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Radical Difluroromethylation of Thiols with Difluoromethylphosphonium Triflate under Photoredox Catalysis

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Abstract

A convenient, visible light-induced radical difluoromethylation of aryl-, heteroaryl-, and alkylthiols with difluoromethyltriphenylphosphonium triflate was developed to afford various difluoromethyl thioethers in moderate to excellent yields. The key reaction features include the use of a readily available CF_2H radical source, mild reaction conditions and excellent chemoselective thiol-difluoromethylation.

Introduction

As an important type of fluorine-containing groups, fluoroalkylthio groups have received growing interest over the past few years.¹ The association of fluoroalkyl groups with sulfur atom generally increases the lipophilicity parameter of these substituents. In particular, the trifluoromethylthio group (SCF₃) has extremely high Hansch parameter ($\pi_R = 1.44$).² Thus, it is not surprising to witness the surge in the number of methods for introduction of SCF₃ into organic compounds recently.³ Compared to SCF₃, its analogous difluoromethylthio group (SCF₂H) is less lipophilic, but gains additional hydrogenbond donor capabilities.⁴ Consequently, SCF₂H essentially serves as a lipophilic hydrogen-bond donor motif for drug discovery, and the SCF₂H substituent has emerged as an important functional group in bioactive molecules, such as pyriprole and flomoxef sodium (Figure 1).⁵



Figure 1. SCF₂H-containing bioactive compounds

Traditionally, the difluoromethylthiolated compounds are prepared by the reaction of thiol (thiolate) or derivative with difluorocarbene *in situ*-generated from the ozone-depleting compound HCF_2CL^6 Recently, impressive advances have been made for the synthesis of these compounds,⁷ involving either $C-SCF_2H^8$ or $CS-CF_2H^{9-13}$ bond formation. The direct difluoromethylthiolation ($C-SCF_2H$ bond formation) of widely available substrates such as halides, boronic acids, carboxylic acids, and amines with the difluoromethylthiolating reagents has emerged as powerful approaches to various difluoromethyl thioethers.⁸ However several steps were required for the preparation of difluoromethylthiolating reagents. The new methods for $CS-CF_2H$ bond formation can be classified Page 3 of 18

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into four reaction types: difluorocarbene-mediated reactions,⁹ electrophilic,¹¹ nucleophilic,¹² and radical¹³ difluoromethylation. First, new difluorocarbene precursors were developed to make the traditional method more environmentally benign.9 Even so, this protocol suffers from the low chemoselectivity when two or more nucleophilic groups exist in the substrate.¹⁰ The electrophilic difluoromethylation of sulfur-containing compounds gave difluoromethyl thioethers only in moderate Difluoromethyl thioethers were formed in high yields from the nucleophilic vields.¹¹ difluoromethylation of disulfides,¹² but half of the disulfides were wasted in these processes. Baran and co-workers reported that the radical difluromethylation of heteroarylthiols with Zn(SO₂CF₂H)₂ in the presence of t-BuOOH gave the corresponding difluoromethyl thioethers in moderate yield (Scheme 1a).^{13a} Yi developed a silver-catalyzed radical difluoromethylation of aryl- and heteroarylthiols with NaSO₂CF₂H using K₂S₂O₈ as oxidant (Scheme 1b).^{13b} Recently, photoredox catalysis has been regarded as a valuable and environmentally benign tool in organic synthesis.¹⁴ Our group very recently disclosed the radical difluoromethylation of alkenes with difluoromethylphosphonium salts under photoredox catalysis.¹⁵ Compared to other CF₂H radical sources, difluoromethylphosphonium salts are more easily available and handled.¹⁶ Herein, we disclose a complementary visible light-induced radical difluoromethylation of thiols with difluoromethyltriphenylphosphonium triflate (Scheme 1c). This method provides a new access to diffuoromethyl thioethers using easily available diffuoromethylating reagent under mild conditions.

Scheme 1. Radical Difluoromethylation of Thiols



Results and Discussion

Initially, we chose 4-(tert-butyl)benzenethiol (1a) as the model substrate to optimize the reaction conditions (Table 1). In our previous studies,^{15b,c} it was found that among the common photocatalysts only *fac*-Ir(ppy)₃ was capable of reduction of diffuoromethylphosphonium salt to CF_2H radical. Thus, chosen as the photocatalyst for difluoromethylation of **1a** fac-Ir(ppy)₃ was with difluoromethylphosphonium salts (2a-d) in the presence of tetramethylethylenediamine (TMEDA) using MeCN solvent under visible light irradiation (entries 1-4). as the Among the difluoromethylphosphonium salts tested, difluoromethylphosphonium triflate (2b) afforded the desired difluoromethyl thioether 3a in highest vield (entry 2). Then, switching TMEDA to other additives including NaHCO₃, 1,8-diazobicyclo[5,4,0]undec-7-ene (DBU), NEt₃, N,N-dimethylaniline, and N,Ndimethyl-4-toluidine led to lower yields (entries 5-9). It was noteworthy that product 3a was formed in 32% yield even in the absence of an additive (entry 10). Subsequently, different solvents including DMF, DMSO, THF, and acetone were investigated (entries 11-14). However, no higher yield was obtained. Finally, the yield of **3a** was increased by prolonging the reaction time and increasing the amount of difluoromethylating reagent (entries 15 and 16). An excess of difluoromethylphosphonium triflate (2b) was required for formation of **3a** in high yield, because part of **2b** was converted into CF₂H₂ under these reaction conditions. Compound **3a** was not formed when the reaction was performed in the absence of

photoredox catalyst or visible light (entries 17 and 18), which indicated that both the photoredox catalyst

and visible light were crucial for this reaction.

