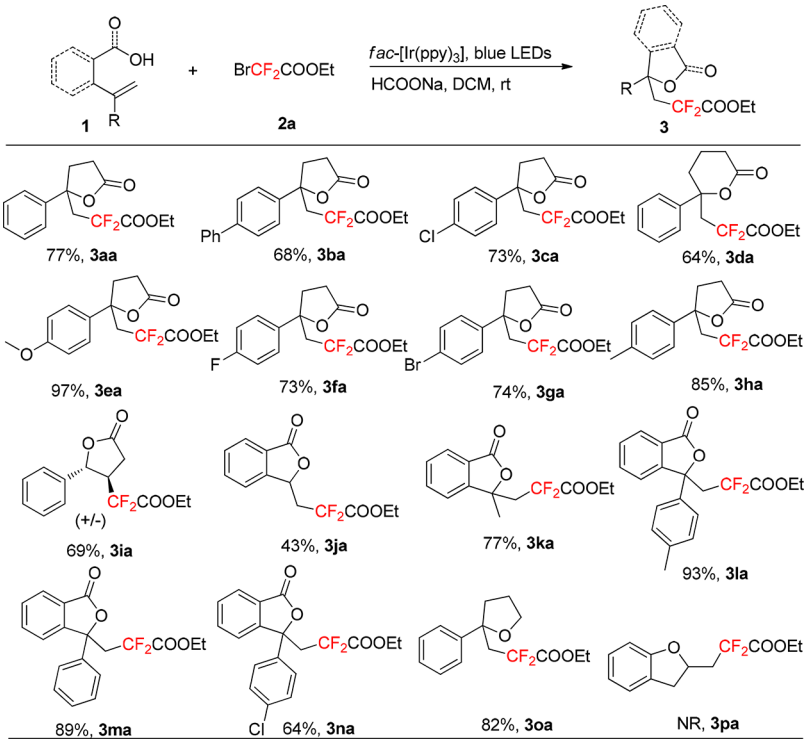
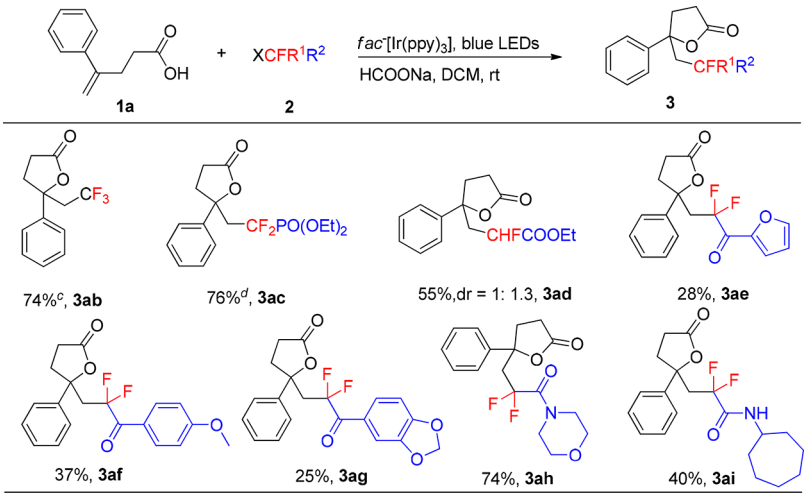
Scheme 2. Substrate Scope of Unsaturated Acids and Alcohols[a]



[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.2 mmol), HCO_2Na (0.4 mmol), *fac*-Ir(ppy)$_3$ (0.004 mmol), DCM (2 mL), at room temperature, 5 W LEDs, for 24 h. Isolated yield.

Scheme 3. Substrate Scope of Bromofluoroalkanes[a,b]



[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.2 mmol), HCOONa (0.4 mmol), fac-Ir(ppy)$_3$ (0.004 mmol), DCM (2 mL), room temperature, 5 W LEDs, 24 h. [b]Isolated yield. [c]Compound **2b** (0.4 mmol, 4 equiv). [d]Compound **2c** (0.4 mmol, 4 equiv).

vinyl group could also work well in these reaction conditions with 69% yield (**3ia**). Because of the importance of the isobenzofuran-1-ones motif in organic and bioorganic chemistry, we tried to examine the *o*-vinyl benzoic acids in the current system. First, we tested the *o*-vinyl benzoic acid for this reaction. It was pleasing that the reaction could take place, affording the expected product in 43% yield (**3ja**). Then, we tried the more congested *o*-vinyl benzoic acids (**1k**−**1n**). Fortunately, these reagents could work very well, giving the product in good yields regardless of alkenoic acids bearing either electron-donating or -withdrawing groups (**3ka**−**3na**). Notably, unsaturated alcohol **1o** was also a suitable substrate, and the reaction proceeded smoothly to give expected α,α-disubstituted tetrahydrofuran **3oa** in good yield (82%). Finally, we extended the substrate to 2-allylphenol **3p**;[19] unfortunately, no reaction occurred under the standard reaction conditions. The chemical structure of difluoroalkylated oxygen heterocycleproducts **3** has been confirmed by X-ray single-crystal analysis of **3ja** (see Supporting Information).

Encouraged by the results from different unsaturated carboxylic acids with $BrCF_2COOEt$, we further examined other bromofluoro precursors, such as ester, keto, amide, and phosphate-bearing bromofluoro compounds, and the results are shown in Scheme 3.

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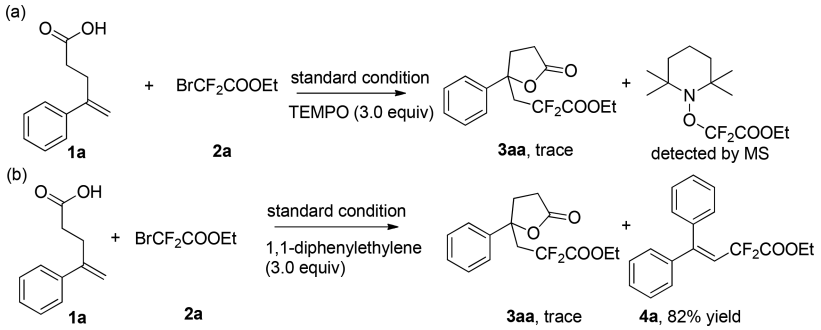
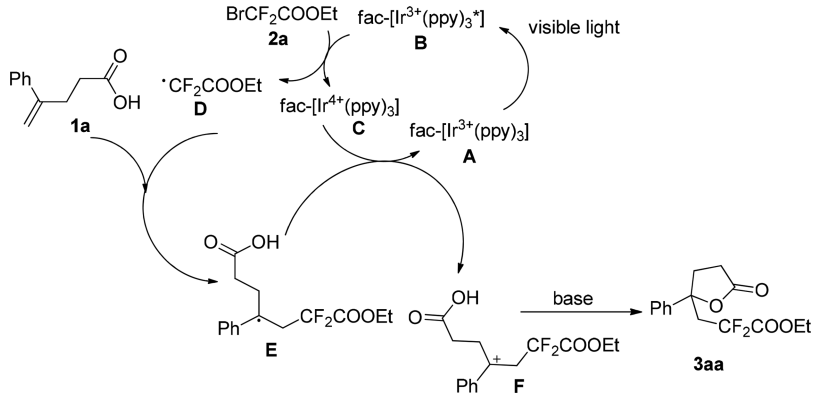
Scheme 4. Control Experiments



Scheme 5. Proposal Mechanism



CF_3SO_2Cl, $BrCF_2PO(OEt)_2$, and BrCHFCOOEt can be applied to this catalytic system and to obtain the products **3ab**−**3ad** in moderate yields, respectively. Bromodifluoroareneketones could also be tolerated in this reaction, however, affording the corresponding product in low yields (**3ae**−**3ag**). Finally, we tested the amide-containing $BrCF_2$ group. In the case of the tertiary amide, it could react smoothly with **1a** to deliver product **3ah** in 74% yield. On the other hand, secondary amide could also work in the current system but afforded **3ai** in obviously lower yield (40%).

