Journal of Fluorine Chemistry 198 (2017) 67–75

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Efficient nucleophilic difluoromethylation of aldehydes with (phenylsulfonyl)difluoromethylzinc and (phenylsulfonyl) difluoromethylcadmium reagents

Fanzhou Jiang, Chuanfa Ni, Jinbo Hu*

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Ling-Ling Road, Shanghai 200032, China

ARTICLE INFO

Article history:
Received 3 November 2016
Received in revised form 6 December 2016
Accepted 6 December 2016
Available online 13 December 2016

Keywords:
Difluoromethylation
Sulfone
Aldehyde
Organozinc reagent
Organocadmium reagent

ABSTRACT

A new strategy for nucleophilic addition to aldehydes with difluoromethyl organometallic reagents has been developed by functionalizing the difluoromethyl moiety with the phenylsulfonyl group (SO_2Ph). This electron-withdrawing group influences both the thermodynamic stability and the nucleophilicity of difluoromethyl organometallic reagents, which plays an important role in the nucleophilic difluoromethylation of aldehydes.

1. Introduction

Fluoroalkylation reactions have undergone extensive development in the field of organofluorine chemistry over the past decades [1]. Among various fluoroalkyl groups, the difluoromethyl group ($-CF_2H$) is considered to be isosteric and isopolar to a carbinol ($-CH_2OH$) or thiol (-SH) unit [2]. It can also behave as a more lipophilic hydrogen donor through hydrogen bonding [3]. Moreover, selective incorporation of a difluoromethylene moiety into medicinal molecules not only has the potential to modify their interaction with neighboring functional groups, but also has an impact on their receptor bindings and metabolic processes [4]. Therefore, difluoromethylated analogues of biologically active molecules promise to be good candidates for pharmaceuticals. Recent years have witnessed the increasing number of methods for the introduction of difluoromethylated building blocks [2d,4] Nucleophilic difluoromethylation has been known as a convenient and efficient method to prepare difluoromethylated compounds [5]. $TMSCF_2H$, as a potentially useful difluoromethanide anion (CF_2H^-) precursor, has been successively applied for the nucleophilic addition to different substrates, such as aldehydes, ketones and imines [6]. In contrast to this organosilicon compound, difluoromethyl organometallic reagents are still supposed to be incapable of undergoing nucleophilic difluoromethylation of carbonyl compounds and related electrophiles [7]. Difluoromethylzinc (HCF_2ZnX) and cadmium (HCF_2CdX) reagents were prepared via direct insertion of the corresponding metal into the C-X bond of CF_2HX (X = Br and I) [7]. These sluggish difluoromethyl reagents demonstrated fairly good thermal stability at even 65 ~ 75 °C and only exhibited reactivities with allylic halides, propargyl halides and other high chemically reactive derivatives. Difluoromethylcopper reagents (HCF_2CuX) derived from difluoromethylcadmium reagent was more reactive with these halides, whereas easily decomposed when the temperature was elevated to higher than −30 °C [7]. The difluoromethylcopper species prepared from $TMSCF_2H$ was extensively investigated and successfully applied to the synthesis of difluoromethylated arenes [8]. Shen's group reported that a structurally well-defined difluoromethyl silver complex could difluoromethylate aryl bromides and iodides under mild conditions in the presence of palladium catalyst [9].

Recently, Mikami and co-workers succeeded in the trifluoromethylation of carbonyl compounds with the stable bis(trifluoromethyl)zinc reagent $Zn(CF_3)_2(TMEDA)$ [10]. As analogues of this isolated organozinc species, the corresponding bis(difluoromethyl) zinc reagent and its analogues were also synthesized for metal catalyzed cross-coupling reactions with aryl halides [11]. However,

* Corresponding author
E-mail address: jinbohu@sioc.ac.cn (J. Hu).

http://dx.doi.org/10.1016/j.jfluchem.2016.12.005
0022-1139/

difluoromethylation of carbonyl compounds with difluoromethylzinc reagents has not been achieved yet.

