

## RESEARCH ARTICLE

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Cite this: *Org. Chem. Front.*, 2022, **9**, 2141Direct C(sp<sup>3</sup>)-H difluoromethylation *via* radical-radical cross-coupling by visible-light photoredox catalysis†Wei Xiong,<sup>‡</sup> Wen-Bing Qin,<sup>‡</sup> Ya-Shi Zhao, Kai-Zhong Fu and Guo-Kai Liu \*

Herein, a radical-radical cross-coupling strategy for direct difluoromethylation of the C(sp<sup>3</sup>)-H bond is reported. This transformation was readily accomplished under transition metal-free photoredox catalysis in the presence of 3 mol% of an organic photocatalyst, allowing the direct difluoromethylation of C(sp<sup>3</sup>)-H of a wide variety of 1,4-dihydroquinoxalin-2-ones in good yields under mild reaction conditions. Moreover, various 3-difluoromethyl quinoxalin-2-ones were also easily furnished in a one-pot manner through this radical difluoromethylation protocol. Mechanistic studies clearly reveal that the radical-radical cross-coupling between a difluoromethyl radical and a C(sp<sup>3</sup>) radical is responsible for this transformation. To the best of our knowledge, this is the first example of radical-radical cross-coupling difluoromethylation of the C(sp<sup>3</sup>)-H bond, which not only provides a promising strategy for a straightforward installation of a CF<sub>2</sub>H group at a C(sp<sup>3</sup>) center but would also promote the development of other new fluorination and fluoroalkylation methods.

Received 11th February 2022,

Accepted 3rd March 2022

DOI: 10.1039/d2qo00192f

rsc.li/frontiers-organic

## Introduction

Nowadays, the incorporation of one or more fluorine atoms into bioactive compounds has become a routine strategy for the development of pharmaceuticals and agrochemicals.<sup>1</sup> Amongst various fluorine-containing units, the CF<sub>2</sub>H group can endow the parent molecule with significantly improved physicochemical and biological properties due to its unique instincts.<sup>2</sup> For example, the CF<sub>2</sub>H group can serve as a competent lipophilic hydrogen bond donor<sup>3</sup> as well as act as metabolically stable bioisosteres of alcohol, thiol, or amine groups.<sup>4</sup> Therefore, the development of strategies and synthetic versions for assembling the CF<sub>2</sub>H unit has attracted considerable attention. Amongst the existing strategies, the difluoromethylation reaction is the most straightforward and efficient approach to access CF<sub>2</sub>H-containing compounds. Consequently, for this purpose, continuous efforts on difluoromethylating reagents and thereby difluoromethylation protocols have been increasingly made in the past decade.<sup>5</sup> Notably, the C(sp<sup>3</sup>)-CF<sub>2</sub>H moiety is of great interest in pharmaceutical chemistry because it is a bioisosteric replacement for aliphatic alcohols

and thiols, two prevalent functional groups in drug design and discovery.<sup>6</sup> As one of the most straightforward and general reactions for the rapid and efficient installation of CF<sub>2</sub>H to a C(sp<sup>3</sup>) center, the direct C(sp<sup>3</sup>)-H activation difluoromethylation represents a greatly reliable and ideal method for the construction of C(sp<sup>3</sup>)-CF<sub>2</sub>H bonds in the late-stage modification of bioactive molecules. However, to date, a direct C(sp<sup>3</sup>)-H difluoromethylation method has been rarely studied and a great challenge. The related research is mainly focused on the electrophilic difluoromethylation of highly activated aliphatic-carbon acids with difluorocarbene in the presence of a strong base due to the fact that a great variety of difluorocarbene precursors were developed by Hu, Shibata, Shen, and our group (Scheme 1a).<sup>7–11</sup>