For obtaining mechanistic insight into this reaction, the radical scavenger 2,2,6,6,-tetramethyl-1-piperidinyloxy (TEMPO) was introduced into the catalytic system. The formation of **3aa** was suppressed, and only the **2a**-TEMPO adduct was detected by MS, indicating that a radical process is involved (Scheme 4a). For the radical process to be verified, another radical scavenger 1,1-diphenylalkene was added to the standard reaction conditions. Only a trace amount of product **3aa** could be detected by MS in the reaction mixture, and 1,1-diphenylalkene-**2a** adduct **4a** could be obtained in 82% yield (Scheme 4b).

On the basis of the experimental results provided above and previous studies,[8] a possible mechanism is illustrated in Scheme 5. At the first step, the photoredox catalyst *fac*-$[Ir^{3+}(ppy)_3]$ **A** is irradiated to the excited state *fac*-$[Ir^{3+}(ppy)_3{}^*]$ **B**, which undergoes single-electron transfer to generate *fac*-$[Ir^{4+}(ppy)_3]$ **C** and radical ·CF_2COOEt **D**. Subsequently, radical **D** adds to the unsaturated carboxylic acids **1a** to generate intermediate **E**. Then, intermediate **E** is oxidized to the carbocation intermediate **F** by the Ir intermediate **C** as well as regeneration of the Ir catalyst **A**. Finally, final product **3aa** is produced by deprotonation of intermediate **F** in the presence of base.

In conclusion, we have developed a novel photoredox-catalyzed strategy for the synthesis of difluoroalkylated oxygen heterocycles through difunctionalization of unsaturated acids/alcohols. Several types of bromofluoroalkane precursors bearing ester, keto, amido, and phosphate groups were developed for this difluoroalkylation and cyclization reaction, affording the corresponding products in good-to-excellent yields. The reaction proceeds smoothly under mild conditions, which provides a new method for the preparation of functionalized difluoroalkylated oxygen heterocycles.

EXPERIMENTAL SECTION

Typical Procedures for the Preparation of Substrates 1a−1h.[20a] To a suspension of methyltriphenylphosphonium bromide (4.6 g, 13.0 mmol) in THF (20 mL) was added sodium *tert*-butoxide (2.5 g, 26.0 mmol) at 0 °C. The mixture was then stirred for 30 min. 4-Oxo-4-arylbutanoic acid (10.0 mmol) was then added to the reaction mixture at 0 °C. The mixture was allowed to warm to room temperature and was then stirred for 16 h. After evaporation of THF, dichloromethane and 1 N NaOH were added. The aqueous layer was washed with dichloromethane. HCl (12 N) was then added until the pH of the aqueous layer was ∼2. The aqueous layer was then extracted with dichloromethane twice and dried over magnesium sulfate. Purification by column chromatography (10% EA−PE) afforded substrates **1a**−**1h**.

*4-Phenylpent-4-enoic Acid (**1a**).*[20a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.23 (m, 5H), 5.32 (s, 1H), 5.10 (d, J = 1.1 Hz, 1H), 2.84 (dd, J = 8.1, 7.4 Hz, 2H), 2.55−2.51 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.6, 146.6, 140.4, 128.5, 127.7, 126.1, 113.0, 33.0, 30.2.

*4-([1,1′-Biphenyl]-4-yl)pent-4-enoic Acid (**1b**).*[20b] ^{1}H NMR (400 MHz, DMSO) δ 12.19 (br s, 1H), 7.69−7.36 (m, 9H), 5.43 (s, 1H), 5.14 (s, 1H), 2.78 (t, J = 6.9 Hz, 2H), 2.42 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 174.3, 146.3, 140.1, 139.8, 139.5, 129.4, 128.0, 127.2, 127.0, 126.8, 113.0, 33.2, 30.0.

*4-(4-Chlorophenyl)pent-4-enoic Acid (**1c**).*[20b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.29 (m, 4H), 5.31 (s, 1H), 5.12 (d, J = 0.9 Hz, 1H), 2.81 (dd, J = 8.0, 7.3 Hz, 2H), 2.52 (dd, J = 8.5, 6.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.8, 145.4, 138.9, 133.5, 128.6, 127.4, 113.5, 32.8, 30.0.

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*5-Phenylhex-5-enoic Acid (**1d**).*[20c] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dt, J = 3.3, 1.9 Hz, 2H), 7.34−7.24 (m, 3H), 5.31 (d, J = 1.2 Hz, 1H), 5.08 (d, J = 1.3 Hz, 1H), 2.59−2.55 (m, 2H), 2.37 (t, J = 7.4 Hz, 2H), 1.83−1.76 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.8, 147.4, 140.8, 128.4, 127.5, 126.1, 113.1, 34.5, 33.3, 23.0.

*4-(4-Methoxyphenyl)pent-4-enoic Acid (**1e**).*[20b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.34 (m, 2H), 6.88−6.86 (m, 2H), 5.25 (s, 1H), 5.02 (d, J = 1.1 Hz, 1H), 3.81 (s, 3H), 2.84−2.80 (m, 2H), 2.55−2.51 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 159.2, 145.8, 132.8, 127.2, 113.8, 111.4, 55.3, 32.9, 30.2.

*4-(4-Fluorophenyl)pent-4-enoic Acid (**1f**).*[20a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.34 (m, 2H), 7.04−7.00 (m, 2H), 5.27 (s, 1H), 5.09 (d, J = 0.8 Hz, 1H), 2.81 (dd, J = 8.0, 7.3 Hz, 2H), 2.52 (dd, J = 8.6, 6.9 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.81 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.1, 162.4 (d, J = 246.6 Hz), 145.6, 136.5 (d, J = 3.4 Hz), 127.7 (d, J = 7.9 Hz), 115.3 (d, J = 21.4 Hz), 113.0 (d, J = 0.8 Hz), 32.9, 30.2.

*4-(4-Bromophenyl)pent-4-enoic Acid (**1g**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.45 (m, 2H), 7.28−7.26 (m, 2H), 5.32 (s, 1H), 5.13 (s, 1H), 2.81 (t, J = 7.6 Hz, 2H), 2.54−2.50 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.4, 145.5, 139.4, 131.6, 127.8, 121.7, 113.6, 32.7, 30.0.

*4-(p-Tolyl)pent-4-enoic Acid (**1h**).*[20b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 5.29 (s, 1H), 5.06 (d, J = 1.1 Hz, 1H), 2.85−2.81 (m, 2H), 2.53 (dd, J = 8.7, 6.9 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.3, 146.3, 137.5, 137.5, 129.1, 126.0, 112.2, 33.0, 30.2, 21.1.

Typical Procedures for the Preparation of Substrates 1j−1n.[21a] To a suspension of methyltriphenylphosphonium bromide (7.14 g, 20.0 mmol) in THF (100 mL) was added potassium *tert*-butoxide (3.36 g, 30.0 mmol) at 0 °C. The mixture was then stirred for 30 min. 2-Ketobenzoic acid (10.0 mmol) was added to the reaction mixture at 0 °C. The mixture was allowed to warm to room temperature and stirred for 16 h. After evaporation of THF, the mixture was treated with 10% NaOH (100 mL). The aqueous layer was washed with CH_2Cl_2 (50 mL) and acidified (pH 1) with 3 N HCl. The aqueous layer was extracted with ethyl acetate (3× 50 mL). The combined extracts were washed with a saturated solution of NaCl (100 mL), dried over $MgSO_4$, and evaporated in vacuo. Purification by column chromatography (10% EA−PE) afforded substrates **1j−1n**.