Table 1. Optimization of Reaction Conditions for Difluoromethylation of Arylthiol^a

	t-Bu la	$\begin{array}{ccc} & & \text{visible light} \\ & & & & f_{ac} \cdot \ln(\text{ppy})_{3} \\ & & & + & Ph & (3 \text{ mol } \%) \\ & & & Ph & additive, solvent \\ & & & 2 \end{array}$	t-Bu	SCF ₂ H
entry	2 (X)	Additive	Solvent	yield $(\%)^b$
1	2a (Br)	TMEDA	MeCN	36
2	2b (OTf)	TMEDA	MeCN	62
3	2c (BF ₄)	TMEDA	MeCN	45
4	2d (PF ₆)	TMEDA	MeCN	51
5	2b (OTf)	NaHCO ₃	MeCN	12
6	2b (OTf)	DBU	MeCN	10
7	2b (OTf)	NEt ₃	MeCN	55
8	2b (OTf)	N,N-dimethylaniline	MeCN	11
9	2b (OTf)	N,N-dimethyl-4-toluidine	MeCN	12
10	2b (OTf)	—	MeCN	32
11	2b (OTf)	TMEDA	DMF	46
12	2b (OTf)	TMEDA	DMSO	49
13	2b (OTf)	TMEDA	THF	28
14	2b (OTf)	TMEDA	Acetone	7
15 ^c	2b (OTf)	TMEDA	MeCN	72
16 ^{<i>d</i>}	2b (OTf)	TMEDA	MeCN	85
17 ^e	2b (OTf)	TMEDA	MeCN	0
18 ^f	2b (OTf)	TMEDA	MeCN	0

^{*a*}Reaction conditions: **1a** (0.1 mmol), difluoromethyltriphenylphosphonium salt (0.3 mmol), *fac*-Ir(ppy)₃ (0.003 mmol), additive (0.2 mmol), solvent (1.0 mL), visible light, rt, under N₂, 24 h. ^{*b*}Yields determined by ¹⁹F NMR spectroscopy using fluorobenzene as an internal standard. ^{*c*}48 h. ^{*d*}Difluoromethyltriphenylphosphonium salt (0.4 mmol). ^{*e*}In the absence of *fac*-Ir(ppy)₃. ^{*f*}In the dark.

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With optimized conditions in hand, the substrate scope of arylthiols was investigated (Scheme 2). The electron-rich, electron-deficient arylthiols electron-neutral, and (1a-l) reacted with difluoromethylphosphonium 2b to afford the corresponding aryl difluoromethyl thioethers (3a-1) in good to excellent yields. An array of functional groups including ether, alcohol, phenol, amine, amide, chloride, bromide, nitrile, and ester were well tolerated under the mild conditions. It is noteworthy that difluoromethylation of (4-mercaptophenyl)methanol (1c) and 4-mercaptophenol (1d) with 4.0 equiv. of **2b** gave only S-difluoromethylated products (**3c** and **3d**). No O-difluoromethylated product was detected. This excellent chemoselectivity highlights the unique property of the current method, which is different from the difluorocarbene-based protocols.⁹ The sterically hindered arylthiol (11) also proceeded smoothly to give product 31 in 88% yield. However, low yield was obtained when naphthalene-2-thiol was subjected to the standard conditions.

Scheme 2. Difluoromethylation of Arylthiols^a



^aReaction conditions: **1** (0.5 mmol), difluoromethyltriphenylphosphonium triflate (2.0 mmol), *fac*-Ir(ppy)₃ (0.015 mmol), TMEDA (1.0 mmol), MeCN (5.0 mL), visible light, rt, under N₂, 48 h. Yields are those of the isolated products.

We next turned our attention to the difluoromethylation of heteroarylthiols for the preparation of heteroaryl difluoromethylthioethers. Compared to the difluoromethylation of 4-(tert-butyl)benzenethiol (1a),benzo[*d*]thiazole-2-thiol the reaction of (4a)faster and required less was difluoromethylphosphonium (2b) (Table 2, entry 1). After screening of the additives and solvents (entries 2-8), the difluoromethylated product (5a) was obtained in up to 92% yield in the presence of N,N-dimethyl-4-toluidine using DMF as the solvent (entry 6). This is due to the solubility of the substrate in DMF.

Table 2. Screening of Additives and Solvents for Difluoromethylation of Heteroarylthiol^a



Lifting		Sorvent	yiela (70)
1	TMEDA	MeCN	68
2	NEt ₃	MeCN	23
3	DBU	MeCN	42
4	N,N-dimethylaniline	MeCN	58
5	N,N-dimethyl-4-toluidine	MeCN	72
6	N,N-dimethyl-4-toluidine	DMF	92
7	N,N-dimethyl-4-toluidine	DMSO	81
8	N,N-dimethyl-4-toluidine	THF	43

^{*a*}Reaction conditions: **4a** (0.1 mmol), difluoromethyltriphenylphosphonium triflate (0.3 mmol), *fac*-Ir(ppy)₃ (0.003 mmol), additive (0.2 mmol), solvent (1.0 mL), visible light, rt, under N₂, 24 h. ^{*b*}Yields determined by ¹⁹F NMR spectroscopy using fluorobenzene as an internal standard.