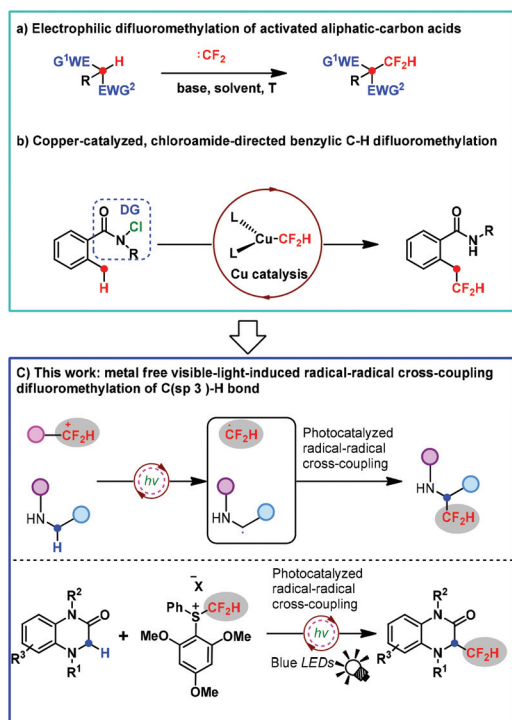
However, these methods usually suffer from limitations such as requirement of highly activated substrates, requirement of excess reagents and strong bases, and undesirable regioselectivity, thus significantly narrowing their practicability and further application. In 2019, Liu and co-workers reported the first copper-catalyzed benzylic C-H difluoromethylation. However, this transformation was accomplished with the aid of a directing group chloroamide to generate a benzylic radical (Scheme 1b).<sup>12</sup>

In spite of the aforementioned preliminary progress, the direct C(sp<sup>3</sup>)-H difluoromethylation remains largely underdeveloped and highly desirable as one of the most straightforward and promising strategies. To address this topic and challenge, we decided to develop an elegant and highly efficient solution by using our bench-stable S-(difluoromethyl)

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† Electronic supplementary information (ESI) available. CCDC 2112795. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d2qo00192f

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Scheme 1 Strategies for difluoromethylation of C(sp<sup>3</sup>)-H bonds.

diarylsulfonium salts **2**,<sup>10</sup> which have proved to be good difluoromethyl radical precursors under photoredox catalysis,<sup>13</sup> as well as electrophilic difluoromethylating reagents and difluorocarbene precursors.<sup>10,14</sup> On the other hand, the photoredox-catalyzed reaction is becoming a more and more popular synthetic version for incorporating the fluoroalkyl group into various organic molecules *via* a radical pathway.<sup>15,16</sup> The direct C(sp<sup>3</sup>)-H radical difluoromethylation remains currently unknown except the copper-catalyzed benzylic C-H difluoromethylation reported by Liu.<sup>12</sup> Consequently, we question whether **2** can achieve the direct C(sp<sup>3</sup>)-H difluoromethylation, serving as a difluoromethyl radical precursor *via* a photoredox-catalyzed radical-radical cross-coupling reaction. In particular, amines could be oxidized to generate N-radicals under photoredox catalysis, thus allowing the generation of α-C radical species *via* single electron transfer (SET) from C to N atoms (Scheme 1c, for the detailed information, see the ESI S2-S4†).<sup>17</sup> Bearing this in mind, we reasoned that reagent **2** and 1,4-dihydroquinoxalin-2-ones would lead to a radical-radical cross-coupling reaction under photoredox catalysis. As a result, we report herein a transition metal-free visible-light-induced direct C(sp<sup>3</sup>)-H difluoromethylation approach *via* the radical-radical cross-coupling reaction in this article (Scheme 1c). To the best of our knowledge, this transformation is the first example involving a radical-radical cross-coupling difluoromethylation of the C(sp<sup>3</sup>)-H bond, allowing for the direct C3-H radical difluoromethylation of a wide variety of 1,4-dihydroquinoxalin-2-ones, which is of great interest to pharmaceuti-

cals and drug candidates as a prevalent scaffold frequently existing in a lot of biologically active compounds.