*2-Vinylbenzoic Acid (**1j**).*[8h] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.9, 1.2 Hz, 1H), 7.63−7.53 (m, 3H), 7.37 (td, J = 7.8, 1.3 Hz, 1H), 5.68 (dd, J = 17.4, 1.2 Hz, 1H), 5.39 (dd, J = 11.0, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 140.7, 136.1, 133.2, 131.3, 127.6, 127.6, 127.2, 116.8.

*2-(Prop-1-en-2-yl)benzoic Acid (**1k**).*[8h] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, J = 7.8, 1.1 Hz, 1H), 7.50 (td, J = 7.5, 1.4 Hz, 1H), 7.35 (td, J = 7.7, 1.3 Hz, 1H), 7.27 (dd, J = 7.1, 1.4 Hz, 1H), 5.14−5.13 (m, 1H), 4.90 (dd, J = 1.7, 0.9 Hz, 1H), 2.12 (dd, J = 1.3, 0.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 146.6, 146.2, 132.5, 130.7, 129.7, 128.0, 127.0, 114.0, 24.3.

*2-(1-(p-Tolyl)vinyl)benzoic Acid (**1l**).*[21a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 7.8, 1.3 Hz, 1H), 7.55 (td, J = 7.5, 1.4 Hz, 1H), 7.42 (td, J = 7.6, 1.3 Hz, 1H), 7.35 (dd, J = 7.6, 1.1 Hz, 1H), 7.12−7.10 (m, 2H), 7.06−7.04 (m, 2H), 5.63 (d, J = 0.9 Hz, 1H), 5.16 (d, J = 0.9 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 149.3, 143.8, 138.1, 137.3, 132.4, 131.5, 130.6, 129.5, 128.8, 127.6, 126.7, 113.5, 21.1.

*2-(1-Phenylvinyl)benzoic Acid (**1m**).*[21a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 7.8, 1.1 Hz, 1H), 7.56 (td, J = 7.5, 1.4 Hz, 1H), 7.42 (td, J = 7.6, 1.3 Hz, 1H), 7.37 (dd, J = 7.6, 0.9 Hz, 1H), 7.25−7.20 (m, 5H), 5.66 (d, J = 1.0 Hz, 1H), 5.22 (d, J = 0.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 149.5, 143.6, 140.9, 132.4, 131.6, 130.6, 129.5, 128.1, 127.7, 127.5, 126.8, 114.4.

*2-(1-(4-Chlorophenyl)vinyl)benzoic Acid (**1n**).*[21a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, J = 7.8, 1.2 Hz, 1H), 7.57 (td, J = 7.5, 1.4 Hz, 1H), 7.44 (td, J = 7.6, 1.3 Hz, 1H), 7.35 (dd, J = 7.6, 1.0 Hz, 1H), 7.23−7.19 (m, 2H), 7.15−7.12 (m, 2H), 5.65 (d, J = 0.7 Hz, 1H), 5.22 (d, J = 0.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 148.6, 143.2, 139.4, 133.3, 132.6, 131.5, 130.9, 129.2, 128.3, 128.0, 127.9, 114.8.

*4-Phenylpent-4-en-1-ol (**1o**).* Compound **1o** was synthesized according to a previously reported method.[21b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dt, J = 8.3, 1.9 Hz, 2H), 7.34−7.30 (m, 2H), 7.26 (ddt, J = 5.8, 4.7, 1.4 Hz, 1H), 5.29 (d, J = 1.3 Hz, 1H), 5.10−5.08 (m, 1H), 3.65 (t, J = 6.5 Hz, 2H), 2.62−2.58 (m, 2H), 1.75−1.68 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 141.0, 128.4, 127.5, 126.1, 112.6, 62.4, 31.6, 31.2.

Typical Procedures for the Preparation of Substrates 2e−2g.[22a] To a mixture of ethyl bromodifluoroacetate (10.2 g, 50 mmol) and tetrahydrofuran (50 mL) was added a solution of arylmagnesium bromide in tetrahydrofuran (3.0 M, 18.3 mL, 55 mmol) at −78 °C under an argon atmosphere. After the solution was stirred at that temperature for 3 h, the mixture was quenched with 3 N HCl and then extracted with diethyl ether. The extract was dried over anhydrous $MgSO_4$, and the solvent was removed. Flash chromatography (silica gel, petroleum ether-ethyl acetate) afforded substrates **2e−2g**.

*2-Bromo-2,2-difluoro-1-(furan-2-yl)ethan-1-one (**2e**).*[22b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.70 (m, 1H), 7.47 (dd, J = 2.7, 1.1 Hz, 1H), 6.61 (dd, J = 3.7, 1.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −59.84 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4 (t, J = 28.4 Hz), 148.9, 144.4, 123.1 (t, J = 3.9 Hz), 112.1, 111.7 (t, J = 317.0 Hz).

*2-Bromo-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (**2f**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 9.1 Hz, 2H), 7.00−6.98 (m, 2H), 3.91 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −57.01 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.1 (t, J = 25.4 Hz), 165.1, 133.3 (t, J = 2.8 Hz), 121.7, 114.3, 113.8 (t, J = 318.6 Hz), 55.7.

*1-(Benzo[d][1,3]dioxol-5-yl)-2-bromo-2,2-difluoroethan-1-one (**2g**).*[22c] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (ddt, J = 8.3, 1.9, 1.0 Hz, 1H), 7.56−7.55 (m, 1H), 6.91 (d, J = 8.3 Hz, 1H), 6.11 (s, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −56.78 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.7 (t, J = 25.5 Hz), 153.6, 148.4, 128.1 (t, J = 3.5 Hz), 123.3, 113.6 (t, J = 318.4 Hz), 110.0 (t, J = 2.6 Hz), 108.4, 102.4.

Typical Procedures for the Preparation of Substrates 2h and 2i.[22d] A 20 mL tube equipped with a magnetic stir bar was charged with lanthanum trifluoromethanesulfonate (0.25 mmol, 5.0 mol %). The tube was backfilled with argon, and then ethyl bromodifluoroacetate (6.0 mmol) and amine (5.0 mmol) were added. The mixture was stirred at the room temperature and monitored by TLC. After the amine was exhausted, the mixture was purified by silica gel column chromatography to give the target amides **2h** and **2i**.

*2-Bromo-2,2-difluoro-1-morpholinoethan-1-one (**2h**).*[22d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77−3.69 (m, 8H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −54.53 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9 (t, J = 26.5 Hz), 110.5 (t, J = 314.3 Hz), 66.5, 66.1, 47.3 (t, J = 3.8 Hz), 43.9.

*2-Bromo-N-cycloheptyl-2,2-difluoroacetamide (**2i**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (brs, 1H), 3.97 (dd, J = 8.4, 4.1 Hz, 1H), 2.01−1.95 (m, 2H), 1.68−1.49 (m, 10H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −60.49 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8 (t, J = 27.9 Hz), 112.0 (t, J = 316.5 Hz), 51.6, 34.5, 27.8, 23.9; HRMS (TOF MS ESI) calcd for $C_9H_{15}BrF_2NO^+$ $[M + H]^+$ 270.0300, found 270.0304.

General Procedure for the Photoredox-Catalyzed Cascade Difluoroalkylation and Intramolecular Cyclization. An oven-dried reaction vial containing unsaturated carboxylic acids **1** (0.2 mmol), *fac*-$[Ir(ppy)_3]$ (0.004 mmol), and HCOONa (0.4 mmol) was evacuated and purged with argon three times. Then, DCM (2 mL) as solution and **2a** (0.2 mmol) were added via syringe. The reaction mixture was stirred for 24 h at room temperature in the presence of 5 W blue LED lamps. When the reaction was completed, the reaction mixture was purified by flash chromatography on silica gel (elute: petroleum ether/ethyl acetate = 5:1) directly to furnish corresponding product **3**.

