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# Synthesis of [1,4]Thiazino[4,3-*a*]indol-10-one Derivatives through Radical Anti Aza-Michael Addition of 2′-Aminochalcones

Pingshun Zhang, Linjie Yang, Wanzhi Chen,* Miaochang Liu,* and Huayue Wu

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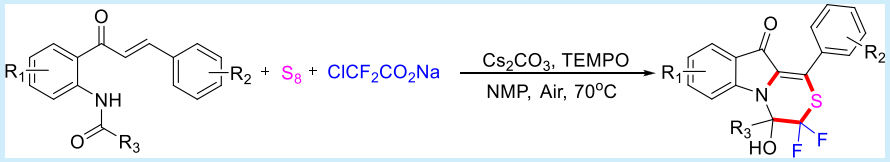


**ABSTRACT:** An efficient method for the synthesis of [1,4]thiazino[4,3-*a*]indole derivatives using sodium chlorodifluoroacetate ($ClCF_2CO_2Na$) and elemental sulfur as the difluoromethylthiolating reagent system has been developed. Three-component reactions of 2′-aminochalcones, sulfur, and $ClCF_2CO_2Na$ under basic conditions using TEMPO as the oxidant afforded [1,4]thiazino[4,3-*a*]indol-10-ones containing a difluoromethyl thioether moiety in good yields. Four bonds including one C−N, two C−S, and one C−C bonds are selectively formed in the sequential transformation process.



Organofluorine compounds exhibit unique physicochemical and chemical reactivities, which have been widely used as materials and pharmaceuticals.[1] Selectively introducing a fluorine atom or fluoroalkyl group can effectively change the biological activity, physical activity, and reactivity of organic molecules (Figure 1).[2] Among various fluorinated moieties

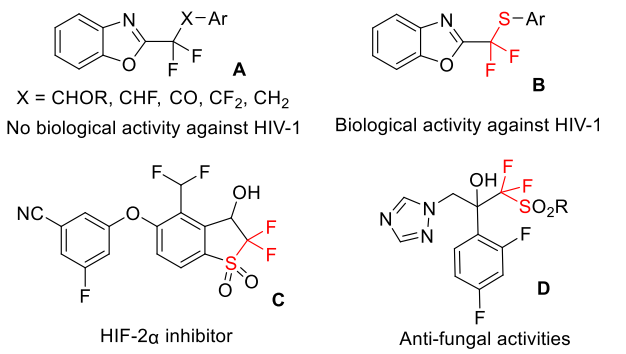


**Figure 1.** Examples of drug molecules containing $-SCF_2-$ scaffolds.

employed to modify the properties of a targeted products, difluoromethylene group $CF_2$ was the most prevailing one.[3] In particular, incorporation of a difluoromethyl thioether moiety $SCF_2$ to a drug molecule often enhances its metabolic property, lipophilicity, and oxidative stability.[4] Thus, the development of efficient approaches to construct difluoromehtyl thioethers are appealing and valuable for pharmaceutical industry.[5]

These difluoromehtyl thioethers are usually synthesized by sequential sulfenylation and fluoroalkylation reactions.[4b] Various compounds containing the $-SCF_2-$ moiety have been employed in the construction of difluoromethyl thiolether as the difluoromethylthiolation agents including $PhSCF_2SiMe_3$,[6] $PhSCF_2Br$,[7] $PhSO_2CF_2H$,[8] and $PhSO_2CF_2SiMe_3$, etc.[9] Cyclic difluoromethyl thioethers have been less studied, and only a few synthetic methods have been reported in recent years. Basically, the synthesis of cyclic difluoromethyl thioethers can be accomplished through nucleophilic reactions of thiols and $CF_2$-containing compounds (Scheme 1, a and b). DBU-catalyzed [4 + 2] annulation between *gem*-difluoroolefins and 2-mercaptobenzaldehydes successfully gave rise to the desired products.[10] The reaction of 2-mercaptophenone and $ClCF_2COONa$ yielded 2,2-difluoro-2,3-dihydrobenzo[*b*]thiophens, which was achieved through reaction of a thiolate with difluorocarbene, followed by intramolecular nucleophilic addition.[11] Alternatively, cyclic difluoromethyl thioethers could be obtained from $SCF_2$-containing compounds (Scheme 1, c and d). In this context, 2,2-difluorothiochromane derivatives were obtained via radical addition of difluoromethyl xanthate to various terminal alkenes[12] or visible-light-induced arylthiofluoroalkylations of unactivated heteroarenes and alkenes.[13]