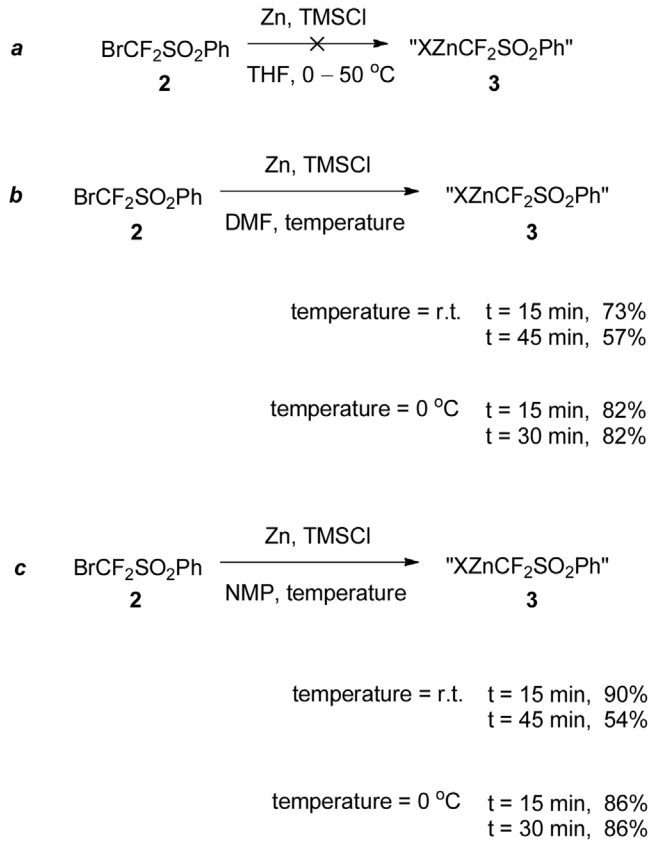
The (phenylsulfonyl)difluoromethyl group ($PhSO_2CF_2$) was regarded as a useful functionality, which can undergo further transformation into various groups, such as difluoromethylene ($—CF_2—$), difluoromethyl (CF_2H) and difluoromethylidene ($=CF_2$) moieties [5b]. In addition, the phenylsulfonyl group could enhance the nucleophilicity of difluoromethyl anion towards different electrophilic substrates [5]. The corresponding difluoromethylated organometallic reagents are expected to be obtained by direct insertion of an appropriate metal into the C—X (X = Br and I) bond of iodo- or bromodifluoromethyl phenyl sulfone ($PhSO_2CF_2I$/$PhSO_2CF_2Br$). Herein, we disclose an efficient nucleophilic difluoromethylation of aldehydes with (phenylsulfonyl)difluoromethylzinc and (phenylsulfonyl)difluoromethylcadmium reagents under mild conditions [12].

2. Results and discussion

Bromodifluoromethyl phenyl sulfone (**2**) could be readily prepared from bromodifluoromethyl phenyl sulfide ($PhSCF_2Br$, **1**) and $NaIO_4$ in the presence of $RuCl_3{\cdot}xH_2O$ according to the literature procedures (Scheme 1) [13]. With this difluoromethyl equivalent in hand, we initially began to investigate the reaction conditions for preparing (phenylsulfonyl)difluoromethylzinc reagent. TMSCl was used to in situ activate zinc powder before $PhSO_2CF_2Br$ was added into the mixture. The moderately polar solvent THF was not effective for the insertion of zinc metal into C – Br bond of $PhSO_2CF_2Br$ (**2**) even at an elevated temperature (50 °C) (Scheme 2**a**). The highly polar solvent DMF was found to be much better and the insertion proceeded smoothly at room temperature within 15 min to afford the corresponding difluoromethylzinc reagent "$XZnCF_2SO_2Ph$ (X = Br, CF_2SO_2Ph)" (**3**) as a mixture of mono- and bisdifluoromethylzinc in 73% ^{19}F NMR yield (Fig. 1). The mono/bis species were tentatively assigned via their characteristic ^{19}F NMR spectra, which exhibited the singlet at −105.6 ppm (25%) and −106.0 ppm (75%), respectively [7b,14]. However, these organozinc species gradually decomposed to difluoromethyl phenyl sulfone ($PhSO_2CF_2H$) at room temperature. A lower temperature could keep "$XZnCF_2SO_2Ph$" (**3**) relatively stable (Scheme 2**b**). Similarly, the reaction between zinc powder and $PhSO_2CF_2Br$ (**2**) conducted in NMP also rapidly produced "$XZnCF_2SO_2Ph$" (**3**), which also maintains stable at 0 °C (Scheme 2**c**).

Using the optimized reaction conditions for the preparation of (phenylsulfonyl)difluoromethylzinc reagent, we made a survey on its reaction with aldehydes, choosing 2-naphthaldehyde as a model substrate. The difluoromethylzinc species prepared in DMF exhibited a higher nucleophilicity than that in NMP. The nucleophilic difluoromethylation proceeded smoothly, providing the difluoromethyl carbinol in excellent yield within 5 h at ambient temperature (Table 1).

Encouraged by the above results, we next examined the substrate scope of the difluoromethylation reaction with (phenylsulfonyl)difluoromethylzinc reagent. As shown in Scheme 3, this method exhibited a good tolerance to both aromatic and aliphatic aldehydes. Aldehydes with electron-withdrawing groups could

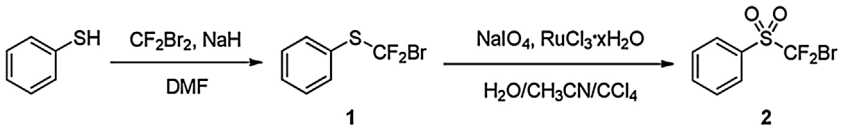


Scheme 2. Optimized reaction conditions for the preparation of (phenylsulfonyl) difluoromethylzinc reagent.

smoothly undergo the reaction to give the corresponding difluoromethyl carbinols, whereas the reaction of aldehydes with electron-donating groups required anhydrous LiCl to promote the nucleophilic addition process due to their relatively low reactivity. Besides aromatic aldehydes with various substituents, this reaction was also amenable to heteroaromatic aldehydes (Table 2).