## Results and discussion

Initially, we started our investigation employing 4-benzyl-1,4-dihydroquinoxalin-2-one **1aa** as a model substrate to optimize the reaction conditions (Table 1). Gratifyingly, the reaction proceeded smoothly under the irradiation of blue light overnight in the presence of 3 mol% photocatalyst **PC I**, 5.0 equivalents of LiOH and 2.0 equivalents of *S*-(difluoromethyl) sulfonium salt **2**, affording 3-difluoromethylated 1,4-dihydroquinoxalin-2-one **3aa** in 63% isolated yield (Table 1, entry 1). Inspired by this exciting result, other conveniently available common photosensitizers were further examined, and all the organic photosensitizers exhibited high catalytic activity to promote

Table 1 Survey of reaction conditions for radical-radical cross-coupling of 1,4-dihydroquinoxalin-2-ones with the *S*-(difluoromethyl)sulfonium salt<sup>a</sup>

| Entry           | PC (3 mmol%)                         | Base (5.0 equiv.)               | Solvent                         | Yield <sup>b</sup> (%) |
|-----------------|--------------------------------------|---------------------------------|---------------------------------|------------------------|
| 1               | <b>PC I</b>                          | LiOH                            | AcOEt                           | 63                     |
| 2               | <b>PC II</b>                         | LiOH                            | AcOEt                           | 74                     |
| 3               | <b>PC III</b>                        | LiOH                            | AcOEt                           | 73                     |
| 4               | Perylene                             | LiOH                            | AcOEt                           | 55                     |
| 5               | Ir(dFppy) <sub>3</sub>               | LiOH                            | AcOEt                           | 52                     |
| 6               | Ru(bpy) <sub>3</sub> Cl <sub>2</sub> | LiOH                            | AcOEt                           | 0                      |
| 7               | —                                    | LiOH                            | AcOEt                           | Trace                  |
| 8 <sup>c</sup>  | <b>PC II</b>                         | LiOH                            | AcOEt                           | 0                      |
| 9               | <b>PC II</b>                         | DBU                             | AcOEt                           | 10                     |
| 10              | <b>PC II</b>                         | Et <sub>3</sub> N               | AcOEt                           | 0                      |
| 11              | <b>PC II</b>                         | NaOH                            | AcOEt                           | 5                      |
| 12              | <b>PC II</b>                         | CsOH·H <sub>2</sub> O           | AcOEt                           | 8                      |
| 13              | <b>PC II</b>                         | KOH                             | AcOEt                           | 43                     |
| 14              | <b>PC II</b>                         | K <sub>2</sub> CO <sub>3</sub>  | AcOEt                           | 18                     |
| 15              | <b>PC II</b>                         | Li <sub>2</sub> CO <sub>3</sub> | AcOEt                           | 60                     |
| 16              | <b>PC II</b>                         | Li <sub>3</sub> PO <sub>4</sub> | AcOEt                           | 69                     |
| 17              | <b>PC II</b>                         | LiOH                            | CH <sub>3</sub> CN              | 57                     |
| 18              | <b>PC II</b>                         | LiOH                            | THF                             | 8                      |
| 19              | <b>PC II</b>                         | LiOH                            | CH <sub>2</sub> Cl <sub>2</sub> | 17                     |
| 20 <sup>d</sup> | <b>PC II</b>                         | LiOH                            | AcOEt                           | 55                     |
| 21 <sup>e</sup> | <b>PC II</b>                         | LiOH                            | AcOEt                           | 56                     |
| 22 <sup>f</sup> | <b>PC II</b>                         | LiOH                            | AcOEt                           | 51                     |

<sup>a</sup> Reaction conditions (unless otherwise specified): **1aa** (0.1 mmol, 1.0 equiv.), photocatalyst (3 mol%), reagent **2** (0.2 mmol, 2.0 equiv.), base (0.5 mmol, 5.0 equiv.), solvent (2.0 mL), room temperature, overnight. <sup>b</sup> Isolated yields. <sup>c</sup> No blue light irradiation. <sup>d</sup> LiOH (0.3 mmol) was used. <sup>e</sup> Reagent **2** (0.15 mmol) was used. <sup>f</sup> The reaction time was shortened to 3 hours.