Obviously, the combination of sulfur and $ClCF_2CO_2Na$ is the most convenient and economic agent for the construction of ambiphilic $-SCF_2^-$ moiety. We have described that three-component reactions of 2′-hydroxychalcones, $ClCF_2CO_2Na$, and sulfur under basic conditions afforded $HCF_2S$-containing

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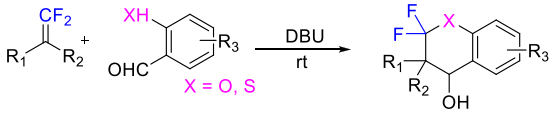
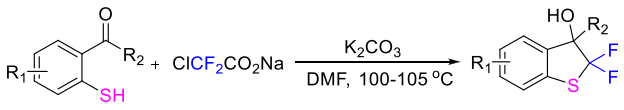
**Scheme 1. Synthesis of Cyclic Difluoromethyl Thiolethers**

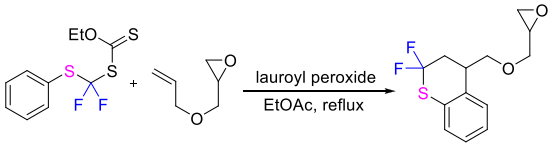
(a) Nucleophilic addition between *gem*-difluoroolefins and benzaldehydes



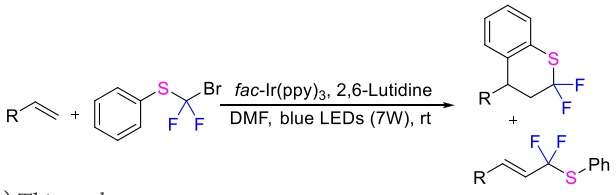

(b) Difluorocarbene-triggered cyclization



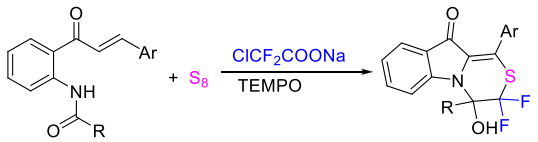

(c) Difluoromethyl xanthate radical addition to terminal alkenes




(d) Visible-light-induced arylthiofluoroalkylation of unactivated alkenes



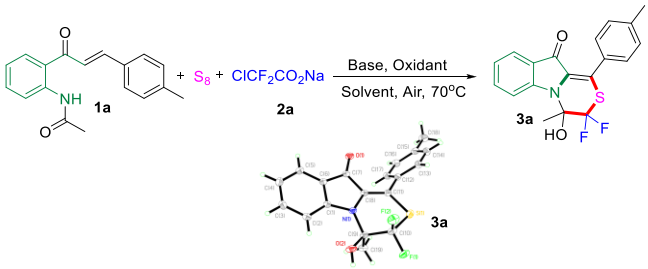

(e) This work




4*H*-chromen-4-one and 9*H*-thieno[3,2-*b*]chromen-9-one derivatives in good yields.[14] The transformation is initiated by oxa-Michael addition. We inferred that in the case of 2′-aminochalcones radical anti-Michael addition would happen to afford difluoroalkylthiolated indole derivatives in the presence of an oxidant. Herein, we report the reaction of 2′-aminochalcones, sulfur, and $ClCF_2CO_2Na$. A variety of indolins-3-one derivatives were obtained in good yields.