*Ethyl 2,2-Difluoro-3-(5-oxo-2-phenyltetrahydrofuran-2-yl)-propanoate (**3aa**).* Pale yellow oil, 45.6 mg (77% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 4.28−4.11 (m, 2H), 2.95−2.35 (m, 6H), 1.31 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.10 (d, J = 6.7 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 163.6 (t, J = 31.7 Hz), 141.9, 128.9, 128.5, 124.8, 114.4 (t, J = 251.9 Hz), 84.8 (t, J = 4.4 Hz), 63.5, 45.8 (t, J = 23.1 Hz), 34.7, 28.1, 14.0; IR (cm^{-1}) 1768, 1093, 1073, 923, 701; HRMS (TOF MS ESI) calcd for $C_{15}H_{17}F_2O_4^+$ $[M + H]^+$ 299.1089, found 299.1081.

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*Ethyl 3-(2-([1,1′-Biphenyl]-4-yl)-5-oxotetrahydrofuran-2-yl)-2,2-difluoropropanoate (**3ba**).* Pale yellow solid, mp 86−88 °C, 50.6 mg (68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.48 (m, 4H), 7.36−7.26 (m, 5H), 4.21−4.05 (m, 2H), 2.92−2.32 (m, 6H), 1.23 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.00 (d, J = 10.1 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 163.4 (t, J = 31.6 Hz), 141.2, 140.6, 140.1, 128.9, 127.7, 127.4, 127.1, 125.2, 114.3 (t, J = 252.0 Hz), 84.6 (t, J = 4.4 Hz), 63.4, 45.6 (t, J = 23.1 Hz), 34.5, 28.0, 13.8; IR (cm^{-1}) 1765, 1222, 1095, 1080, 766, 733, 693; HRMS (TOF MS ESI) calcd for $C_{21}H_{21}F_2O_4^+$ $[M + H]^+$ 375.1402, found 375.1396.

*Ethyl 3-(2-(4-Chlorophenyl)-5-oxotetrahydrofuran-2-yl)-2,2-difluoropropanoate (**3ca**).* Colorless liquid, 48.6 mg (73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.28 (m, 2H), 7.24−7.21 (m, 2H), 4.24−4.09 (m, 2H), 2.81−2.30 (m, 6H), 1.26 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −100.37−102.08 (m, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 163.3 (t, J = 31.5 Hz), 140.2, 134.3, 128.9, 126.2, 114.1 (t, J = 251.0 Hz), 84.2 (t, J = 4.3 Hz), 63.5, 45.5 (t, J = 23.1 Hz), 34.6, 27.8, 13.8; IR (cm^{-1}) 1768, 1190, 1092, 1012, 922, 832; HRMS (TOF MS ESI) calcd for $C_{15}H_{16}ClF_2O_4^+$ $[M + H]^+$ 333.0700, found 333.0702.

*Ethyl 2,2-Difluoro-3-(6-oxo-2-phenyltetrahydro-2H-pyran-2-yl)-propanoate (**3da**).* Yellow oil, 40.1 mg (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.30 (m, 2H), 7.27−7.23 (m, 3H), 4.30−4.15 (m, 2H), 2.77−2.61 (m, 2H), 2.43−2.26 (m, 4H), 1.72−1.64 (m, 1H), 1.46−1.34 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −99.68 (q, J = 263.8 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 162.7 (t, J = 31.0 Hz), 141.1, 127.9, 127.0, 123.8, 113.3 (t, J = 251.4 Hz), 83.1 (dd, J = 6.7, 3.0 Hz), 62.3, 46.6 (t, J = 23.3 Hz), 30.2 (d, J = 2.9 Hz), 28.0, 15.9, 12.8; IR (cm^{-1}) 2921, 2852, 1756, 1456, 1376, 813, 763; HRMS (TOF MS ESI) calcd for $C_{16}H_{19}F_2O_4^+$ $[M + H]^+$ 313.1246, found 313.1245.

*Ethyl 2,2-Difluoro-3-(2-(4-methoxyphenyl)-5-oxotetrahydrofuran-2-yl)propanoate (**3ea**).* White oil, 63.6 mg (97% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.18 (m, 2H), 6.84−6.80 (m, 2H), 4.20−4.04 (m, 2H), 3.73 (s, 3H), 2.82−2.69 (m, 2H), 2.66−2.42 (m, 3H), 2.38−2.28 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.12 (d, J = 4.8 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 162.4 (t, J = 31.6 Hz), 158.4, 132.3, 125.0, 113.2 (t, J = 251.0 Hz), 112.9, 83.6 (t, J = 4.1 Hz), 62.3, 54.3, 44.7 (t, J = 22.9 Hz), 33.3, 27.0, 12.7; IR (cm^{-1}) 1769, 1514, 1252, 1178, 1092, 1030, 922, 833; HRMS (TOF MS ESI) calcd for $C_{16}H_{19}F_2O_5^+$ $[M + H]^+$ 329.1195, found 329.1197.

*Ethyl 2,2-Difluoro-3-(2-(4-fluorophenyl)-5-oxotetrahydrofuran-2-yl)propanoate (**3fa**).* White oil, 46.2 mg (73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.25 (m, 2H), 7.03−6.98 (m, 2H), 4.23−4.08 (m, 2H), 2.85−2.30 (m, 6H), 1.25 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −100.41−102.10 (m, 2F), −113.64 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 163.3 (t, J = 31.7 Hz), 162.4 (d, J = 247.9 Hz), 137.5 (d, J = 3.2 Hz), 126.6 (d, J = 8.3 Hz), 115.6 (d, J = 21.7 Hz), 114.1 (t, J = 251.0 Hz), 84.3 (t, J = 4.3 Hz), 63.4, 45.6 (t, J = 23.0 Hz), 34.7, 27.9, 13.8; IR (cm^{-1}) 1769, 1511, 1223, 1090, 1013, 922, 839, 816, 778; HRMS (TOF MS ESI) calcd for $C_{15}H_{16}F_3O_4^+$ $[M + H]^+$ 317.0995, found 317.0994.

*Ethyl 3-(2-(4-Bromophenyl)-5-oxotetrahydrofuran-2-yl)-2,2-difluoropropanoate (**3ga**).* Yellow oil, 55.7 mg (74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.43 (m, 2H), 7.20−7.15 (m, 2H), 4.24−4.08 (m, 2H), 2.85−2.69 (m, 2H), 2.67−2.52 (m, 2H), 2.45−2.30 (m, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −100.36−102.06 (m, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 163.3 (t, J = 31.6 Hz), 140.8, 131.9, 126.4, 122.4, 114.1 (t, J = 252.3 Hz), 84.2 (t, J = 4.3 Hz), 63.5, 45.4 (t, J = 23.1 Hz), 34.6, 27.8, 13.8; IR (cm^{-1}) 1769, 1222, 1190, 1090, 1008, 922, 829, 777; HRMS (TOF MS ESI) calcd for $C_{15}H_{16}BrF_2O_4^+$ $[M + H]^+$ 377.0195, found 377.0193.

*Ethyl 2,2-Difluoro-3-(5-oxo-2-(p-tolyl)tetrahydrofuran-2-yl)-propanoate (**3ha**).* White liquid, 53.1 mg (85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.10 (m, 4H), 4.20−4.04 (m, 2H), 2.86−2.69 (m, 2H), 2.68−2.59 (m, 1H), 2.55−2.42 (m, 2H), 2.37−2.29 (m, 1H), 2.27 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.06 (d, J = 5.4 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.3, 163.4 (t, J = 31.7 Hz), 138.6, 138.1, 129.3, 124.6, 114.3 (t, J = 251.9 Hz), 84.7 (t, J = 4.0 Hz), 63.3, 45.6 (t, J = 23.0 Hz), 34.4, 28.0, 21.0, 13.8; IR (cm^{-1}): 1770, 1225, 1182, 1092, 922, 822, 777; HRMS (TOF MS ESI) calcd for $C_{16}H_{19}F_2O_4^+$ $[M + H]^+$ 313.1246, found 313.1250.