The optimized reaction conditions (Table 2, entry 6) were suitable for the conversion of a series of

heteroarylthiols to the corresponding difluoromethyl thioethers in moderate to excellent yields (Scheme

3). Benzo[*d*]thiazole-2-thiols (**4a-f**) bearing electron-withdrawing and electron-donating groups were well tolerated. Moreover, the difluoromethylation of 4-thiopyridine (**4g**), 2-thiopyridine (**4h**), and 2-thiopyrimidine (**4i**) occurred in excellent yields. In all cases, only *S*-difluoromethylated products were obtained and no *N*-difluoromethylated product was detected.¹⁰

Scheme 3. Difluoromethylation of Heteroarylthiols



^aReaction conditions: **4** (0.5 mmol), difluoromethyltriphenylphosphonium triflate (1.5 mmol), *fac*-Ir(ppy)₃ (0.015 mmol), *N*,*N*-dimethyl-4-toluidine (1.0 mmol), DMF (5.0 mL), visible light, rt, under N₂, 24 h. Yields are those of the isolated products.

The alkylthiols are challenging substrates for the radical difluoromethylation process. Benzylthiol **6a** and alkylthiol **6b** were respectively converted into difluoromethyl thioethers **7a** and **7b** in low yields (Scheme 4). These results are consistent with the analogous radical trifluoromethylation of alkylthiols.¹⁷

 Scheme 4. Difluoromethylation of Alkyl Thiols



To gain insight into the reaction mechanism, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), a well known radical scavenger, was added into the standard reaction conditions of **1a**. The desired product **3a** was not obtained and a TEMPO-CF₂H adduct **8** was formed (Scheme 5a). This result provides supportive evidence that a CF₂H radical may be involved as a reactive species in this reaction. Moreover, in some cases, the formation of disulfides in the reaction mixture was detected. Thus, the difluoromethylation of disulfide **9**¹⁸ under the standard reaction conditions was investigated, and difluoromethylated product **3a** was also obtained in high yield (Scheme 5b). Additionally, the fluorescence quenching experiments at different concentration of difluoromethylphosphonium **2b** showed that **2b** exhibited fluorescence quenching of excited state **fac*-Ir^{III}(ppy)₃ (see the Supporting Information). This result suggested that electron transfer probably occurred from **fac*-Ir^{III}(ppy)₃ to **2b** firstly.

Scheme 5. Mechanistic Experiments



Based on the above results, a proposed mechanism for the reaction is outlined in Scheme 6. First, irradiation with visible light excites fac-Ir^{III}(ppy)₃ into *fac-Ir^{III}(ppy)₃, which is then oxidized by difluoromethylphosphonium **2b** via a single electron transfer (SET) to give fac-Ir^{IV}(ppy)₃ and CF₂H radical. Subsequently, CF₂H radical reacts with thiolate affording the corresponding radical anion intermediate, which undergoes a SET to give the final product difluoromethyl thioether (*path a*). On the other hand, thiolate might be oxidized by fac-Ir^{IV}(ppy)₃ to sulfur radical, which is easily converted into the disulfide. The reaction of CF₂H radical and disulfide could also give the difluoromethyl thioether (*path b*). The excellent chemoselective thiol-difluoromethylation suggest that *path b* is the more likely reaction pathway, although *path a* can not be ruled out. However, the exact reaction mechanism remains unclear at the moment.





Conclusion

We have developed an efficient and practical radical difluoromethylation of aryl-, heteroaryl-, and alkylthiols with readily available difluoromethyltriphenylphosphonium triflate by visible light photoredox catalysis. This protocol provides an attractive approach to a range of difluoromethyl ACS Paragon Plus Environment

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thioethers under mild conditions with excellent S/X (X = O, N)-selectivities. Further exploration of the reaction mechanism and the application of this method are underway in our laboratory.

Experimental Section

General Experimental Methods. ¹H NMR (TMS as the internal standard) and ¹⁹F NMR spectra (CFCl₃ as the outside standard and low field is positive) were recorded on a 400 MHz spectrometer. ¹³C NMR was recorded on 400 MHz spectrometer. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. HRMS data using EI were obtained on a GC-TOF mass spectrometer. Unless otherwise noted, all reagents were obtained commercially and used without further purification. Substrates were purchased from commercial sources or were prepared according to literature procedures.

General procedure for difluoromethylation of aryl thiols

A 50 mL Schlenk flask equipped with a rubber septum and a magnetic stir bar was charged with difluoromethyltriphenylphosphonium triflate **2b** (925.0 mg, 2.0 mmol, 4.0 equiv.) and *fac*-Ir(ppy)₃ (9.8 mg, 0.015 mmol, 3 mol%). Then thiol **1** (0.5 mmol, 1.0 equiv.), TMEDA (0.15 mL, 1.0 mmol, 2.0 equiv.), and MeCN (5 mL) was added. The flask was sealed with 3M vinyl electrical tape. The mixture was degassed three times by the freeze-pump-thaw procedure. The flask was placed at a distance of 2 cm from the blue LEDs. The mixture was stirred under nitrogen atmosphere and irradiated by blue 30 W LEDs for 48 h. After the reaction was complete, 10% H₂O₂ (5 mL) was added to the reaction mixture (Note: H₂O₂ was used to oxidize PPh₃ to Ph₃PO for the purification of the desired products easier). The reaction mixture was extracted by Et₂O. The organic phase was dried by anhydrous sodium sulfate, concentrated in vacuo, and the residue was purified with silica gel column chromatography to provide the desired product.