this reaction, leading to moderate to good yields; **PC II** achieved 74% isolated yield of the desired product (Table 1, entries 2–4). A metal photosensitizer Ir(dFppy)<sub>3</sub> was also compatible with this reaction to deliver the product in 52% isolated yield (Table 1, entry 5), whereas Ru(bpy)<sub>3</sub>Cl<sub>2</sub> did not work (Table 1, entry 6). Predictably, the reaction was shut down in the absence of light or the photocatalyst (Table 1, entries 7 and 8), hence suggesting that the process might proceed through a radical pathway. Next, screening of various bases was carried out. Compared to inorganic bases, organic bases were clearly less effective to drive this reaction (Table 1, entries 9 and 10). Interestingly, alkaline lithium seems to be superior to other inorganic bases. Li<sub>2</sub>CO<sub>3</sub> and Li<sub>3</sub>PO<sub>4</sub> also gave the products in good yields of 60% and 69%, respectively (Table 1, entries 15 and 16), whereas dramatically diminished yields were obtained when KOH, NaOH, CsOH and K<sub>2</sub>CO<sub>3</sub> were used (Table 1, entries 11–14). The effect of solvents on the transformation efficiency was also surveyed. Thus, the use of CH<sub>3</sub>CN instead of AcOEt decreased the yield to 57% (Table 1, entry 17). THF and CH<sub>2</sub>Cl<sub>2</sub> also led to inferior results (Table 1, entries 18 and 19). The reduction of the amount of LiOH or the difluoromethylating reagent was obviously harmful to the yields of the desired product (Table 1, entries 20 and 21). The conversion efficiency was also eroded when the reaction time was shortened to 3 hours (Table 1, entry 22).

To showcase the generality of this radical–radical cross-coupling difluoromethylation protocol, we further explored the substrate scope under the optimized reaction conditions (Table 1, entry 3). As illustrated in Table 2, a wide range of *N*4-benzyl-1,4-dihydroquinoxalin-2-ones were readily transformed to the desired products in moderate to good yields. The structure of **3aa** was confirmed by X-ray crystallographic analysis. Notably, many functional groups were tolerated, regardless of their electron-donating and electron-withdrawing properties, including halogens (F, Cl, and Br), CF<sub>3</sub>O, CH<sub>3</sub>, CH<sub>3</sub>O, C(CH<sub>3</sub>)<sub>3</sub>, *etc.* Most substitution sites, *i.e.*, C6, C7 and C8, were compatible with the reaction conditions. However, C5-substituents led to significantly low reactivity (**3ae** and **3am**). Next, the influence of protection groups on *N*4 was investigated. Various benzyls were well tolerated to give the corresponding products in good yields, and the electronic properties of *para*-substituents on benzyls did not show a noticeable influence on the transformation efficiency (**3aa**, **3aq**, and **3ar**). *N*4-methyl and *N*4-allyl-protected 1,4-dihydroquinoxalin-2-ones also reacted well to give good yields (**3as** and **3at**). However, electron-withdrawing benzoyl on *N*4 shut down the desired transformation (**3au**). Moreover, *N*1 and *N*4 di-substituted substrates were also suitable substrates and provided **3av** and **3aw** in moderate yields. A tertiary C(sp<sup>3</sup>)–H bond, *e.g.*, 3-methyl-1,4-dihydroquinoxalin-2-one, also smoothly underwent the reaction to give the desired product, albeit in a lower isolated yield of 38% (**3ax**), because its poor solubility eroded the reaction efficiency and a large amount of **1ax** was recovered. Remarkably, *N*4-unprotected substrates were also compatible with this transformation, furnishing the corresponding difluoromethylated products in moderate to good yields (**3ba–3be**). Finally, a