*Ethyl 2,2-Difluoro-2-(5-oxo-2-phenyltetrahydrofuran-3-yl)-acetate (**3ia**).* Pale yellow solid, 39.4 mg (69% yield), mp 54−55 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.30 (m, 5H), 5.60 (d, J = 5.2 Hz, 1H), 4.29−4.16 (m, 2H), 3.35−3.23 (m, 1H), 2.92−2.79 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.43 (q, J = 267.8 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 162.5 (t, J = 32.1 Hz), 137.9, 129.2, 129.0, 125.6, 114.4 (t, J = 254.4 Hz), 79.1 (t, J = 4.3 Hz), 63.7, 47.6 (t, J = 23.4 Hz), 28.3 (t, J = 4.0 Hz), 13.8; IR (cm^{-1}) 2929, 1779, 1765, 1144, 1095, 991, 766, 736, 700, 487; HRMS (TOF MS ESI) calcd for $C_{14}H_{15}F_2O_4^+$ $[M + H]^+$ 285.0933, found 285.0933.

*Ethyl 2,2-Difluoro-3-(3-oxo-1,3-dihydroisobenzofuran-1-yl)-propanoate (**3ja**).* Pale yellow solid, 23.2 mg (43% yield), mp 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.7 Hz, 1H), 7.75−7.71 (m, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.52 (d, J = 7.7 Hz, 1H), 5.70 (dd, J = 9.0, 3.2 Hz, 1H), 4.46−4.35 (m, 2H), 2.85−2.73 (m, 1H), 2.66−2.52 (m, 1H), 1.40 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.22 (dd, J = 1762.4, 265.8 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 163.3 (t, J = 32.0 Hz), 148.1, 134.5, 129.8, 126.1, 125.7, 122.0, 114.2 (dd, J = 253.7, 250.8 Hz), 74.7 (dd, J = 7.4, 3.7 Hz), 63.6, 40.3 (t, J = 24.0 Hz), 13.9; IR (cm^{-1}) 1765, 1286, 1186, 1089, 1058, 749, 693, 682; HRMS (TOF MS ESI) calcd for $C_{13}H_{13}F_2O_4^+$ $[M + H]^+$ 271.0776, found 271.0778.

*Ethyl 2,2-Difluoro-3-(1-methyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)propanoate (**3ka**).* Colorless oil, 43.8 mg (77% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.80 (m, 1H), 7.63 (td, J = 7.6, 1.1 Hz, 1H), 7.48 (td, J = 7.6, 0.8 Hz, 1H), 7.37 (d, J = 7.7 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 2.88 (q, J = 15.0 Hz, 1H), 2.66 (q, J = 15.0 Hz, 1H), 1.65 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.57 (d, J = 0.8 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 163.4 (t, J = 31.6 Hz), 152.4, 134.4, 129.6, 126.0, 125.2, 121.3, 114.1 (t, J = 252.4 Hz), 82.9 (t, J = 4.3 Hz), 63.5, 43.7 (t, J = 23.4 Hz), 26.9, 13.8; IR (cm^{-1}) 1758, 1086, 1029, 763, 694; HRMS (TOF MS ESI) calcd for $C_{14}H_{15}F_2O_4^+$ $[M + H]^+$ 285.0933, found 285.0934.

*Ethyl 2,2-Difluoro-3-(3-oxo-1-(p-tolyl)-1,3-dihydroisobenzofuran-1-yl)propanoate (**3la**).* Colorless oil, 66.7 mg (93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 1H), 7.60 (td, J = 7.8, 1.1 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.44 (td, J = 7.6, 0.9 Hz, 1H), 7.30−7.28 (m, 2H), 7.08 (d, J = 8.0 Hz, 2H), 4.24−4.11 (m, 2H), 3.35 (ddd, J = 21.8, 15.2, 8.3 Hz, 1H), 3.08 (td, J = 15.7, 9.0 Hz, 1H), 2.23 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.26 (dd, J = 1242.5, 267.6 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 163.4 (t, J = 31.5 Hz), 151.2, 138.6, 136.8, 134.4, 129.6, 129.6, 126.0, 125.0, 124.5, 122.7, 114.0 (dd, J = 254.7, 251.3 Hz), 85.2 (dd, J = 6.1, 2.5 Hz), 63.5, 43.9 (t, J = 23.4 Hz), 21.0, 13.8; IR (cm^{-1}) 1762, 1229, 1113, 1068, 723, 693, 538; HRMS (TOF MS ESI) calcd for $C_{20}H_{19}F_2O_4^+$ $[M + H]^+$ 361.1246, found 361.1249.

*Ethyl 2,2-Difluoro-3-(3-oxo-1-phenyl-1,3-dihydroisobenzofuran-1-yl)propanoate (**3ma**).* Yellow oil, 61.5 mg (89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.72−7.68 (m, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.51−7.48 (m, 2H), 7.40−7.30 (m, 3H), 4.33−4.20 (m, 2H), 3.44 (ddd, J = 21.8, 15.2, 8.2 Hz, 1H), 3.18 (td, J = 15.6, 9.0 Hz, 1H), 1.33 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.31 (dd, J = 1300.4, 267.9 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 162.4 (t, J = 31.5 Hz), 150.0, 138.7, 133.4, 128.6, 127.9, 127.6, 125.0, 123.9, 123.5, 121.7, 112.9 (dd, J = 254.7, 251.3 Hz), 84.1 (dd, J = 6.3, 2.5 Hz), 62.4, 42.9 (t, J = 23.5 Hz), 12.7; IR (cm^{-1}) 1762, 1286, 1230, 1064, 778, 699, 622; HRMS (TOF MS ESI) calcd for $C_{19}H_{17}F_2O_4^+$ $[M + H]^+$ 347.1089, found 347.1089.

*Ethyl 3-(1-(4-Chlorophenyl)-3-oxo-1,3-dihydroisobenzofuran-1-yl)-2,2-difluoropropanoate (**3na**).* White oil, 48.6 mg (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 1H), 7.73−7.69 (m, 1H), 7.60−7.57 (m, 2H), 7.45−7.43 (m, 2H), 7.36−7.33 (m, 2H), 4.34−4.21 (m, 2H), 3.39 (ddd, J = 20.7, 15.2, 8.5 Hz, 1H), 3.18−3.08 (m, 1H), 1.34 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.31 (dd, J = 1032.8, 268.5 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 163.3 (t, J = 31.4 Hz), 150.7, 138.2, 134.8, 134.6, 129.9, 129.1,

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126.3, 126.1, 124.8, 122.6, 113.8 (dd, J = 254.5, 252.1 Hz), 84.6 (dd, J = 5.8, 3.5 Hz), 63.6, 43.9 (t, J = 23.5 Hz), 13.8; IR (cm^{-1}) 1762, 1286, 1230, 1094, 1067, 1012, 762, 691; HRMS (TOF MS ESI) calcd for $C_{19}H_{16}ClF_2O_4^+$ $[M + H]^+$ 381.0700, found 381.0699.

*Ethyl 2,2-Difluoro-3-(2-phenyltetrahydrofuran-2-yl)propanoate (**3oa**).* Pale yellow oil, 46.5 mg (82% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.23 (m, 4H), 7.19−7.13 (m, 1H), 4.21−4.07 (m, 2H), 3.84−3.74 (m, 2H), 2.72−2.59 (m, 2H), 2.30−2.23 (m, 1H), 2.15−2.10 (m, 1H), 1.91−1.84 (m, 1H), 1.70−1.59 (m, 1H), 1.25 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.25 (dd, J = 680.5, 264.5 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9 (dd, J = 32.8, 31.2 Hz), 145.0, 127.2, 125.9, 123.8, 114.3 (t, J = 250.1 Hz), 82.1 (dd, J = 6.7, 3.2 Hz), 67.1, 61.4, 44.7 (t, J = 22.0 Hz), 37.2 (d, J = 3.0 Hz), 24.1, 12.9; IR (cm^{-1}) 2961, 1795, 1257, 1009, 863, 787; HRMS (TOF MS ESI) calcd for $C_{15}H_{19}F_2O_3^+$ $[M + H]^+$ 285.1297, found 285.1292.