We began our optimization tests by using *N*-(2-(3-(*p*-tolyl)acryloyl)phenyl)acetamide **1a** as the model substrate. Reaction of **1a**, sulfur, and $ClCF_2CO_2Na$ **2a** was initially performed in DMF in the presence of $KOCH_3$ and 2,2,6,6-tetramethylpiperidinooxy (TEMPO). As expected, an indole derivative **3a** containing a $SCF_2$ unit was generated in 32% yield through anti-aza Michael addition (Table 1, entry 1). Unexpectedly, further cyclization to form a thiazine ring was observed due to unusual nucleophilic addition of $-SCF_2^-$ to the amide group. The structure of **3a** was identified by NMR spectroscopy and finally determined by X-ray diffraction analysis. Next, we examined the effect of various solvents. Strongly polar solvents are preferred (Table 1, entries 2 and 3).

**Table 1. Optimization of Reaction Conditions**[a]




| entry | base | oxidant | solvent | yield (%) |
|---|---|---|---|---|
| 1 | $KOCH_3$ | TEMPO | DMF | 32 |
| 2 | $KOCH_3$ | TEMPO | NMP | 60 |
| 3 | $KOCH_3$ | TEMPO | HMPA | 45 |
| 4 | NaO*t*-Bu | TEMPO | NMP | 14 |
| 5 | $Cs_2CO_3$ | TEMPO | NMP | 78 |
| 6 | KOAc | TEMPO | NMP | 23 |
| 7 | DBU | TEMPO | NMP | 15 |
| 8 | $Cs_2CO_3$ | DTBP | NMP | 52 |
| 9 | $Cs_2CO_3$ | $K_2S_2O_8$ | NMP | 43 |
| 10 | $Cs_2CO_3$ | 1,4-BQ | NMP | 27 |

[a]Reaction conditions: chalcone **1a** (0.2 mmol), $ClCF_2CO_2Na$ **2a** (0.6 mmol), $S_8$ (1.2 mmol), base (0.6 mmol) oxidant (0.4 mmol), 3 Å molecular sieve (100 mg), and solvent (1.5 mL) at 70 °C in air for 30 h. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene; TEMPO = 2,2,6,6-tetramethyl-1-piperidinyloxy; DTBP = 2-(*tert*-butylperoxy)-2-methylpropane; BQ = benzoquinone.

Compound **3a** was isolated in 60% yield when NMP was the solvent. The effect of various inorganic and organic bases was examined (Table 1, entries 4−7). It seems that organic bases are less efficient, and $Cs_2CO_3$ is the most suitable base in which case **3a** was isolated in 78% yield. Finally, we checked the influence of the oxidant, and we found that TEMPO is the best oxidant among the inorganic and organic oxidants examined (Table 1, entries 5 and 8−10). Unexpectedly, pyridine-*N*-oxide with the similar structure as TEMPO is totally ineffective. The full optimization details are listed in the Supporting Information (Table S2).

After optimization, we explored the substrate scope of **1**. As shown in Scheme 2, the double cyclization reaction involving difluoromethylthiolation of a variety of 2′-amidochalcones bearing electron-donating and electron-withdrawing substituents such as alkyl, phenyl, alkoxy, cyano, acetyl, $CF_3$, $NO_2$, $CH_3SO_2$, and halogen groups at the 4-positions occurred under the mild conditions furnishing **3a**−**3m** in good yields (49−85%). The results told that electron-donating groups are preferred. Unexpectedly, the transformation of *N*-(2-(3-(4-(dimethylamino)phenyl)acryloyl)phenyl)acetamide **1n** failed to give the corresponding product **3n**, and most of **1n** was recovered. The reason is not clear at the present. The *m*-substituted substrates having an electron-donating and electron-withdrawing group, including of alkoxy, $CF_3$, and halogen were well tolerated and gave **3o**−**3r** in good yields. Unfortunately, the reactions of *N*-(2-(3-(2-methoxyphenyl)-acryloyl)phenyl)acetamide and *N*-(2-(3-(2-chlorophenyl)-acryloyl)phenyl)acetamide afforded **3s** and **3t** in relatively lower yields, 41% and 38%, respectively, due to steric hindrance. The polysubstituted substrates having alkoxy and alkyls groups were successfully transformed to **3u**−**3x** in 59−73% yields. The naphthalene derivatives reacted similarly with sulfur and $ClCF_2CO_2Na$ to give **3y** and **3z**, respectively.