**Table 2** Scope of visible-light-induced radical–radical cross-coupling difluoromethylation of 1,4-dihydroquinoxalin-2-ones with the *S*-(difluoromethyl)sulfonium salt<sup>a</sup>

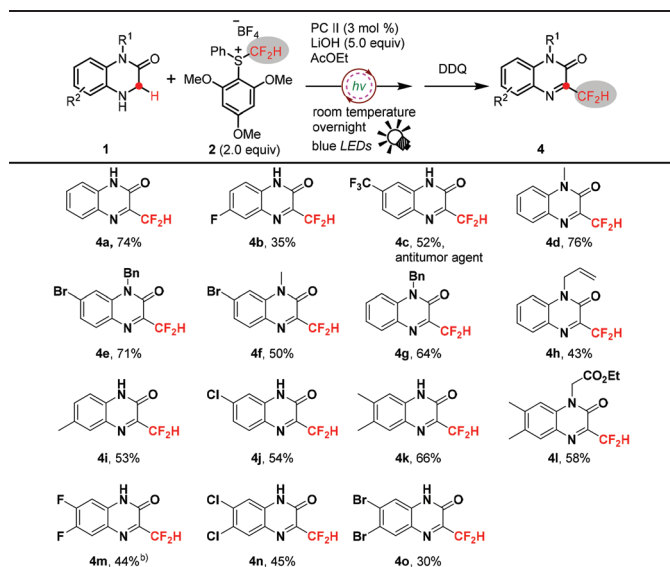
|                                              |                                                               |                                                |                                                |
|----------------------------------------------|---------------------------------------------------------------|------------------------------------------------|------------------------------------------------|
| <b>3aa</b> , 74%                             | <b>3ar</b> , 73%                                              | <b>3as</b> , 66%                               | <b>3at</b> , 54%                               |
| <b>3au</b> , 0%                              | <b>3av</b> , R = Bn, 55%                                      | <b>3ax</b> , 38%                               | <b>3ba</b> , 50%; <b>4a</b> , 25% <sup>c</sup> |
| <b>3bb</b> , 36%; <b>4b</b> , trace          | <b>3aw</b> , R = Me, 38%                                      | <b>3bd</b> , 58%; <b>4d</b> , 11% <sup>c</sup> | <b>3be</b> , 70%; <b>4e</b> , ND               |
| <b>3ac</b> , R = 7-Me, 82%                   | <b>3bc</b> , 52% <sup>d</sup> ; <b>4c</b> , 5% <sup>d,d</sup> |                                                |                                                |
| <b>3ad</b> , R = 6-Me, 72%                   |                                                               |                                                |                                                |
| <b>3ae</b> , R = 5-Me, trace                 |                                                               |                                                |                                                |
| <b>3af</b> , R = 6-OMe, 37%                  |                                                               |                                                |                                                |
| <b>3ag</b> , R = 7-OMe, 58%                  |                                                               |                                                |                                                |
| <b>3ah</b> , R = 7- <i>t</i> -Bu, 70%        |                                                               |                                                |                                                |
| <b>3ai</b> , R = 7-OCF <sub>3</sub> , 45%    |                                                               |                                                |                                                |
| <b>3aj</b> , R = 8-F, 53%                    |                                                               |                                                |                                                |
| <b>3ak</b> , R = 7-F, 88% (60%) <sup>b</sup> |                                                               |                                                |                                                |
| <b>3al</b> , R = 6-F, 57%                    |                                                               |                                                |                                                |
| <b>3am</b> , R = 5-F, 22%                    |                                                               |                                                |                                                |
| <b>3an</b> , R = 6,7-di-F, 58%               |                                                               |                                                |                                                |
| <b>3ao</b> , R = 7-Cl, 76%                   |                                                               |                                                |                                                |
| <b>3ap</b> , R = 7-Br, 59%                   |                                                               |                                                |                                                |