*5-Phenyl-5-(2,2,2-trifluoroethyl)dihydrofuran-2(3H)-one (**3ab**).* White solid, 36.1 mg (74% yield), mp 59−61 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.32 (m, 5H), 2.93−2.77 (m, 2H), 2.68−2.58 (m, 3H), 2.51−2.41 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −60.54 (s, 3F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 141.1, 128.8, 128.5, 124.6, 124.6 (q, J = 277.0 Hz), 84.3 (dd, J = 4.3, 2.2 Hz), 45.2 (q, J = 27.6 Hz), 34.1 (d, J = 1.3 Hz), 28.0; IR (cm^{-1}): 1775, 1382, 1248, 1122, 928, 701; HRMS (TOF MS ESI) calcd for $C_{12}H_{12}F_3O_2^+$ $[M + H]^+$ 245.0784, found 245.0782.

*Diethyl (1,1-Difluoro-2-(5-oxo-2-phenyltetrahydrofuran-2-yl)-ethyl)phosphonate (**3ac**).* Yellow oil, 54.9 mg (76% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.31 (m, 5H), 4.30−4.17 (m, 4H), 2.93−2.59 (m, 5H), 2.49−2.40 (m, 1H), 1.36 (dt, J = 12.5, 7.1 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.58 (ddd, J = 676.8, 300.1, 104.2 Hz, 2F); ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.73 (t, J = 104.2 Hz, 1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9, 142.9, 128.8, 128.3, 124.8, 119.8 (td, J = 262.7, 216.1 Hz), 85.8 (d, J = 9.4 Hz), 65.0 (t, J = 8.0 Hz), 44.3 (td, J = 19.0, 14.6 Hz), 34.1, 28.4, 16.5 (dd, J = 5.3, 2.4 Hz); IR (cm^{-1}) 1778, 1267, 1178, 1012, 921, 701, 533; HRMS (TOF MS ESI) calcd for $C_{16}H_{22}F_2O_5P^+$ $[M + H]^+$ 363.1167, found 363.1171.

*Ethyl 2-Fluoro-3-(5-oxo-2-phenyltetrahydrofuran-2-yl)-propanoate (**3ad**).* White oil, 30.6 mg (55% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.24 (m, 5H), 4.99−4.64 (m, 1H), 4.21−4.00 (m, 2H), 2.66−2.33 (m, 6H), 1.23−1.16 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −189.48 (s, 0.43F), −190.14 (s, 0.56F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 175.8, 169.3 (d, J = 10.1 Hz), 169.1 (d, J = 9.9 Hz), 142.6, 141.1, 129.1, 129.0, 128.5, 128.4, 125.2, 124.7, 87.0 (d, J = 33.0 Hz), 86.9 (d, J = 41.0 Hz), 85.4, 85.0, 62.2, 62.1, 44.2 (d, J = 19.5 Hz), 43.9 (d, J = 20.0 Hz), 34.9 (d, J = 3.1 Hz), 34.6 (d, J = 3.3 Hz), 28.6, 28.4, 14.2, 14.2; IR (cm^{-1}) 1777, 1755, 1178, 1089, 1024, 701; HRMS (TOF MS ESI) calcd for $C_{15}H_{18}FO_4^+$ $[M + H]^+$ 281.1184, found 281.1185.

*5-(2,2-Difluoro-3-(furan-2-yl)-3-oxopropyl)-5-phenyldihydrofuran-2(3H)-one (**3ae**).* Pale yellow oil, 17.7 mg (28% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 1.0 Hz, 1H), 7.30−7.20 (m, 6H), 6.50 (dd, J = 3.7, 1.7 Hz, 1H), 3.05−2.86 (m, 2H), 2.67−2.48 (m, 3H), 2.40−2.30 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −99.50 (q, J = 280.7 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8 (t, J = 30.8 Hz), 174.3, 147.9, 146.8, 140.7, 127.6, 127.2, 123.7, 122.2 (t, J = 5.7 Hz), 116.3 (t, J = 254.8 Hz), 111.7, 84.0 (t, J = 2.8 Hz), 43.6 (t, J = 2.2 Hz), 34.0, 27.0; IR (cm^{-1}) 1773, 1668, 1460, 1191, 1073, 1029, 921, 760, 700; HRMS (TOF MS ESI) calcd for $C_{17}H_{15}F_2O_4^+$ $[M + H]^+$ 321.0933, found 321.0935.

*5-(2,2-Difluoro-3-(4-methoxyphenyl)-3-oxopropyl)-5-phenyldihydrofuran-2(3H)-one (**3af**).* Pale yellow oil, 26.8 mg (37% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 9.0 Hz, 2H), 7.33−7.20 (m, 5H), 6.86−6.82 (m, 2H), 3.80 (s, 3H), 2.95 (t, J = 16.9 Hz, 2H), 2.74−2.47 (m, 3H), 2.41−2.25 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −95.46−97.36 (m, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.0 (t, J = 298.0 Hz), 175.6, 164.5, 142.5, 132.8, 128.6, 128.1, 124.7, 124.4, 118.5 (t, J = 256.0 Hz), 114.0, 85.5, 55.6, 44.5 (t, J = 21.7 Hz), 34.7, 28.2; IR (cm^{-1}) 1778, 1688, 1596, 1263, 1169, 700; HRMS (TOF MS ESI) calcd for $C_{20}H_{19}F_2O_4^+$ $[M + H]^+$ 361.1246, found 361.1247.

*5-(3-(Benzo[d][1,3]dioxol-5-yl)-2,2-difluoro-3-oxopropyl)-5-phenyldihydrofuran-2(3H)-one (**3ag**).* Yellow oil, 18.5 mg (25% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.3, 1.0 Hz, 1H), 7.35−7.21 (m, 6H), 6.77 (d, J = 8.3 Hz, 1H), 5.98 (s, 2H), 2.94 (t, J = 16.9 Hz, 2H), 2.71−2.48 (m, 3H), 2.41−2.33 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −96.00 (q, J = 290.7 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.6 (t, J = 29.8 Hz), 174.5, 151.9, 147.1, 141.4, 127.6, 127.1, 126.3 (t, J = 4.5 Hz), 124.9 (t, J = 2.6 Hz), 123.7, 117.3 (t, J = 256.2 Hz), 108.6 (t, J = 2.9 Hz), 107.2, 101.1, 84.3 (t, J = 2.0 Hz), 43.5 (t, J = 21.8 Hz), 33.8, 27.2; IR (cm^{-1}) 1777, 1687, 1445, 1242, 1034, 923, 701; HRMS (TOF MS ESI) calcd for $C_{20}H_{17}F_2O_5^+$ $[M + H]^+$ 375.1039, found 375.1040.

*5-(2,2-Difluoro-3-morpholino-3-oxopropyl)-5-phenyldihydrofuran-2(3H)-one (**3ah**).* Yellow solid, 49.9 mg (74% yield), mp 122−124 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.23 (m, 5H), 3.69−3.45 (m, 8H), 2.97−2.87 (m, 2H), 2.68 (dt, J = 12.3, 8.7 Hz, 1H), 2.56 (ddd, J = 16.7, 8.8, 4.3 Hz, 1H), 2.50−2.43 (m, 1H), 2.35 (dt, J = 17.0, 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −95.93 (dd, J = 744.6, 282.7 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 160.6 (t, J = 28.3 Hz), 141.6, 127.6, 127.0, 123.6, 116.7 (t, J = 256.7 Hz), 84.3, 65.5, 65.5, 45.5 (t, J = 6.0 Hz), 44.0 (t, J = 21.7 Hz), 42.6, 33.8, 27.1; IR (cm^{-1}) 1763, 1665, 1110, 712, 600; HRMS (TOF MS ESI) calcd for $C_{17}H_{20}F_2NO_4^+$ $[M + H]^+$ 340.1355, found 340.1354.