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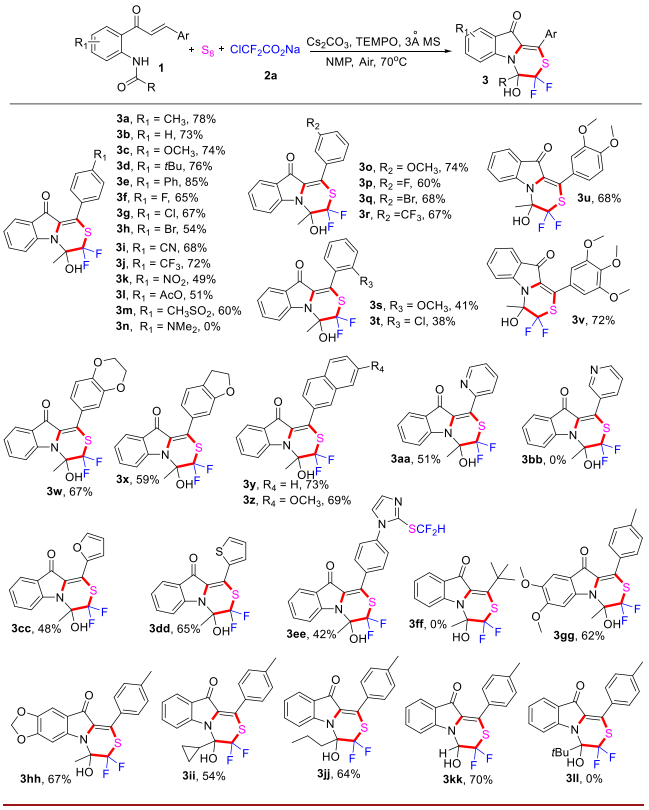
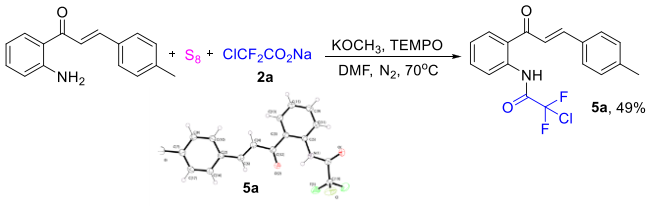
**Scheme 2. Scope of Substrates 1**




We also tested the reactions of 2′-acetamionchalcone analogues containing a furyl, thiophene-yl, or 2-pyridine groups. These heterocyclic compounds also proceeded smoothly, and the corresponding [1,4]thiazino[4,3-*a*]indole derivatives **3aa**−**3dd** were obtained in 73−84% yields. Unfortunately, the 3-pyridine derivative was totally unreactive, and no desired product was isolated. It was interestingly observed that the sequential reaction of 4-imidazolyl-2′-acetamionchalcone afforded [1,4]thiazino[4,3-*a*]indol-10-one derivative **3ee** in 42% yield, and further difluoromethylthiolation simultaneously occurred at 2-position of imidazole group. 2-(Difluoromethylthio)-1*H*-imidazoles are known compounds which have been prepared through nucleophilic substitution of *S*-(difluoromethyl)sulfonium salt[15] or radical coupling of $Zn(SO_2CF_2H)$[16] with 1*H*-imidazole-2-thiols. The three-component reaction is not compatible with the unsaturated ketone with an alkyl substituent at 3-position, and thus, **3ff** was not obtained. Finally, 2′-acetamionchalcones containing alkoxy groups at the 4′- and 5′-positions also gave the desired [1,4]thiazino[4,3-*a*]indol-10-ones **3gg** and **3hh** in moderate yields. The *N*-acetyl group could also be replaced by other aliphatic acyl groups with isolated yields of 54−70%. However, reactions of 2′-benzoamino and 2′-pivalamino compounds yielded complicated mixtures.