Having accomplished the nucleophilic difluoromethylation of aldehydes with (phenylsulfonyl)difluoromethylzinc reagent, we continued our study with investigations of the preparation and reaction of other organometallic species for (phenylsulfonyl) difluoromethylation of aldehydes.

The generation of (phenylsulfonyl)difluoromethylcadmium reagent was found to be feasible via the insertion of cadmium metal into C—Br bond of $PhSO_2CF_2Br$ (**2**). This reaction performed in DMF could complete within 15 min and the organocadmium species was stable at the temperature of 0 °C (Scheme 3). The cadmium reagent "$XCdCF_2SO_2Ph$ (X = Br, CF_2SO_2Ph)" (**5**) was formed as a mixture of mono- and bisdifluoromethylcadmium in 90% ^{19}F NMR yield when the reaction was conducted at room temperature (Fig. 2). The mono/bis species were tentatively assigned via their characteristic ^{19}F NMR spectrum, which showed the expected singlet at −100.5 ppm (42%) and −100.9 ppm (58%),



Scheme 1. Preparation of bromodifluoromethyl phenyl sulfone.

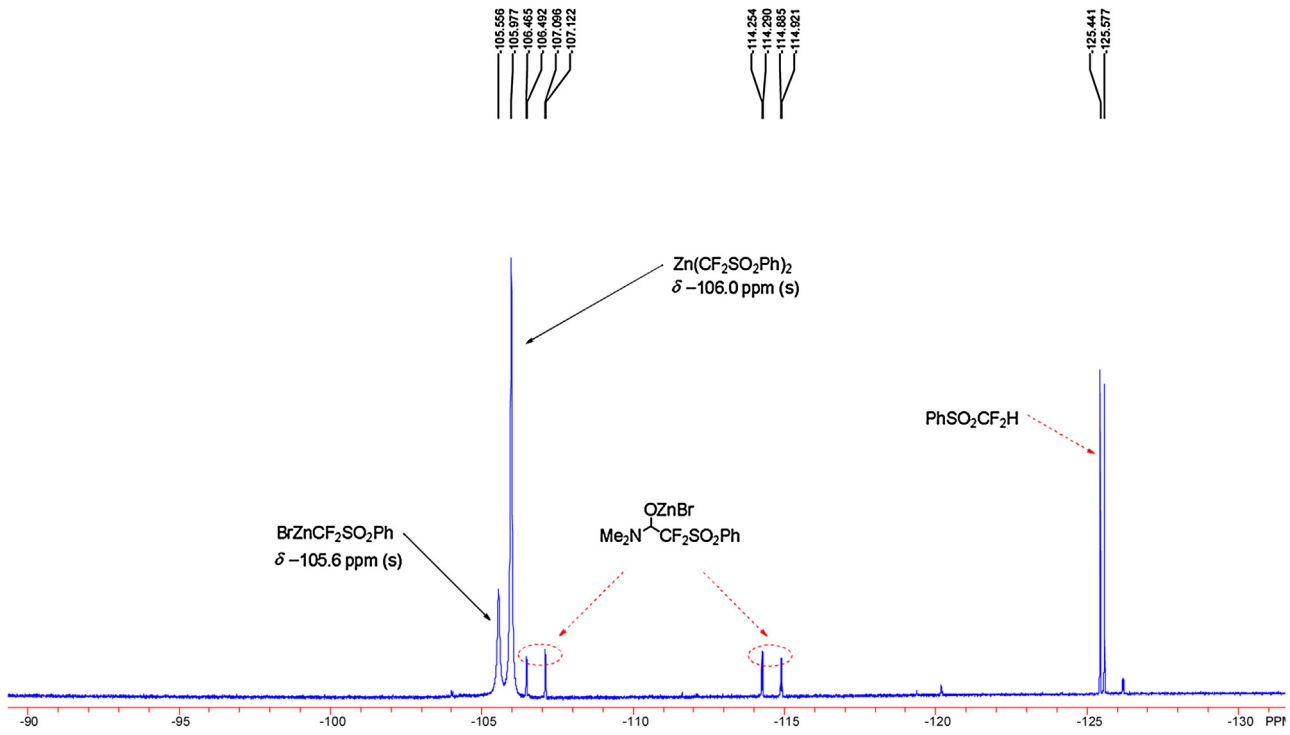
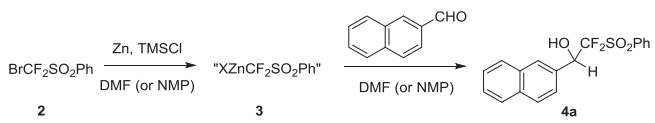