*N-Cycloheptyl-2,2-difluoro-3-(5-oxo-2-phenyltetrahydrofuran-2-yl)propanamide (**3ai**).* White solid, 29.1 mg (40% yield), mp 96−98 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.22 (m, 5H), 6.04 (d, J = 6.1 Hz, 1H), 3.75−3.67 (m, 1H), 2.97−2.78 (m, 2H), 2.62−2.30 (m, 4H), 1.91−1.85 (m, 1H), 1.75−1.71 (m, 1H), 1.58−1.48 (m, 4H), 1.45−1.25 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −102.38 (q, J = 262.5 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 162.2 (t, J = 27.4 Hz), 142.0, 128.6, 128.1, 124.6, 116.3 (t, J = 255.0 Hz), 84.9 (t, J = 3.2 Hz), 50.9, 44.1 (t, J = 22.8 Hz), 35.7, 34.5, 34.4, 27.9, 23.9 (d, J = 1.2 Hz); IR (cm^{-1}) 3322, 2919, 2850, 1779, 1669, 1539, 1194, 1070, 702; HRMS (TOF MS ESI) calcd for $C_{20}H_{26}F_2NO_3^+$ $[M + H]^+$ 366.1875, found 366.1883.

Control Experiment with the Addition of 1,1-Diphenylethylene. An oven-dried reaction vial containing unsaturated carboxylic acids **1a** (0.2 mmol), *fac*-$[Ir(ppy)_3]$ (0.004 mmol), 1,1-diphenylethylene (0.4 mmol), and HCOONa (0.4 mmol) was evacuated and purged with argon three times. Then, DCM (2 mL) as solution and **2a** (0.2 mmol) were added via syringe. The reaction mixture was stirred for 24 h at room temperature in the presence of 5 W blue LED lamps. When the reaction was completed, the reaction mixture was purified by flash chromatography on silica gel (elute: petroleum ether/ethyl acetate = 5:1) directly to furnish corresponding product **4a** with 82% yield.

*Ethyl 2,2-Difluoro-4,4-diphenylbut-3-enoate (**4a**).*[23] Colorless liquid, 49.6 mg (82% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.11 (m, 10H), 6.19 (t, J = 11.8 Hz, 1H), 3.83 (q, J = 7.2 Hz, 2H), 1.09 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −90.95 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (t, J = 34.0 Hz), 150.0 (t, J = 9.5 Hz), 139.4, 136.0, 128.8 (t, J = 1.9 Hz), 128.1, 127.6, 127.4, 127.0, 126.9, 118.4 (t, J = 28.4 Hz), 111.5 (t, J = 245.0 Hz), 61.7, 12.6.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01279.

Full spectroscopic data for compounds **3**, copies of ^1H and ^{13}C NMR spectra, and X-ray single crystal analysis of **3ja** (PDF)

Crystallographic information for **3ja** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hanjl@nju.edu.cn.

ORCID

Jianlin Han: 0000-0002-3817-0764

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881−1886. (b) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116*, 422−518. (c) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359−4369. (d) Meanwell, N. A. *J. Med. Chem.* **2011**, *54*, 2529−2591. (e) Fujiwara, T.; O'Hagan, D. *J. Fluorine Chem.* **2014**, *167*, 16−29. (f) Zhang, W. *Chem. Rev.* **2009**, *109*, 749−795. (g) Miró, J.; del Pozo, C. *Chem. Rev.* **2016**, *116*, 11924−11966. (h) Ni, C.; Hu, J. *Chem. Soc. Rev.* **2016**, *45*, 5441−5454. (i) Campbell, M. G.; Ritter, T. *Chem. Rev.* **2015**, *115*, 612−633.

(2) (a) Miller, P. W.; Long, N. J.; Vilar, R.; Gee, A. D. *Angew. Chem., Int. Ed.* **2008**, *47*, 8998−9033. (b) Preshlock, S.; Tredwell, M.; Gouverneur, V. *Chem. Rev.* **2016**, *116*, 719−766.

(3) (a) Chen, P. H.; Liu, G. S. *Synthesis* **2013**, *45*, 2919−2939. (b) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214−8264. (c) Zhang, C. *Org. Biomol. Chem.* **2014**, *12*, 6580−6589. (d) Chatalova-Sazepin, C.; Hemelaere, R.; Paquin, J. F.; Sammis, G. M. *Synthesis* **2015**, *47*, 2554−2569. (e) Xu, P.; Guo, S.; Wang, L. Y.; Tang, P. P. *Synlett* **2015**, *26*, 36−39. (f) Koike, T.; Akita, M. *Acc. Chem. Res.* **2016**, *49*, 1937−1945. (g) Hasegawa, M.; Yoshida, K.; Yanagisawa, A. *Chem. Lett.* **2016**, *45*, 294−296.

(4) (a) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1−PR43. (b) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475−4521. (c) Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8950−8958. (d) Egami, H.; Sodeoka, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 8294−8308. (e) Alonso, C.; Martinez de Marigorta, E.; Rubiales, G.; Palacios, F. *Chem. Rev.* **2015**, *115*, 1847−1935. (f) Charpentier, J.; Fruh, N.; Togni, A. *Chem. Rev.* **2015**, *115*, 650−682. (g) Liu, X.; Xu, C.; Wang, M.; Liu, Q. *Chem. Rev.* **2015**, *115*, 683−730. (h) Yang, X.; Wu, T.; Phipps, R. J.; Toste, F. D. *Chem. Rev.* **2015**, *115*, 826−870.

(5) (a) Zhang, C.-P.; Chen, Q.-Y.; Guo, Y.; Xiao, J.-C.; Gu, Y.-C. *Coord. Chem. Rev.* **2014**, *261*, 28−72. (b) Chen, B.; Vicic, D. A.; Braun, T.; Hughes, R. P. Transition-Metal-Catalyzed Difluoromethylation, Difluoromethylenation, and Polydifluoromethylenation Reactions. *Top. Organomet. Chem.* **2014**, *52*, 113−141.

(6) (a) Belhomme, M.-C.; Besset, T.; Poisson, T.; Pannecoucke, X. *Chem. - Eur. J.* **2015**, *21*, 12836−12865. (b) Pan, X.; Xia, H.; Wu, J. *Org. Chem. Front.* **2016**, *3*, 1163−1185. (c) Huang, H.; Li, Y. *J. Org. Chem.* **2017**, *82*, 4449−4457. (d) Yang, X.; Yang, X.; Zhu, S.; Ye, L.; Chen, Y.; Chen, G.; Wu, F. H. *Chin. J. Chem.* **2010**, *28*, 2269−2273. (e) Wang, J. X.; Wu, J. J.; Chen, H.; Zhang, S. W.; Wu, F. H. *Chin. Chem. Lett.* **2015**, *26*, 1381−1384. (f) Yang, X.; Fang, X.; Yang, X.; Zhao, M.; Han, Y.; Shen, Y.; Wu, F. H. *Tetrahedron* **2008**, *64*, 2259−2269. (g) Yang, X.; Zhu, Y.; Fang, X.; Yang, X.; Wu, F. H.; Shen, Y. *J. Fluorine Chem.* **2007**, *128*, 174−178. (h) Nguyen, Q. P. B.; Kim, B. M.; Song, M. S.; Yoon, K. H.; Chai, K. Y. *Bull. Korean Chem. Soc.* **2014**, *35*, 313−315.