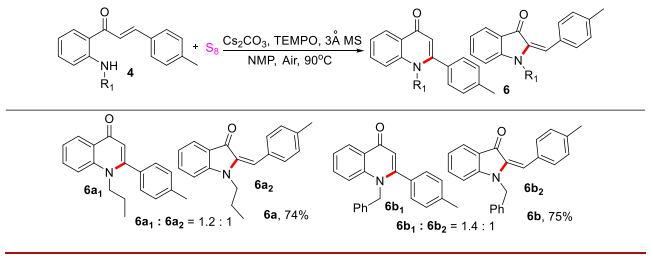
It has been reported that unprotected 2′-aminochalcones were easily converted to 2,3-dihydroquinolin-4(1*H*)-ones via simple aza-Michael addition.[17] Under the conditions stated in Scheme 2, only 2′-(2-chloro-2,2-difluoroacetamido)chalcone **5a** was isolated in 49% yield from the reaction of 2′-aminochalcone under our conditions, as shown in Scheme 3. Then we turned to 2′-alkylaminochalcones (Scheme 4). Both sulfur and fluorine were not involved in the products, and the

**Scheme 3. Reaction of Unprotected 2′-Aminochalcone**



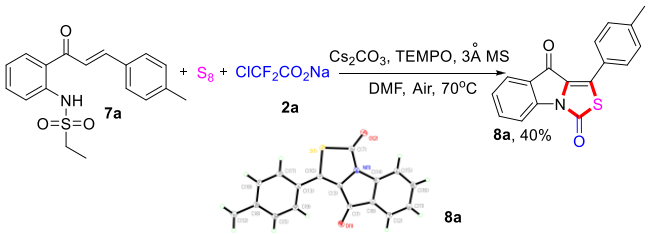

mixtures of **6a** and **6b** were afforded in 74% and 75% yields, respectively.

**Scheme 4. Scope of Substrates 4**




When *N*-(2-(3-(*p*-tolyl)acryloyl)phenyl)ethanesulfonamide **7a** was treated with sulfur and $ClCF_2CO_2Na$ in DMF in the presence of $Cs_2CO_3$ and TEMPO, the reaction did occur, but affording the fused compound 1-(*p*-tolyl)-3*H*,9*H*-thiazolo[3,4-*a*]indol-3,9-dione **8a** as a light-yellow solid in 40% yield (Scheme 5). Probably, the SC═O moiety is originated from hydrolysis of thiocarbonyl fluoride ($S{=}CF_2$) *in situ* generated from sulfur and $ClF_2COONa$, as reported.[18]

**Scheme 5. Reaction of Substrates 7a**




The three-component reaction of 2-acylamino chalcone is quite fascinating since four bonds including one C−N, two C−S, and one C−C bonds have to be selectively formed in one-pot. The synthetic utility of the reaction was demonstrated by a scale-up experiment. Compound **3e** was obtained in 78.6% yield at a gram-scale. To gain some mechanistic insights into the transformation, a few control experiments were performed. The control experiments clearly showed that the cyclization was initiated via radical anti-Michael addition (see the Supporting Information). It was reported that the nucleophilic aza-Michael addition of 2′-aminochalcone affords 2,3-dihydroquinolin-4(1*H*)-ones due to 6-endo-trig cyclization.[17] The present anti-Michael addition and 5-exo-trig cyclization of 2′-aminochalcone indicate its radical nature.[19] Based on the above observations and the literature reports,[20] a plausible radical mechanism is proposed (Scheme 6). The reaction was initiated by deprotonation of **1** giving acylamido anion **A**, which was readily oxidized by TEMPO to generate the acylamido radical **B**. The subsequent intraradical addition of **B**