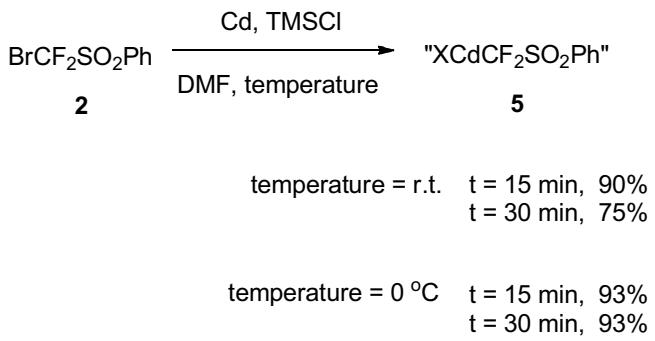
Fig. 1. The composition of (phenylsulfonyl)difluoromethylzinc reagent prepared in DMF at room temperature.

Table 1
Survey of nucleophilic difluoromethylation of 2-naphthaldehyde with (phenylsulfonyl)difluoromethylzinc reagent.



entry[a]	solvent	time (h)	temperature (°C)	yield (%)[b]
1	DMF	3 h	r.t.	70
2	DMF	5 h	r.t.	92
3	DMF	5 h	0	42
4	NMP	10 h	r.t.	49

[a] The amount of $PhSO_2CF_2Br$ and Zn is 2.0 and 3.0 equivalents relative to that of 2-naphthaldehyde, respectively.
[b] Determined by ^{19}F NMR analysis of the crude reaction mixture using $PhCF_3$ as an internal standard.



Scheme 3. Optimized reaction conditions for the preparation of (phenylsulfonyl) difluoromethylcadmium reagent.

respectively, for the CF_2 group with the distinctive $^{111}Cd/^{113}Cd$ satellites [7b,14–16].

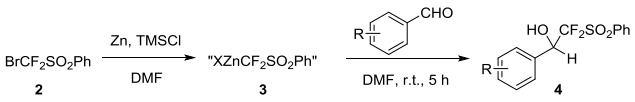
Then we investigated the optimal reaction conditions for difluoromethylation of the model substrate 2-naphthaldehyde with (phenylsulfonyl)difluoromethylcadmium reagent. The nucleophilic addition reaction could occur at room temperature in good yield as determined by ^{19}F NMR spectroscopy analysis. In contrast to the reaction of organozinc reagent, a certain amount of by-product was detected by GC–MS analysis. We proposed that it might result from the formylation of (phenylsulfonyl)difluoromethyl carbinol product by DMF. Further investigation demonstrated that anhydrous LiCl could not only guarantee the efficiency of the desired addition reaction, but also inhibit the formation of the formylated by-product. Compared with the nucleophilic addition to 2-naphthaldehyde with (phenylsulfonyl)difluoromethylzinc reagent, this reaction proceeded more easily even at the temperature of 0 °C, suggesting that (phenylsulfonyl)difluoromethylcadmium reagent had a better nucleophilicity toward aldehydes than the (phenylsulfonyl)difluoromethylzinc species (Table 3).

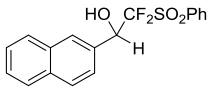
Similar to the reaction of (phenylsulfonyl)difluoromethylzinc species, this method also proved to be amenable to diverse substrates including both (hetero)aryl and aliphatic aldehydes (Table 4). However, the further formylation of the (phenylsulfonyl) difluoromethyl carbinols in the absence of LiCl was found to be general. Therefore, the addition of anhydrous LiCl is of great importance to inhibit the undesired formylation process.

3. Conclusions

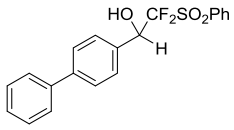
In summary, we have developed a new method for nucleophilic difluoromethylation of aldehydes by using (phenylsulfonyl) difluoromethylzinc and (phenylsulfonyl)difluoromethylcadmium reagents. The phenylsulfonyl group plays a crucial role in increasing the stability of the difluoromethyl anion. Meanwhile, the introduction of phenylsulfonyl group can also enhance the nucleophilicity of the difluoromethanide anion towards various

Table 2
Nucleophilic difluoromethylation of various aldehydes with (phenylsulfonyl)difluoromethylzinc reagent[a].