(4-(*Tert-butyl*)*phenyl*)(*difluoromethyl*)*sulfane (3a*). Compound **3a** was obtained as a light yellow liquid (93.4 mg, 86%), hexane/Et₂O = 9:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.51 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 6.80 (t, *J* = 57.2 Hz, 1H), 1.33 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 153.2, 135.2, 126.5, 122.5 (t, *J* = 3.0 Hz), 121.2 (t, *J* = 274.1 Hz), 37.8, 31.2; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.4 (d, *J* = 57.2 Hz, 2F); MS (EI): *m/z* 216 (M⁺). These data matched with the reported results.^{8b}

 (*Difluoromethyl*)(4-methoxyphenyl)sulfane (3b). Compound 3b was obtained as a yellow liquid (88.6 mg, 93%), hexane as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.49-7.51 (m, 2H), 6.89-6.91 (m, 2H), 6.73 (t, *J* = 57.2 Hz, 1H), 3.81 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 161.2, 137.6, 121.0 (t, *J* = 273.3 Hz), 116.1 (t, *J* = 3.0 Hz), 114.9, 55.3; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -92.3 (d, *J* = 57.5 Hz, 2F); MS (EI): *m/z* 190 (M⁺). These data matched with the reported results.^{8b}

(4-((Difluoromethyl)thio)phenyl)methanol (3c). Compound 3c was obtained as a yellow liquid (67.9 mg, 71%), DCM/MeOH = 50:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.53 (d, *J* = 8.0 Hz, 2H), 7.32(d, *J* = 8.0 Hz, 2H), 6.79 (t, *J* = 56.8 Hz, 1H), 4.62 (s, 2H), 2.61-2.68 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 142.7, 135.6, 127.6, 124.8 (t, *J* = 3.0 Hz), 121.8 (t, *J* = 273.3 Hz), 64.3; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.5 (d, *J* = 57.2 Hz, 2F); IR (thin film) v 3341, 2926, 1492, 1320, 1297, 1067, 817 cm⁻¹; MS (EI): *m/z* 190 (M⁺); HRMS (EI-TOF): *m/z* [M⁺] Calculated for C₈H₈F₂OS: 190.0264; Found: 190.0267.

4-((Difluoromethyl)thio)phenol (3d). Compound 3d was obtained as a light brown liquid (76.9 mg, 87%), hexane/EA = 5:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.45 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.73 (t, J = 57.2 Hz, 1H), 5.34-5.39 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.3, 137.9, 120.9 (t, J = 274.1 Hz), 116.4; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -92.3 (d, J = 57.2 Hz, 2F); MS (EI): m/z 176 (M⁺). These data matched with the reported results.^{13b}

N-(4-((difluoromethyl)thio)phenyl)acetamide (3e). Compound **3e** was obtained as a light yellow solid (92.6 mg, 85%), hexane/EA = 1:1 as eluent for the column chromatography. ¹H NMR (400 MHz, d₆-DMSO) δ ppm 10.1 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.32 (t, *J* = 56.4 Hz, 1H), 2.04 (s, 3H); ¹³C NMR (100 MHz, d₆-DMSO) δ ppm 169.1, 141.5, 136.6, 121.4 (t, *J* = 271.8 Hz), 120.0, 118.3 (t, *J* = 3.1 Hz), 24.4; ¹⁹F NMR (376 MHz, d₆-DMSO) δ ppm -92.9 (d, *J* = 56.0 Hz, 2F); MS (EI): *m/z* 217 (M⁺). These data matched with the reported results.^{8b}

4-((Difluoromethyl)thio)-N,N-dimethylaniline (3f). Compound 3f was obtained as a light brown liquid (84.7 mg, 83%), hexane/Et₂O = 9:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.42 (d, J = 9.2 Hz, 2H), 6.69 (t, J = 57.6 Hz, 1H), 6.66 (d, J = 8.8 Hz, 2H), 2.98 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 151.5, 137.4, 121.4 (t, J = 273.3 Hz), 112.5, 109.8 (t, J = 3.1 Hz), 40.1; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -92.6 (d, J = 57.2 Hz, 2F); MS (EI): m/z 203 (M⁺). These data matched with the reported results.^{8a}

(4-Chlorophenyl)(difluoromethyl)sulfane (3g). Compound 3g was obtained as a colorless liquid (79.6 mg, 82%), hexane as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.49-7.52 (m, 2H), 7.34-7.37 (m, 2H), 6.79 (t, *J* = 56.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 136.7,

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136.5, 129.6, 124.2 (t, J = 3.0 Hz), 120.3 (t, J = 274.8 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.7 (d, J = 56.0 Hz, 2F); MS (EI); m/z 194 (M⁺). These data matched with the reported results.^{8b}

(4-Bromophenyl)(difluoromethyl)sulfane (3h). Compound 3h was obtained as a light yellow liquid (98.7 mg, 83%), hexane/Et₂O = 9:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.42-7.52 (m, 4H), 6.79 (t, *J* = 56.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 136.9, 132.6, 124.9 (t, *J* = 3.0 Hz), 124.7, 120.2 (t, *J* = 274.1 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.7 (d, *J* = 56.0 Hz, 2F); MS (EI): *m/z* 238 (M⁺). These data matched with the reported results.^{8b}

(*Difluoromethyl*)(4-(trifluoromethyl)phenyl)sulfane (3i). Compound 3i was obtained as a light yellow liquid (82.1 mg, 72%), pentane as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.68 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 6.87 (t, *J* = 56.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 134.9, 131.7 (q, *J* = 32.6 Hz), 130.9, 126.1 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 271.1 Hz), 120.1 (t, *J* = 274.8 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -63.0 (s, 3F), -91.3 (d, *J* = 55.6 Hz, 2F); MS (EI): *m/z* 228 (M⁺). These data matched with the reported results.^{9f}