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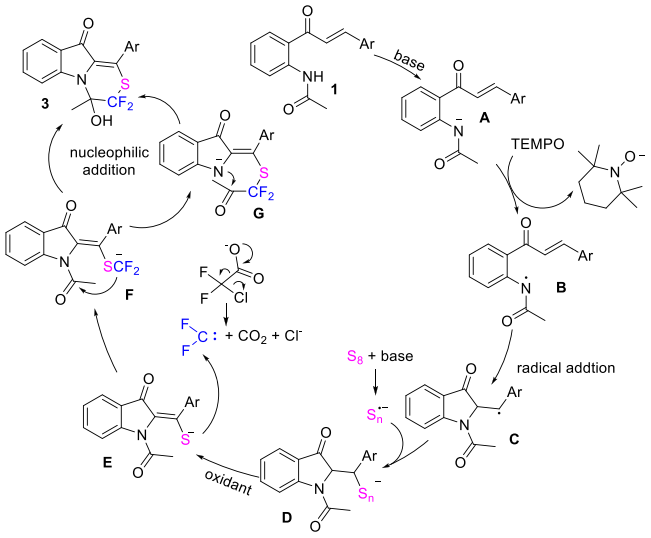
**Scheme 6. Plausible Mechanism**




led to cyclization affording new radical **C**. Intermediate **C** would capture an $S_n^{\bullet-}$ radical ion, *in situ* generated from sulfur and a base.[21] The resulting thiolate **D** would be oxidatively dehydrogenated to **E**. The oxidation could be furnished by either TEMPO or sulfur or both. The nucleophilic addition of thiolate **E** toward a $F_2C$: molecule would form difluorinated carbanion **F**. Finally, the intranucleophilic addition of carbanion toward acetyl would generate the target product **3**.

In summary, the combination of $ClCF_2CO_2Na$ and sulfur has been utilized as a difluoromethylthiolating agent. The three-component reaction of 2′-aminochalcone, sulfur, and $ClCF_2CO_2Na$ in the presence of TEMPO selectively afforded [1,4]thiazino[4,3-*a*]indoles, which were formed through radical anti-Michael addition and nucleophilic addition of difluorocarbanion to amide. It provides a simple and atom-economic way to synthesize functionalized indoles containing a difluoromethyl thioether moiety.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c02160.

Experimental procedures and spectra (PDF)

### Accession Codes

CCDC 2079900−2079901 and 2080082 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

## ■ AUTHOR INFORMATION


### Corresponding Authors

**Wanzhi Chen** − *Department of Chemistry, Zhejiang University, Hangzhou 310027, China;* orcid.org/0000-0002-7076-1521; Email: chenwzz@zju.edu.cn

**Miaochang Liu** − *College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou 325027, China;* orcid.org/0000-0002-4603-3022; Email: mcl@wzu.edu.cn

### Authors

**Pingshun Zhang** − *Department of Chemistry, Zhejiang University, Hangzhou 310027, China*

**Linjie Yang** − *Department of Chemistry, Zhejiang University, Hangzhou 310027, China*

**Huayue Wu** − *College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou 325027, China;* orcid.org/0000-0003-3431-561X

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c02160


### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES


(1) (a) Wang, J.; Sánchez-Roselló, M.; Aceña, J.; Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001−2011). *Chem. Rev.* **2014**, *114*, 2432−2506. (b) Gillis, E. P.; Eastman, K. J.; Hill, M. D.; Donnelly, D. J.; Meanwell, N. A. Applications of Fluorine in Medicinal Chemistry. *J. Med. Chem.* **2015**, *58*, 8315−8359.

(2) Müller, K.; Faeh, C.; Diederich, F. Fluorine in Pharmaceuticals: Looking Beyond Intuition. *Science* **2007**, *317*, 1881−1886.

(3) Hirai, G.; Watanabe, T.; Yamaguchi, K.; Miyagi, T.; Sodeoka, M. Stereocontrolled and Convergent Entry to $CF_2$-Sialosides: Synthesis of $CF_2$-Linked Ganglioside GM4. *J. Am. Chem. Soc.* **2007**, *129*, 15420−15421.

(4) (a) Ni, C.; Hu, M.; Hu, J. Good Partnership between Sulfur and Fluorine: Sulfur-Based Fluorination and Fluoroalkylation Reagents for Organic Synthesis. *Chem. Rev.* **2015**, *115*, 765−825. (b) Dilman, A. D.; Levin, V. V. Difluorocarbene as a Building Block for Consecutive Bond-Forming Reactions. *Acc. Chem. Res.* **2018**, *51*, 1272−1280.