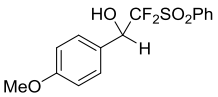




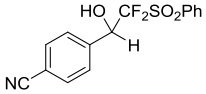
4a, 88%



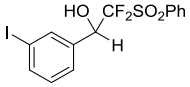
4b, 86%



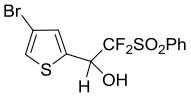
4c, 80%[b]



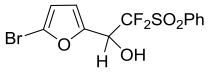
4d, 88%



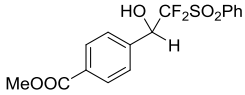
4e, 90%



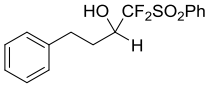
4f, 88%



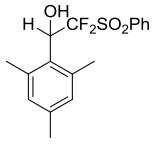
4g, 84%[c]



4h, 95%



4i, 78%



4j, 93%[c]

[a] The amount of $PhSO_2CF_2Br$ and Zn is 2.0 and 3.0 equivalents relative to that of the aldehyde, respectively. Isolated yield is reported.
[b] 2.0 equivalents of LiCl is added to the mixture.
[c] 1.0 equivalent of LiCl is added to the mixture.

aldehydes. By taking advantage of the dual roles of phenylsulfonyl group, an efficient nucleophilic addition of difluoromethyl organometallic reagent to aldehydes has been achieved under mild conditions. This method also promises to be useful for the development of other new difluoromethylation reactions.

4. Experimental

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. Chlorotrimethylsilane (TMSCl) was distilled over CaH_2. The solvent DMF and NMP were distilled over CaH_2. The solvent THF was distilled over Na. Infrared (IR) spectra were recorded on a *Shimadzu IR-440 or Bio-Rad FTS-185* spectrometer. ^1H, ^{13}C and ^{19}F NMR spectra were recorded on a *Bruker DPX-400 NMR*, Agilent *MR-400 NMR or MR-500 NMR* spectrometer. ^1H NMR chemical shifts were determined relative to internal $(CH_3)_4Si$ (TMS) at δ 0.0 or to the signal of a residual protonated solvent: $CDCl_3$ δ 7.26. ^{13}C NMR chemical shifts were determined relative to internal TMS at δ 0.0. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ at δ 0.0. MS (EI-MS) were obtained on a Agilent *5975C* gas chromatography and *HP5989A* mass spectrometer. HRMS (EI) were recorded on a *SATURN 2000* mass spectrometer. MS (ESI) were obtained on an *AGILENT1100* mass spectrometer. HRMS (ESI) were recorded on a *FTMS-7* mass spectrometer.

4.1. Preparation of (bromodifluoromethyl)(phenyl)sulfane (1)

Under an inert atmosphere, NaH (5.760 g, 240 mmol, 60% in w. t.) was added to a dried round-bottom flask. Anhydrous DMF (250 mL) was added and the mixture was stirred in an ice-water cold bath. Five minutes later, PhSH (20.5 mL, 200 mmol) was gradually injected into the flask. After the injection, the mixture continued to be stirred in the cold bath for another 10 min. The cold bath was removed and the temperature was elevated to room temperature for 20 min. The mixture was stirred in the ice-water cold bath once again. After 5 min, CF_2Br_2 (27.3 mL, 320 mmol) was added into the mixture in three parts, and then the cold bath was removed 10 min later. The mixture was allowed to warm to room temperature for another 4 h. Excess sodium hydride was quenched by dropwise addition of water (150 mL), and 2 M HCl was used to neutralize the reaction mixture. After extraction with ethyl acetate for three times, the organic phase was washed with brine, and then dried over anhydrous Na_2SO_4. After the solution was filtered and most of the solvent was evaporated under vacuum, the residue was distilled under vacuum (about 2 mmHg) and the fraction from 63 to 66 °C was collected. The collection was distilled again to give (bromodifluoromethyl)(phenyl)sulfane (**1**) as a colorless liquid (20.239 g, 42%).

(Bromodifluoromethyl)(phenyl)sulfane (**1**)[17a]