<sup>a</sup> Reaction conditions (unless otherwise specified): **1** (0.1 mmol, 1.0 equiv.), **PC II** (3 mol%), reagent **2** (0.2 mmol, 2.0 equiv.), LiOH (0.5 mmol, 5.0 equiv.), AcOEt (2.0 mL), room temperature, overnight. Isolated yields. <sup>b</sup> 2.0 mmol scale. <sup>c</sup> Yield was calculated according to the <sup>19</sup>F NMR ratio of **3** and **4**; **4** refers to Table 3. <sup>d</sup> CH<sub>3</sub>CN was used as the solvent.

larger scale transformation of **1ak** (2.0 mmol) was demonstrated with 60% isolated yield.

Interestingly, when *N*4-unprotected substrates 1,4-dihydroquinoxalin-2-ones **1ba–1bd** were subjected to this reaction, oxidation products 3-difluoromethyl-quinoxalin-2-ones **4a–4d** were detected as the minor products (Table 2). It is reasonable to presume that **4a–4d** might be derived from the oxidation of the corresponding desired **3ba–3bd**. We therefore further expanded the application of this method for the synthesis of 3-difluoromethyl functionalized quinoxalin-2-ones **4**, which belong to a class of pharmaceutically important compounds and were hitherto difficult to synthesize, although many methods were reported for the functionalization of quinoxalin-2-ones.<sup>18</sup> Thus, as shown in Table 3, various 3-difluoromethyl-quinoxalin-2-ones were readily accessed in moderate to good yields *via* a facile one-pot process with the addition of an oxidant DDQ.

Notably, in these cases of low yields, *i.e.* **4b** and **4o**, the poor solubility of substrates **1bb** and **1bo** significantly diminished the desired transformation, and the unreacted starting materials were oxidized to the corresponding quinoxalin-2-ones as the main side-products after adding DDQ. Importantly, **4c**, an antitumor agent,<sup>19</sup> was conveniently syn-

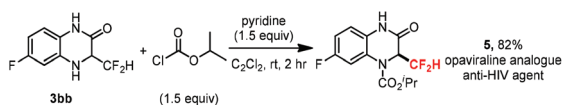
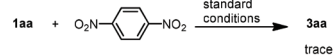
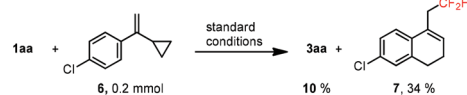
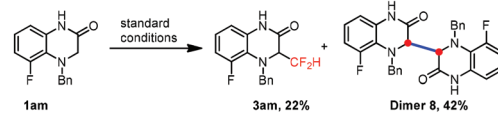
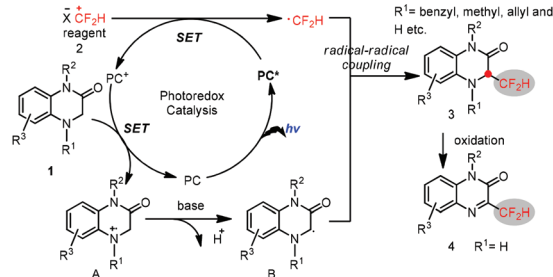
**Table 3** Synthesis of 3-difluoromethylquinoxalin-2-ones<sup>a</sup>

<sup>a</sup> Reaction conditions (unless otherwise specified): **1** (0.1 mmol, 1.0 equiv.), **PC II** (3 mol%), reagent **2** (0.2 mmol, 2.0 equiv.), LiOH (0.5 mmol, 5.0 equiv.), AcOEt (2.0 mL), room temperature, overnight. Then DDQ (0.2 mmol, 2.0 equiv.) was added. Isolated yields. <sup>b</sup> CH<sub>3</sub>CN was used as the solvent.

thesized from **1bc** in 52% isolated yield with this simple one-pot method.