4-((Difluoromethyl)thio)benzonitrile (3j). Compound **3j** was obtained as a colorless liquid (83.5 mg, 90%), hexane/Et₂O = 9:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.64 (s, 4H), 6.89 (t, *J* = 56.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 134.5, 132.7, 119.7 (t, *J* = 275.6 Hz), 117.9, 113.2; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.3 (d, *J* = 56.0 Hz, 2F); MS (EI): *m/z* 185 (M⁺). These data matched with the reported results.^{8b}

Methyl 4-((difluoromethyl)thio)benzoate (3k). Compound **3k** was obtained as a light yellow liquid (85.3 mg, 78%), hexane/EA = 5:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 8.00 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 6.87 (t, *J* = 56.4 Hz, 1H), 3.90 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 166.2, 134.0, 132.2 (t, *J* = 3.0 Hz), 131.0, 130.3, 120.4 (t, *J* = 274.1 Hz), 52.3; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.2 (d, *J* = 57.2 Hz, 2F); MS (EI): *m/z* 218 (M⁺). These data matched with the reported results.^{8b}

(2,6-Dichlorophenyl)(difluoromethyl)sulfane (3l). Compound 3I was obtained as a light yellow liquid (100.6 mg, 88%), hexane as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.44 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 6.88 (t, *J* = 57.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 142.5, 132.0, 129.0, 125.1 (t, *J* = 3.8 Hz), 120.1 (t, *J* = 277.1 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -92.0 (d, *J* = 58.7 Hz, 2F); MS (EI): *m/z* 228 (M⁺). These data matched with the reported results.^{9c}

General procedure for difluoromethylation of heteroaryl thiols

A 50 mL Schlenk flask equipped with a rubber septum and a magnetic stir bar was charged with difluoromethyltriphenylphosphonium triflate **2b** (690.0 mg, 1.5 mmol, 3.0 equiv.) and *fac*-Ir(ppy)₃ (9.8

mg, 0.015 mmol, 3 mol%). Then thiol **4** (0.5 mmol, 1.0 equiv.), *N*,*N*-dimethy-4-toluidine (0.14 mL, 1.0 mmol, 2.0 equiv.), and DMF (5 mL) was added. The flask was sealed with 3M vinyl electrical tape. The mixture was degassed three times by the freeze-pump-thaw procedure. The flask was placed at a distance of 2 cm from the blue LEDs. The mixture was stirred under nitrogen atmosphere and irradiated by blue 30 W LEDs for 24 h. After the reaction was complete, 10% H₂O₂ (5 mL) was added to the reaction mixture. The reaction mixture was extracted by Et₂O. The organic phase was dried by anhydrous sodium sulfate, concentrated in vacuo, and the residue was purified with silica gel column chromatography to provide the desired product.

2-((Difluoromethyl)thio)benzo[d]thiazole (5a). Compound 5a was obtained as a light yellow liquid (100.2 mg, 90%), hexane/DCM = 10:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.98 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 7.2 Hz, 1H), 7.63 (t, J = 56.0 Hz, 1H), 7.46-7.50 (m, 1H), 7.37-7.41 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.0, 152.9, 135,9, 126.6, 125.6, 122.8, 121.2, 120.3 (t, J = 275.6 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -93.2 (d, J = 56.0 Hz, 2F); MS (EI): m/z 217 (M⁺). These data matched with the reported results.^{9c}

6-Chloro-2-((difluoromethyl)thio)benzo[d]thiazole (5b). Compound 5b was obtained as a light yellow liquid (107.2 mg, 85%), hexane/DCM = 10:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.96 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.65 (t, J = 56.0 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 159.5, 153.6, 134.0, 132.8, 126.0, 122.6, 121.8, 120.0 (t, J = 276.4 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -93.5 (d, J = 55.6 Hz, 2F); IR (thin film) v 1547, 1430, 1287, 1064, 997, 801, 780 cm⁻¹; MS (EI): m/z 251 (M⁺); HRMS (EI-TOF): m/z [M⁺] Calculated for C₈H₄ClF₂NS₂: 250.9442; Found: 250.9438.

6-Bromo-2-((difluoromethyl)thio)benzo[d]thiazole (5c). Compound 5c was obtained as a yellow liquid (137.7 mg, 93%), hexane/DCM = 10:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 8.09-8.10 (m, 1H), 7.63-7.66 (m, 1H), 7.65 (t, J = 56.0 Hz, 1H), 7.46-7.49 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.0, 152.9, 135,9, 126.6, 125.6, 122.8, 121.2, 120.3 (t, J = 275.6 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -93.2 (d, J = 56.0 Hz, 2F); IR (thin film) v 1542, 1462, 1427, 1287, 1071, 997, 893, 780 cm⁻¹; MS (EI): m/z 295 (M⁺); HRMS (EI-TOF): m/z [M⁺] Calculated for C₈H₄BrF₂NS₂: 294.8937; Found: 294.8936.

4-Bromo-2-((difluoromethyl)thio)-6-(trifluoromethyl)benzo[d]thiazole (5d). Compound 5d was obtained as a yellow liquid (151.5 mg, 83%), hexane/DCM = 10:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 8.02 (s, 1H), 7.88 (s, 1H), 7.80 (t, J = 55.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 162.7, 152.8, 136.1, 128.5 (q, J = 33.4 Hz), 127.1 (q, J = 6.1 Hz), 123.0 (q, J = 271.8 Hz), 119.9 (t, J = 276.4 Hz), 117.8 (q, J = 4.6 Hz), 116.5; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -61.7 (s, 3F), -93.9 (d, J = 55.6 Hz, 2F); IR (thin film) v 1460, 1391, 1306, 1170, 1134,

1087, 1009, 880 cm⁻¹; MS (EI): m/z 363 (M⁺); HRMS (EI-TOF): m/z [M⁺] Calculated for C₉H₃BrF₅NS₂: 362.8810; Found: 362.8809.