(5) (a) Wehn, P. M.; Rizzi, J. P.; Dixon, D. D.; Grina, J. A.; Schlachter, S. T.; Wang, B.; Xu, R.; Yang, H.; Du, X.; Han, G.; Wang, K.; Cao, Z.; Cheng, T.; Czerwinski, R. M.; Goggin, B. S.; Huang, H.; Halfmann, M. M.; Maddie, M. A.; Morton, E. L.; Olive, S. R.; Tan, H.; Xie, S.; Wong, T.; Josey, J. A.; Wallace, E. M. Design and Activity of Specific Hypoxia-Inducible Factor-2$\alpha$ (HIF-2$\alpha$) Inhibitors for the Treatment of Clear Cell Renal Cell Carcinoma: Discovery of Clinical Candidate (*S*)-3-((2,2-Difluoro-1-hydroxy-7-(methylsulfonyl)-2,3-dihydro-1*H*-inden-4-yl)oxy)-5-fluorobenzonitrile (PT2385). *J. Med. Chem.* **2018**, *61*, 9691−9721. (b) Eto, H.; Kaneko, Y.; Takeda, S.; Tokizawa, M.; Sato, S.; Yoshida, K.; Namiki, S.; Ogawa, M.; Maebashi, K.; Ishida, K.; Matsumoto, M.; Asaoka, T. New Antifungal 1,2,4-Triazoles with Difluoro(substituted sulfonyl)methyl Moiety. *Chem. Pharm. Bull.* **2001**, *49*, 173−182.

(6) (a) Bootwicha, T.; Panichakul, D.; Kuhakarn, C.; Prabpai, S.; Kongsaeree, P.; Tuchinda, P.; Reutrakul, V.; Pohmakotr, M. Fluoride-Catalyzed Addition of $PhSCF_2SiMe_3$ to *N*-Substituted Cyclic Imides Followed by Radical Cyclization: General Synthetic Strategy of *gem*-Difluoromethylenated 1-Azabicyclic Compounds. *J. Org. Chem.* **2009**, *74*, 3798−3805. (b) Pharikronburee, V.; Punirun, T.; Soorukram, D.; Kuhakarn, C.; Tuchinda, P.; Reutrakul, V.; Pohmakotr, M. Fluoride-Catalyzed Nucleophilic Addition of $PhSCF_2SiMe_3$ to Anhydrides: Aynthesis of $\gamma$-Difluoromethylated $\gamma$-Lactams. *Org. Biomol. Chem.* **2013**, *11*, 2022−2033.

(7) Betterley, N. M.; Surawatanawong, P.; Prabpai, S.; Kongsaeree, P.; Kuhakarn, C.; Pohmakotr, M.; Reutrakul, V. Electrophilic Difluoro(phenylthio)methylation: Generation, Stability, and Reactivity of $\alpha$-Fluorocarbocations. *Org. Lett.* **2013**, *15*, 5666−5669.

(8) Ni, C.; Liu, J.; Zhang, L.; Hu, J. A Remarkably Efficient Fluoroalkylation of Cyclic Sulfates and Sulfamidates with $PhSO_2CF_2H$: Facile Entry into β-Difluoromethylated or β-Difluoromethylenated Alcohols and Amines. *Angew. Chem., Int. Ed.* **2007**, *46*, 786−789. (b) Li, Y.; Hu, J. Facile Synthesis of Chiral α-Difluoromethyl Amines from *N*-(*tert*-Butylsulfinyl)aldimines. *Angew. Chem., Int. Ed.* **2005**, *44*, 5882−5886.

(9) (a) Ismalaj, E.; Bars, D. L.; Billard, T. Direct Electrophilic (Benzenesulfonyl)Difluoromethylthiolation with a Shelf-Stable Reagent. *Angew. Chem., Int. Ed.* **2016**, *55*, 4790−4793. (b) Zhu, L.; Li, Y.; Zhao, Y.; Hu, J. Nucleophilic (Phenylsulfonyl)difluoromethylation of Alkyl Halides using $PhSO_2CF_2SiMe_3$: Preparation of *gem*-Difluoroalkenes and Trifluoromethyl Compounds. *Tetrahedron Lett.* **2010**, *51*, 6150−6152.