Quinoxalinones constitute a prevalent skeleton, frequently occurring in many biologically active compounds and pharmaceuticals, and possessing a wide variety of biological activities such as antiviral, anti-inflammatory, antidiabetic, antimicrobial, and anticancer properties. In order to further demonstrate the potential application of this significant method, we herein explored a rapid synthesis of difluoromethyl modified opaviraline (GW420867X) **5** from **3bb** in 82% yield (Scheme 2), which is an anti-HIV-1 reverse transcriptase inhibitor.<sup>20</sup> This process further demonstrates the synthetic utility of this radical–radical cross-coupling difluoromethylation reaction in the late-stage CF<sub>2</sub>H-modification of drugs and biologically active compounds.

The mechanistic insight into this reaction was preliminarily studied. Thus, only a trace of **3aa** was found under the standard reaction conditions in the presence of 1,4-dinitrobenzene (Scheme 3a), suggesting the existence of difluoromethyl radical species. Furthermore, a radical clock experiment was also conducted (Scheme 3a). The yield of the desired product **3aa** was downgraded to 10%, along with the rearranged product **7** as the major product in 34% isolated yield.

**Scheme 2** Synthesis of the opaviraline analogue.**a) Evidence of difluoromethyl radical species****b) Radical-clock experiment****c) Isolation of 1am's dimer 8: evidence for yielding α-C radical****d) Proposed mechanism****Scheme 3** Mechanistic studies and the proposed mechanism.

Moreover, in the low-yield case of **3am** (22%), the dimer product **8** was isolated as the major product in 42% yield (Scheme 3c), which is strong evidence for obtaining the α-C radical from 1,4-dihydroquinoxalin-2-ones under photoredox catalysis conditions. Consequently, these experimental results above confirmed that a radical–radical cross-coupling process is involved during the reaction.

Based on the results of these mechanistic experiments, the radical–radical cross-coupling reaction mechanism was proposed as depicted in Scheme 3d. Initially, the *S*-(difluoromethyl)diarylsulfonium salt **2** is reduced by the excited PC\* to generate the <sup>•</sup>CF<sub>2</sub>H radical along with PC<sup>+</sup>, followed by single electron transfer between substrate **1** and PC<sup>+</sup> to render a cationic nitrogen radical **A**. **A** is delivered to the sp<sup>3</sup> carbon radical **B** via deprotonation in the presence of a base, thus allowing for a radical–radical cross-coupling between the <sup>•</sup>CF<sub>2</sub>H radical and sp<sup>3</sup> carbon radical **B** to generate the desired product **3**, which can be readily oxidized to **4** for the N4-unprotected 1,4-dihydroquinoxalin-2-ones.

## Conclusions

In conclusion, we have developed the first approach for a direct difluoromethylation of the C(sp<sup>3</sup>)–H bond via a radical–radical cross-coupling strategy, featuring transition metal-free photoredox catalysis, broad substrate scope and functional group tolerance, and mild reaction conditions. A wide variety of 1,4-dihydroquinoxalin-2-ones were smoothly converted to 3-difluoromethyl-1,4-dihydroquinoxalin-2-ones and 3-difluoro-

methylquinoxalin-2-ones in moderate to good yields. Employing this protocol, pharmacologically antiviral agent **5** and anticancer agent **4c** were readily accessed in good yields, proving its potential utility in medicinal chemistry. Furthermore, mechanistic studies support the radical–radical cross-coupling process between a difluoromethyl radical and a C(sp<sup>3</sup>) radical involved in this reaction. This pioneering radical–radical cross-coupling strategy for significantly efficient C(sp<sup>3</sup>)–H difluoromethylation not only provides a powerful tool for the straightforward assembly of CF<sub>2</sub>H-containing bioactive molecules in the late-stage synthesis but would also promote the development of other new fluorination and fluoroalkylation methods, which is of great interest in synthetic chemistry and pharmaceutical chemistry.