(7) (a) Blasko, G.; Gula, D. J.; Shamma, M. *J. Nat. Prod.* **1982**, *45*, 105−122. (b) Kaiser, C.; Spagnuolo, C. J.; Adams, T. C.; Audia, V. H.; Dupont, A. C.; Hatoum, H.; Lowe, V. C.; Prosser, J. C.; Sturm, B. L.; Noronha-Blob, L. *J. Med. Chem.* **1992**, *35*, 4415−4424. (c) Lambert, J. D.; Rice, J. E.; Hong, J.; Hou, Z.; Yang, C. S. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 873−876. (d) Omura, S.; Fukuyama, T.; Murakami, Y.; Okamoto, H.; Ryu, I. *Chem. Commun.* **2009**, 6741−6743. (e) Luo, F.; Pan, S.; Pan, C.; Qian, P.; Cheng, J. *Adv. Synth. Catal.* **2011**, *353*, 320−324.

(8) (a) Nicolai, S.; Erard, S.; Gonzalez, D. F.; Waser, J. *Org. Lett.* **2010**, *12*, 384−387. (b) Guo, W.; Cheng, H. G.; Chen, L. Y.; Xuan, J.; Feng, Z. J.; Chen, J. R.; Lu, L. Q.; Xiao, W. J. *Adv. Synth. Catal.* **2014**, *356*, 2787−2793. (c) Chen, T.; Foo, T. J. Y.; Yeung, Y.-Y. *ACS Catal.* **2015**, *5*, 4751−4755. (d) Gao, Y.; Li, X.; Chen, W.; Tang, G.; Zhao, Y. *J. Org. Chem.* **2015**, *80*, 11398−11406. (e) Gao, Y.; Li, X.; Xu, J.; Wu, Y.; Chen, W.; Tang, G.; Zhao, Y. *Chem. Commun.* **2015**, *51*, 1605−1607. (f) Moriyama, K.; Nishinohara, C.; Sugiue, T.; Togo, H. *RSC Adv.* **2015**, *5*, 85872−85878. (g) Xu, C.; Shen, Q. *Org. Lett.* **2015**, *17*, 4561−4563. (h) Hemric, B. N.; Shen, K.; Wang, Q. *J. Am. Chem. Soc.* **2016**, *138*, 5813−5816. (i) Nakatsuji, H.; Sawamura, Y.; Sakakura, A.; Ishihara, K. *Angew. Chem., Int. Ed.* **2014**, *53*, 6974−6977. (j) Liu, X.; An, R.; Zhang, X.; Luo, J.; Zhao, X. *Angew. Chem., Int. Ed.* **2016**, *55*, 5846−5850. (k) Paull, D. H.; Fang, C.; Donald, J. R.; Pansick, A. D.; Martin, S. F. *J. Am. Chem. Soc.* **2012**, *134*, 11128−11131. (l) Niu, W.; Yeung, Y.-Y. *Org. Lett.* **2015**, *17*, 1660−1663.

(9) (a) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 12462−12465. (b) Zhu, R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2013**, *52*, 12655−12658.

(10) Yasu, Y.; Arai, Y.; Tomita, R.; Koike, T.; Akita, M. *Org. Lett.* **2014**, *16*, 780−783.

(11) Parmar, D.; Maji, M. S.; Rueping, M. *Chem. - Eur. J.* **2014**, *20*, 83−86.

(12) Geary, G. C.; Hope, E. G.; Stuart, A. M. *Angew. Chem., Int. Ed.* **2015**, *54*, 14911−14914.

(13) (a) Xiao, F.; Wu, F.; Yang, X.; Shen, Y.; Shi, X. *J. Fluorine Chem.* **2005**, *126*, 319−323. (b) Yang, X.; Yang, X.; Zhu, S.; Ye, L.; Chen, Y.; Chen, G.; Wu, F. *Chin. J. Chem.* **2010**, *28*, 2269−2273. (c) Wu, F.; Yang, X.; Wang, Z.; Huang, W. *J. Fluorine Chem.* **2007**, *128*, 84−86. (d) Yang, X.; Yuan, W.; Gu, S.; Yang, X.; Xiao, F.; Shen, Q.; Wu, F. *J. Fluorine Chem.* **2007**, *128*, 540−544. (e) Zou, X.; Wu, F.; Shen, Y.; Xu, S.; Huang, W. *Tetrahedron* **2003**, *59*, 2555−2560.

(14) Du, B.; Wang, Y.; Mei, H.; Han, J.; Pan, Y. *Adv. Synth. Catal.* **2017**, *359*, 1684−1690.

(15) (a) Sha, W. X.; Zhang, L. J.; Zhang, W. Z.; Mei, H. B.; Soloshonok, V. A.; Han, J. L.; Pan, Y. *Org. Biomol. Chem.* **2016**, *14*, 7295−7303. (b) Sha, W.; Zhang, L.; Wu, X.; Mei, H.; Han, J.; Soloshonok, V. A.; Pan, Y. *J. Fluorine Chem.* **2017**, *196*, 14−23.

(16) (a) Skubi, K. L.; Blum, T. R.; Yoon, T. P. *Chem. Rev.* **2016**, *116*, 10035−10074. (b) Levin, M. D.; Kim, S.; Toste, F. D. *ACS Cent. Sci.* **2016**, *2*, 293−301. (c) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322−5363. (d) Hopkinson, M. N.; Sahoo, B.; Li, J. L.; Glorius, F. *Chem. - Eur. J.* **2014**, *20*, 3874−3886. (e) Cavalcanti, L. N.; Molander, G. A. *Top. Curr. Chem.* **2016**, *374*, 39. (f) Zhang, M.; Li, W.; Duan, Y.; Xu, P.; Zhang, S.; Zhu, C. *Org. Lett.* **2016**, *18*, 3266−3269.

(17) Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 9034−9037.

(18) Zhang, H.-R.; Chen, D.-Q.; Han, Y.-P.; Qiu, Y.-F.; Jin, D.-P.; Liu, X.-Y. *Chem. Commun.* **2016**, *52*, 11827−11830.

(19) Liao, J.; Fan, L.; Guo, W.; Zhang, Z.; Li, J.; Zhu, C.; Ren, Y.; Wu, W.; Jiang, H. *Org. Lett.* **2017**, *19*, 1008−1011.

(20) (a) Takemiya, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 6042−6043. (b) Zhou, L.; Tan, C. K.; Jiang, X.; Chen, F.; Yeung, Y. Y. *J. Am. Chem. Soc.* **2010**, *132*, 15474−15476. (c) Aursnes, M.; Tungen, J. E.; Hansen, T. V. *J. Org. Chem.* **2016**, *81*, 8287−8295.

(21) (a) Song, S.; Zhu, S. F.; Yu, Y. B.; Zhou, Q. L. *Angew. Chem., Int. Ed.* **2013**, *52*, 1556−1559. (b) Alves, T. M. F.; Costa, M. O.; Bispo, B. A. D.; Pedrosa, F. L.; Ferreira, M. A. B. *Tetrahedron Lett.* **2016**, *57*, 3334−3338.

(22) (a) Nihei, T.; Iwai, N.; Matsuda, T.; Kitazume, T. *J. Org. Chem.* **2005**, *70*, 5912−5915. (b) Chung, W. J.; Higashiya, S.; Welch, J. T. *J. Fluorine Chem.* **2001**, *112*, 343−347. (c) John, J. P.; Colby, D. A. *J. Org. Chem.* **2011**, *76*, 9163−9168. (d) Wang, L.; Wei, X. J.; Jia, W. L.; Zhong, J. J.; Wu, L. Z.; Liu, Q. *Org. Lett.* **2014**, *16*, 5842−5845.

(23) Lai, Y.-L.; Lin, D.-Z.; Huang, J.-M. *J. Org. Chem.* **2017**, *82*, 597−605.

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