(10) Li, J.; Xu, C.; Wei, N.; Wang, M. Synthesis of 2,2-Difluorinated 4-Isoflavanols/4-Thioisoflavanols via a Base-Catalyzed [4 + 2] Annulation Reaction of *gem*-Difluoroolefins. *J. Org. Chem.* **2017**, *82*, 11348−11357.

(11) Liang, H.; Liu, R.; Zhou, M.; Fu, Y.; Ni, C.; Hu, J. Difluorocarbene-Triggered Cyclization: Synthesis of (Hetero)arene Fused 2,2-Difluoro-2,3-dihydrothiophenes *Org. Org. Lett.* **2020**, *22*, 7047−7051.

(12) Salomon, P.; Zard, S. Z. A Convergent Route to Geminal Difluorosulfides and to Functionalized Difluorothiochromans, a New Family of Organofluorine Compounds. *Org. Lett.* **2014**, *16*, 1482−1485.

(13) Choi, Y.; Yu, C.; Kim, J. S.; Cho, E. J. Visible-Light-Induced Arylthiofluoroalkylations of Unactivated Heteroaromatics and Alkenes. *Org. Lett.* **2016**, *18*, 3246−3249.

(14) Zhang, P.; Chen, W.; Liu, M.; Wu, H. Synthesis of 3-$HCF_2S$-Chromones through Tandem Oxa-Michael Addition and Oxidative Difluoromethylthiolation. *Org. Lett.* **2019**, *21*, 9326−9329.

(15) Liu, G. K.; Qin, W. B.; Li, X.; Lin, L. T.; Wong, H. N. C. Difluoromethylation of Phenols and Thiophenols with the S-(Difluoromethyl)sulfonium Salt: Reaction, Scope, and Mechanistic Study. *J. Org. Chem.* **2019**, *84*, 15948−15957.

(16) Fujiwara, Y.; Dixon, J. A.; Rodriguez, R. A.; Baxter, R. D.; Dixon, D. D.; Collins, M. R.; Blackmond, D. G.; Baran, P. S. A New Reagent for Direct Difluoromethylation. *J. Am. Chem. Soc.* **2012**, *134*, 1494−1497.

(17) Cheng, S.; Zhao, L.; Yu, S. Enantioselective Synthesis of Azaflavanones Using Organocatalytic 6-*endo* Aza-Michael Addition. *Adv. Synth. Catal.* **2014**, *356*, 982−986.

(18) (a) Li, Z.; Dong, J.; Yuan, Z.; Yang, D.; Weng, Z. One-Pot Synthesis of 3-Difluoromethyl Benzoxazole-2-thiones. *Org. Lett.* **2018**, *20*, 6407−6410. (b) Yu, J.; Lin, J.; Xiao, J. Reaction of Thiocarbonyl Fluoride Generated from Difluorocarbene with Amines. *Angew. Chem., Int. Ed.* **2017**, *56*, 16669−16673.

(19) Lovett, G. H.; Sparling, B. A. Decarboxylative Anti-Michael Addition to Olefins Mediated by Photoredox Catalysis. *Org. Lett.* **2016**, *18*, 3494−3497.

(20) Chen, J.; Hu, X.; Lu, L.; Xiao, W. Visible Light Photoredox-Controlled Reactions of N-Radicals and Radical Ions. *Chem. Soc. Rev.* **2016**, *45*, 2044−2056.

(21) (a) Hojo, M.; Sawyer, D. T. Hydroxide-Induced Reduction of Elemental Sulfur ($S_8$) to the Trisulfur Anion Radical ($S3^{\bullet-}$). *Inorg. Chem.* **1989**, *28*, 1201−1202. (b) Zhang, G.; Yi, H.; Chen, H.; Bian, C.; Liu, C.; Lei, A. Trisulfur Radical Anion as the Key Intermediate for the Synthesis of Thiophene via the Interaction between Elemental Sulfur and NaO*t*Bu. *Org. Lett.* **2014**, *16*, 6156−6159.



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