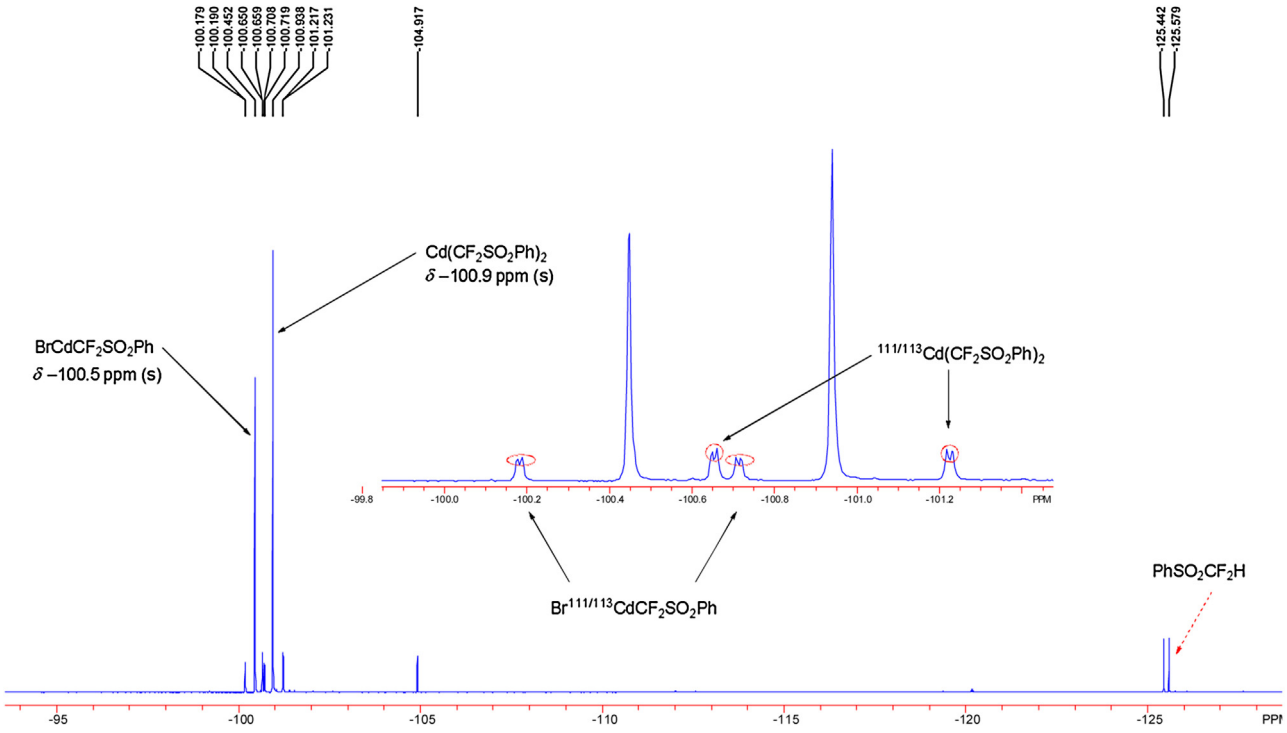
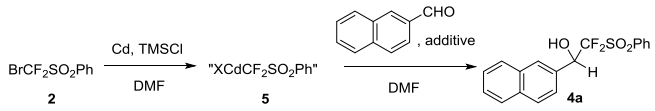


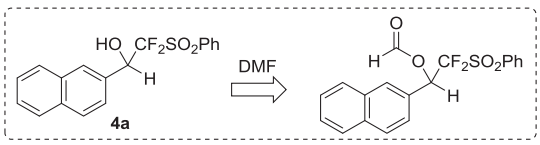
Fig. 2. The composition of (phenylsulfonyl)difluoromethylcadmium reagent prepared in DMF at room temperature.

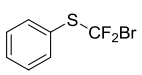
Table 3
Survey of nucleophilic difluoromethylation of 2-naphthaldehyde with (phenylsulfonyl)difluoromethylcadmium reagent.



entry[a]	additive	time (h)	temperature (°C)	yield (%)[b]
1	–	3 h	r.t.	75
2	–	5 h	r.t.	92
3	–	5 h	0	91
4	LiCl (1.0 eq)	5 h	r.t.	93
5	LiCl (2.0 eq)	5 h	r.t.	82

[a] The amount of $PhSO_2CF_2Br$ and Cd is 2.0 and 3.0 equivalents relative to that of 2-naphthaldehyde, respectively.
[b] Determined by ^{19}F NMR analysis of the crude reaction mixture using $PhCF_3$ as an internal standard. [c]The formylation product is detected by GC–MS analysis.



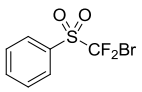


Colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −22.12 (s). MS (EI, m/z): 238 (M^+, 14.29), 159 (100.00), 77 (25.29), 109 (16.17), 240 (14.90), 238 (14.29), 160 (9.76), 65 (7.84), 161 (5.72).

4.2. Preparation of (bromodifluoromethyl)(phenyl)sulfone (**2**)

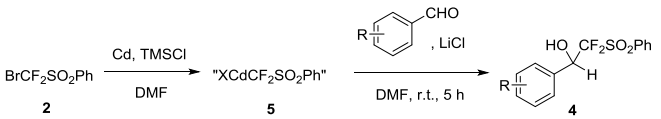
(Bromodifluoromethyl)(phenyl)sulfane (**1**) (20.239 g, 84.7 mmol) was added to a dried round-bottom flask. Acetonitrile (60 mL), water (150 mL) and CCl_4 (60 mL) were added and the mixture was stirred at room temperature. $NaIO_4$ (36.233 g, 169.4 mmol) and $RuCl_3{\cdot}xH_2O$ (15 mg) were added into the mixture. After 30 min, another portion of $NaIO_4$ (36.233 g, 169.4 mmol) was added. The mixture continued to be stirred until the completion of the reaction as monitored by thin layer chromatography (TLC). The crude mixture was filtered by the diatomaceous earth and the precipitate was washed with CH_2Cl_2. After most of the solvent was evaporated under vacuum, the water phase was extracted with ethyl acetate for three times. The organic layer was dried over anhydrous Na_2SO_4. After the solution was filtered and evaporated under vacuum, the residue was subjected to silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to give bromodifluoromethyl phenyl sulfone (**2**) as a white solid (17.932 g, 78%).