## Experimental

### General information

<sup>1</sup>H NMR spectra were recorded on either a Bruker Ascend 400 MHz (400 MHz) spectrometer, a Bruker Ascend 500 MHz (500 MHz) spectrometer or a Bruker Ascend 600 MHz (600 MHz) spectrometer at ambient temperature unless otherwise indicated. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard in CDCl<sub>3</sub>, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet-doublet, m = multiplet, and br = broad), coupling constants (Hz), and assignment. <sup>13</sup>C NMR spectra were recorded on either a Bruker Ascend 500 MHz (126 MHz) spectrometer or a Bruker Ascend 600 MHz (151 MHz) spectrometer at ambient temperature and were proton decoupled. Chemical shifts are reported in ppm from tetramethylsilane on the scale with the solvent resonance employed as the internal standard. <sup>19</sup>F NMR spectra were recorded on a Bruker Ascend 400 MHz (377 MHz) spectrometer or a Bruker Ascend 500 MHz (471 MHz) spectrometer at ambient temperature. Chemical shifts are reported in ppm from CFCl<sub>3</sub> as the internal standard. Single crystal X-ray diffraction data for the compounds were collected on a Rigaku Oxford Diffraction SuperNova dual source at 100 K using Cu-Kα radiation. ESI-MS analysis was performed in the positive ionization mode on an Agilent 1260-Infinity LC/MSD resolution mass spectrometer. All high-resolution mass spectra were obtained on a Thermo Scientific Q-Exactive (HR/AM) Orbitrap mass spectrometer. Commercially available reagents were used as received. Reactions were monitored by TLC (detection with UV light). Flash chromatography: silica gel (300–400 mesh). Visible light irradiation was performed using blue LED lamps (3 W × 4; λ = 450 nm) for the preparative scale.

### General procedure for the visible-light photoredox catalyzed direct C(sp<sup>3</sup>)–H difluoromethylation of 3,4-dihydroquinoxalin-2(1H)-ones

To a 25 mL Schlenk tube equipped with a magnetic stir bar were added the derivative of 3,4-dihydroquinoxalin-2(1H)-one **1** (0.1 mmol, 1.0 equiv.), **2** (83.0 mg, 0.2 mmol, 2.0 equiv.), **PC II**

(1.7 mg, 0.003 mmol, 3 mol%), and LiOH (12.0 mg, 0.5 mmol, 5.0 equiv.). Then the flask was flushed with argon, followed by the addition of EtOAc (2 mL). The tube was placed at a distance of ~2 mm away from (3 W × 4) blue LED lamps (λ = 450 nm), and the reaction mixture was stirred under the irradiation of blue LEDs. After stirring overnight, the solvent was evaporated *in vacuo* and the residue was purified by flash column chromatography on silica gel (petrol ether/ethyl acetate) to afford product **3**.

### General procedure for the synthesis of 3-difluoromethylquinoxalin-2-ones

To a 25 mL Schlenk tube equipped with a magnetic stir bar were added the derivative of 3,4-dihydroquinoxalin-2(1H)-one **1** (0.1 mmol, 1.0 equiv.), **2** (83.0 mg, 0.2 mmol, 2.0 equiv.), **PC II** (1.7 mg, 0.003 mmol, 3 mol%), and LiOH (12.0 mg, 0.5 mmol, 5.0 equiv.). Then the flask was flushed with argon, followed by the addition of EtOAc (2 mL). The tube was placed at a distance of ~2 mm away from 3 W blue LED lamps (λ = 450 nm), and the reaction mixture was stirred under the irradiation of blue LEDs. After stirring overnight, DDQ (45.5 mg, 0.2 mmol, 2.0 equiv.) was added and the mixture was stirred at 80 °C for another 2 hours; then the solvent was evaporated *in vacuo* and the residue was purified by flash column chromatography on silica gel (petrol ether/ethyl acetate) to afford product **4**.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

The authors wish to acknowledge the NSFC (92056201), the Guangdong Basic and Applied Basic Research Foundation (2020A1515010874), and the SZU Top Ranking Project (86000000210). We would like to thank the Instrumental Analysis Center of Shenzhen University for analytical work.

## Notes and references

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