2-((*Difluoromethyl*)thio)-6-nitrobenzo[d]thiazole (5e). Compound 5e was obtained as a light yellow solid (85.3 mg, 65%), hexane/DCM = 1:1 as eluent for the column chromatography. MP: 94-95 °C. ¹H NMR (400 MHz, CDCl₃) δ ppm 8.74-8.75 (m, 1H), 8.33-8.36 (m, 1H), 8.02-8.05 (m, 1H), 7.78 (t, J = 55.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.9 (t, J = 3.8 Hz), 156.2, 145.0, 135.8, 122.7, 122.2, 119.7 (t, J = 276.3 Hz), 117.7; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -93.9 (d, J = 54.5 Hz, 2F); IR (thin film) v 1597, 1515, 1431, 1324, 1076, 1028, 1004, 741 cm⁻¹; MS (EI): *m/z* 262 (M⁺); HRMS (EI-TOF): *m/z* [M⁺] Calculated for C₈H₄F₂N₂O₂S₂: 261.9682; Found: 261.9677.

2-((Difluoromethyl)thio)-6-ethoxybenzo[d]thiazole (5f). Compound 5f was obtained as a light yellow solid (111.3 mg, 85%), hexane/DCM = 1:1 as eluent for the column chromatography. MP: 44-46 °C. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.87 (d, J = 8.8 Hz, 1H), 7.45(t, J = 56.4 Hz, 1H), 7.24 (d, J = 2.4 Hz, 1H), 7.07 (dd, J = 2.8 Hz, J = 8.8 Hz, 1H), 4.06 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 157.5, 147.5, 138.0, 125.7, 123.6, 120.3 (t, J = 276.4 Hz), 116.5, 104.2, 64.1, 12.7; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -92.7 (d, J = 55.6 Hz, 2F); IR (thin film) v 1600, 1470, 1448, 1258, 1225, 1084, 998, 822 cm⁻¹; MS (EI): *m/z* 261 (M⁺); HRMS (EI-TOF): *m/z* [M⁺] Calculated for C₁₀H₉F₂NOS₂: 261.0094; Found: 261.0089.

4-((Difluoromethyl)thio)pyridine (5g). Compound 5g was obtained as a brown liquid (54.5 mg, 67%), hexane/EA = 1:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 8.53-8.55 (m, 2H), 7.35-7.36 (m, 2H), 6.95 (t, J = 55.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 150.2, 138.4, 126.2, 119.7 (t, J = 274.9 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -91.2 (d, J = 55.6 Hz, 2F); MS (EI): m/z 161 (M⁺). These data matched with the reported results.^{8a}

2-((Difluoromethyl)thio)pyridine (5h). Compound 5h was obtained as a brown liquid (73.0 mg, 91%), hexane/EA = 10:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 8.45-8.46 (m, 1H), 7.68(t, J = 56.4 Hz, 1H), 7.55-7.59 (m, 1H), 7.22-7.24 (m, 1H), 7.10-7.13 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 153.1 (t, J = 3.1 Hz), 150.1, 137.1, 124.3 (t, J = 2.3 Hz), 121.7, 121.3 (t, J = 269.5 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -96.3 (d, J = 56.0 Hz, 2F); MS (EI): m/z 161 (M⁺). These data matched with the reported results.^{8a}

2-((Difluoromethyl)thio)-4,6-dimethylpyrimidine (5i). Compound 5i was obtained as a brown liquid (89.2 mg, 94%), hexane/EA = 10:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.81 (t, J = 56.0 Hz, 1H), 6.78 (s, 1H), 2.39 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 167.8, 166.4, 121.2 (t, J = 268.0 Hz), 117.4, 23.7; ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -99.1 (d, J = 55.6 Hz, 2F); MS (EI): m/z 190 (M⁺). These data matched with the reported results.^{9f}

General procedure for difluoromethylation of alkyl thiols

A 50 mL Schlenk flask equipped with a rubber septum and a magnetic stir bar was charged with difluoromethyltriphenylphosphonium triflate **2b** (690.0 mg, 1.5 mmol, 3.0 equiv.) and *fac*-Ir(ppy)₃ (9.8 mg, 0.015 mmol, 3 mol%). Then thiol **6** (0.5 mmol, 1.0 equiv.), DBU (0.15 mL, 1.0 mmol, 2.0 equiv.), and DMSO (5 mL) was added. The flask was sealed with 3M vinyl electrical tape. The mixture was degassed three times by the freeze-pump-thaw procedure. The flask was placed at a distance of 2 cm from the blue LEDs. The mixture was stirred under nitrogen atmosphere and irradiated by blue 30 W LEDs for 48 h. After the reaction was complete, 10% H₂O₂ (5 mL) was added to the reaction mixture. The reaction mixture was extracted by Et₂O. The organic phase was dried by anhydrous sodium sulfate, concentrated in vacuo, and the residue was purified with silica gel column chromatography to provide the desired product.