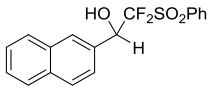
((Bromodifluoromethyl)sulfonyl)benzene (**2**)[17a]



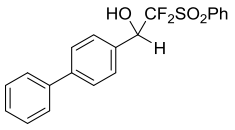
White solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.9 Hz, 2H), 7.83 (t, J = 7.5 Hz, 1H), 7.66 (t, J = 7.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −57.62 (s). MS (EI, m/z): 270 (M^+, 5.55), 141 (100.00), 77 (78.67), 51 (14.69), 125 (8.63), 142 (8.11), 50 (6.29), 272 (6.14), 143 (5.8).

Table 4
Nucleophilic difluoromethylation of various aldehydes with (phenylsulfonyl)difluoromethylcadmium reagent[a].

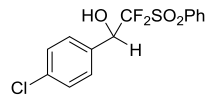




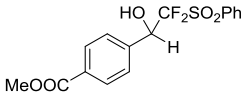
4a, 90%



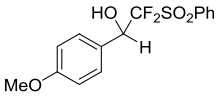
4b, 88%



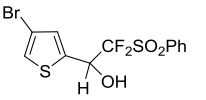
4k, 88%



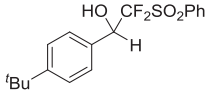
4 h, 84%



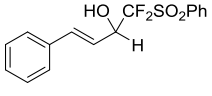
4c, 80%[b]



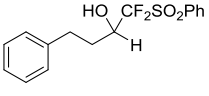
4f, 79%



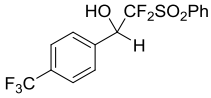
4l, 68%



4m, 80%



4i, 72%



4n, 86%

[a] The amount of $PhSO_2CF_2Br$,Cd and LiCl is 2.0, 3.0 and 1.0 equivalents relative to that of the aldehyde, respectively. Isolated yield is reported.
[b] 2.0 equivalents of LiCl are added to the mixture.

4.3. Nucleophilic difluoromethylation of aldehydes with organozinc and organocadmium reagents

4.3.1. Typical procedures for nucleophilic difluoromethylation of aldehydes with (phenylsulfonyl)difluoromethylzinc reagent (Method A)

In the glove box, zinc powder (206.0 mg, 3.15 mmol) was added into a Schlenk tube. Anhydrous DMF (10.5 mL) was added and the mixture was stirred at room temperature. Chlorotrimethylsilane (66.5 μL, 0.52 mmol) was then added into the mixture to activate zinc powder. Five minutes later, $PhSO_2CF_2Br$ (**2**) (2.1 mmol) was added into the suspension. The reaction proceeded smoothly in 15 min to give (phenylsulfonyl)difluoromethylzinc reagent ("$XZnCF_2SO_2Ph$", **3**). The mixture was kept at room temperature to precipitate the remaining zinc powder, and the solution was directly used for next step.

In the glove box, 2-naphthaldehyde (156.2 mg, 1.0 mmol) was added into another Schlenk tube. Anhydrous DMF (5 mL) was added and the mixture was stirred at room temperature. The DMF solution of "$XZnCF_2SO_2Ph$" (**3**) (10 mL, corresponding to the reaction of ca. 2.0 mmol of $PhSO_2CF_2Br$ and ca. 3.0 mmol of zinc powder) was added to the solution of 2-naphthaldehyde dropwise. The mixture was stirred at room temperature for 5 h, and aqueous HCl (2 M, 10 mL) was added to quench the reaction. After extraction with ethyl acetate for three times, the organic phase was washed with brine, and then dried over anhydrous Na_2SO_4. After the solution was filtered and evaporated under vacuum, the residue was subjected to silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to give the corresponding difluoromethylated carbinol **4a** as a white solid (307.5 mg, 88%).

4.3.2. Typical procedures for nucleophilic difluoromethylation of aldehydes with (phenylsulfonyl)difluoromethylcadmium reagent (Method B)

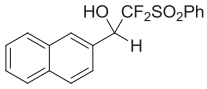
In the glove box, cadmium powder (354.1 mg, 3.15 mmol) was added into a Schlenk tube. Anhydrous DMF (10.5 mL) was added and the mixture was stirred at room temperature. Chlorotrimethylsilane (66.5 μL, 0.52 mmol) was then added into the mixture to activate cadmium powder. Two and a half minutes later, $PhSO_2CF_2Br$ (**2**) (569.3 mg, 2.1 mmol) was added into the suspension. The reaction proceeded smoothly in 15 min to give (phenylsulfonyl)difluoromethylcadmium reagent ("$XCdCF_2SO_2Ph$", **5**). The mixture was kept at room temperature to precipitate the remaining zinc powder, and the solution was directly used for next step.