Benzyl(difluoromethyl)sulfane (7a). Compound 7a was obtained as a light yellow liquid (32.5 mg, 37%), hexane/DCM = 5:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.28-7.35 (m, 5H), 6.73 (t, J = 56.4 Hz, 1H), 4.02 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 136.2, 128.9, 128.8, 128.5, 128.3, 127.7, 120.2 (t, J = 271.1 Hz), 31.7 (t, J = 3.8 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -94.5 (d, J = 56.0 Hz, 2F); MS (EI): m/z 174 (M⁺). These data matched with the reported results.^{9c}

Benzyl(difluoromethyl)sulfane (7b). Compound **7b** was obtained as a light yellow liquid (39.4 mg, 42%), hexane/DCM = 5:1 as eluent for the column chromatography. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.32-7.35 (m, 2H), 7.22-7.28 (m, 3H), 6.78 (t, *J* = 56.4 Hz, 1H), 2.97-3.09 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 139.6, 128.6, 128.6, 126.7, 120.6 (t, *J* = 271.8 Hz), 36.8, 28.6 (t, *J* = 3.0 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ ppm -92.7 (d, *J* = 56.0 Hz, 2F); MS (EI): *m/z* 188 (M⁺). These data matched with the reported results.^{8a}

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Supporting Information Available: Preliminary mechanistic experiments, as well as copies of ¹H, ¹⁹F, and ¹³C NMR spectra. These material are available free of charge via the Internet at http://pubs.acs.org.

References

For selected reviews, see: (a) Liang, T.; Neumann, C. N.; Ritter, T. Angew. Chem., Int. Ed. 2013, 52, 8214. (b) Chu, L.; Qing, F.-L. Acc. Chem. Res. 2014, 47, 1513. (c) Toulgoat, F.; Alazet, S.; Billard, T. Eur. J. Org. Chem. 2014, 2415. (d) Xu, X.-H.; Matsuzaki, K.; Shibata, N. Chem. Rev. 2015, 115,

731. (e) Zhang, K.; Xu, X.-H.; Qing, F.-L. Chin. J. Org. Chem. 2015, 35, 556. (f) Shao, X.; Xu, C.;

Lu, L.; Shen, Q. Acc. Chem. Res. 2015, 48, 1227. (g) Chachignon, H.; Cahard, D. Chin. J. Chem.

- 2016, 34, 445. (h) Barata-Vallejo, S.; Bonesi, S.; Postigo, A. Org. Biomol. Chem. 2016, 14, 7150.
- (2) Hansch, C.; Leo, A.; Unger, S. H.; Kim, K. H.; Nikaitani, D.; Lien, E. J. J. Med. Chem. 1973, 16, 1207.
- (3) For selected examples, see: (a) Teverovskiy, G.; Surry, D. S.; Buchwald, S. L. Angew. Chem. Int. Ed. 2011, 50, 7312. (b) Chen, C.; Xie, Y.; Chu, L.; Wang, R.-W.; Zhang, X.; Qing, F.-L. Angew. Chem. Int. Ed. 2012, 51, 2492. (c) Baert, F.; Colomb, J.; Billard, T. Angew. Chem. Int. Ed. 2012, 51, 10382. (d) Zhang, C.-P.; Vicic, D. A. J. Am. Chem. Soc. 2012, 134, 183. (e) Chen, C.; Chu, L.; Qing, F.-L. J. Am. Chem. Soc. 2012, 134, 12454. (f) Weng, Z.; He, W.; Chen, C.; Lee, R.; Tan, D.; Lai, Z.; Kong, D.; Yuan, Y.; Huang, K.-W. Angew. Chem. Int. Ed. 2013, 52, 1548. (g) Shao, X.; Wang, X. Q.; Yang, T.; Lu, L.; Shen, Q. Angew. Chem. Int. Ed. 2013, 52, 3457. (h) Yang, Y.-D.; Azuma, A.; Tokunaga, E.; Yamasaki, M.; Shiro, M.; Shibata, N. J. Am. Chem. Soc. 2013, 135, 8782. (i) Pluta, R.; Nikolaienko, P.; Rueping, M. Angew. Chem. Int. Ed. 2014, 53, 1650. (j) Liu, J.-B.; Xu, X.-H.; Chen, Z.-H.; Qing, F.-L. Angew. Chem. Int. Ed. 2015, 54, 897. (k) Jiang, L.; Qian, J.; Yi, W.; Lu, G.; Cai, C.; Zhang, W. Angew. Chem. Int. Ed. 2015, 54, 14965.
- (4) (a) Rico, I.; Wakselman, C. *Tetrahedron Lett.* **1981**, *22*, 323. (b) Asakura, S.; Kawasaki, H.; Hiraoka, M.; Yoshimura, T.; Hanai, R. *Pak. J. Weed Sci. Res.* **2012**, *18*, 719.
- (5) (a) Fourie, J. J.; Horak, I. G.; de la Puente Redondo, V. Vet. Rec. 2010, 167, 442. (b) Ito, M.; Ishigami, T. Infection 1991, 19, S253.
- (6) (a) Hine, J.; Porter, J. J. J. Am. Chem. Soc. 1957, 79, 5493. (b) Langlois, B. R. J. Fluorine Chem. 1988, 41, 247. (c) Chen, Q. Y.; Wu, S. W. J. Fluorine Chem. 1989, 44, 433.
- (7) For a recent review, see: Xiong, H.-Y.; Pannecoucke, X.; Besset, T. Chem. Eur. J. 2016, 22, 16734.
- (8) (a) Bayarmagnai, B.; Matheis, C.; Jouvin, K.; Goossen, L. J. Angew. Chem., Int. Ed. 2015, 54, 5753.
 (b) Wu, J.; Gu, Y.; Leng, X.; Shen, Q. Angew. Chem., Int. Ed. 2015, 54, 7648. (c) Zhu, D.; Gu, Y.; Lu, L.; Shen, Q. J. Am. Chem. Soc. 2015, 137, 15047. (d) Zhu, D.; Shao, X.; Hong, X.; Lu, L.; Shen, Q. Angew. Chem., Int. Ed. 2016, 55, 15807. (e) Jiang, L.; Yi, W.; Liu, Q. Adv. Synth. Catal. 2016, 358, 3700. (f) Candish, L.; Pitzer, L.; Gómez-Suárez, A.; Glorius, F. Chem. Eur. J. 2016, 22, 4753. (g) Arimori, S.; Matsubara, O.; Takada, M.; Shiro, M.; Shibata, N. R. Soc. open sci. 2016, 3: 160102.
- (9) (a) Wang, F.; Huang, W.; Hu, J. Chin. J. Chem. 2011, 29, 2717. (b) Fier, P. S.; Hartwig, J. F. Angew. Chem., Int. Ed. 2013, 52, 2092. (c) Li, L.; Wang, F.; Ni, C.; Hu, J. Angew. Chem., Int. Ed. 2013, 52, 12390. (d) Zheng, J.; Lin, J.-H.; Cai, J.; Xiao, J.-C. Chem. Eur. J. 2013, 19, 15261. (e) Thomoson, C. S.; Dolbier, W. R., Jr. J. Org. Chem. 2013, 78, 8904. (f) Mehta, V. P.; Greaney, M. F. Org. Lett. 2013, 15, 5036. (g) Deng, X.-Y.; Lin, J.-H.; Zheng, J.; Xiao, J.-C. Chem. Commun. 2015, 51, 8805. (h) Fuchibe, K.; Bando, M.; Takayama, R.; Ichikawa, J. J. Fluorine Chem. 2015, 171, 133. (i) Prakash, G. K. S.; Krishnamoorthy, S.; Kar, S.; Olah, G. A. J. Fluorine Chem. 2015, 180, 186.
- (10) (a) Petko, K. I.; Yagupolskii, L. M. J. Fluorine Chem. 2001, 108, 211. (b) Zhang, W.; Wang, F.;
 Hu, J. Org. Lett. 2009, 11, 2109. (c) Mehta, V. P.; Greaney, M. F. Org. Lett. 2013, 15, 5036.

- (11) Prakash, G. K. S.; Zhang, Z.; Wang, F.; Ni, C.; Olah, G. A. J. Fluorine Chem. 2011, 132, 792.
- (12) (a) Howard, J. L.; Schotten, C.; Alston, S. T.; Browne, D. L. Chem. Commun. 2016, 52, 8448. (b)
 Han, J.-B.; Qin, H.-L.; Ye, S.-H.; Zhu, L.; Zhang, C.-P. J. Org. Chem. 2016, 81, 2506. (c) Lin, Y.-M.; Yi, W.-B.; Shen, W.-Z.; Lu, G.-P. Org. Lett. 2016, 18, 592.
- (13) (a) Fujiwara, Y.; Dixon, J. A.; Rodriguez, R. A.; Baxter, R. D.; Dixon, D. D.; Collins, M. R.; Blackmond, D. G.; Baran, P. S. J. Am. Chem. Soc. 2012, 134, 1494. (b) Ma, J.-J.; Liu, Q.-R.; Lu, G.-P.; Yi, W.-B. J. Fluorine Chem. 2017, 193, 113.
- (14) For selected reviews, see: (a) Yoon, T. P.; Ischay, M. A.; Du, J. Nat. Chem. 2010, 2, 527. (b) Narayanam, J. M. R.; Stephenson, C. R. J. Chem. Soc. Rev. 2011, 40, 102. (c) Xuan, J.; Xiao, W.-J. Angew. Chem. Int. Ed. 2012, 51, 6828. (d) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Chem. Rev. 2013, 113, 5322. (e) Hopkinson, M. N.; Sahoo, B.; Li, J.; Glorius, F. Chem. Eur. J. 2014, 20, 3874. (f) Xuan, J.; Zhang, Z.-G.; Xiao, W.-J. Angew. Chem. Int. Ed. 2015, 54, 15632. (g) Koike, T.; Akita, M. Acc. Chem. Res. 2016, 49, 1937. (h) Chatterjee, T.; Iqbal, N.; You, Y.; Cho, E. J. Acc. Chem. Res. 2016, 49, 2284.
- (15) (a) Lin, Q.-Y.; Xu, X.-H.; Zhang, K.; Qing, F.-L. Angew. Chem., Int. Ed. 2016, 55, 1479. (b) Ran,
 Y.; Lin, Q.-Y.; Xu, X.-H.; Qing, F.-L. J. Org. Chem. 2016, 81, 7001. (c) Lin, Q.-Y.; Ran, Y.; Xu,
 X.-H.; Qing, F.-L. Org. Lett. 2016, 18, 2419.
- (16) Burton, D. J.; Yang, Z.-Y.; Qiu, W. Chem. Rev. 1996, 96, 1641.
- (17) (a) Anselmi, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C. J. Fluorine Chem. 2000, 105, 41. (b) Straathof, N. J. W.; Tegelbeckers, B. J. P.; Hessel, V.; Wang, X.; Noël, T. Chem. Sci. 2014, 5, 4768.
- (18) Talla, A.; Driessen, B.; Straathof, N. J. W.; Milroy, L.-G.; Brunsveld, L.; Hessel, V.; Noël, T. *Adv. Synth. Catal.* **2013**, *357*, 2180.