In the glove box, 2-naphthaldehyde (156.2 mg, 1.0 mmol) and anhydrous LiCl (42.4 mg, 1.0 mmol) was added into another Schlenk tube. Anhydrous DMF (5 mL) was added and the mixture was stirred at room temperature. The DMF solution of "$XCdCF_2SO_2Ph$" (**5**) (10 mL, corresponding to the reaction of ca. 2.0 mmol of $PhSO_2CF_2Br$ and ca. 3.0 mmol of zinc powder) was added to the solution of 2-naphthaldehyde dropwise. The mixture was stirred at room temperature for 5 h, and aqueous HCl (2 M, 10 mL) was added to quench the reaction. After extraction with ethyl acetate for three times, the organic phase was washed with brine, and then dried over anhydrous Na_2SO_4. After the solution

was filtered and evaporated under vacuum, the residue was subjected to silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to give the corresponding difluoromethylated carbinol **4a** as a white solid (314.7 mg, 90%).

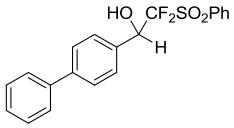
4.3.3. Characterization data for the isolated carbinol compounds ***4***

2,2-Difluoro-1-(naphthalen-2-yl)-2-(phenylsulfonyl)ethan-1-ol (**4a**) [17c]



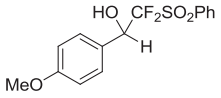
88% yield (Method A); 90% yield (Method B). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.4 Hz, 2H), 7.97 (s, 1H), 7.89–7.80 (m, 3H), 7.75 (t, J = 7.5 Hz, 1H), 7.64–7.55 (m, 3H), 7.54–7.47 (m, 2H), 5.76 (d, J = 20.8 Hz, 1H), 3.43 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.68 (d, J = 237.9 Hz), −118.98 (dd, J = 238.0, 21.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 133.9, 133.0, 132.8, 131.1, 130.7, 129.4, 128.4, 128.4, 128.2, 127.8, 126.9, 126.5, 125.0, 120.5 (dd, J = 298.8, 289.1 Hz), 71.5 (dd, J = 26.4, 19.8 Hz). MS (EI, m/z): 348 (M^+, 11.24), 157 (100.00), 129 (46.89), 128 (27.56), 127 (14.75), 159 (11.93), 77 (11.71), 158 (11.47).

1-([1,1′-Biphenyl]-4-yl)-2,2-difluoro-2-(phenylsulfonyl)ethan-1-ol (**4b**)



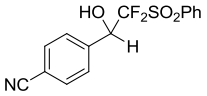
86% yield (Method A); 88% yield (Method B). White solid. m.p.: 141–143 °C. IR (KBr): 3559.7, 3092.9, 3062.2, 3030.3, 1599.8, 1581.9, 1567.1, 1519.4, 1487.5, 1448.3, 1408.1, 1387.4, 1331.6, 1312.9, 1253.3, 1200.5, 1186.6, 1154.0, 1109.2, 1089.4, 1081.3, 1023.8, 1001.3, 856.4, 833.5, 794.3, 753.2, 753.2, 720.6, 669.8, 684.5, 629.4, 617.2, 589.0, 555.8, 530.3, 431.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.4 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.66–7.52 (m, 8H), 7.44 (t, J = 7.6 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 5.63 (d, J = 20.5 Hz, 1H), 3.34 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.82 (d, J = 237.8 Hz), −119.17 (dd, J = 237.8, 21.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 140.5, 135.7, 132.8, 132.6, 130.8, 129.5, 128.9, 128.6, 127.7, 127.3, 127.3, 120.3 (dd, J = 298.7, 288.9 Hz), 71.2 (dd, J = 26.5, 19.9 Hz). MS (EI, m/z): 374 (M^+, 5.72), 183 (100.00), 155 (22), 184 (14.91), 77 (13.9), 152 (10.59), 153 (8.03), 154 (7.84), 165(7.45). HRMS (EI): m/z calcd. For $C_{20}H_{16}O_3F_2S$ (M^+) 374.0788, found 374.0797. Anal. Calcd for $C_{20}H_{16}F_2O_3S$: C, 64.16; H, 4.31. Found: C, 64.10; H, 4.54.

2,2-Difluoro-1-(4-methoxyphenyl)-2-(phenylsulfonyl)ethan-1-ol (**4c**) [17c]



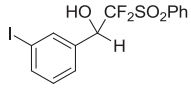
80% yield (Method A, 2.0 equiv of LiCl was used as an additive); 80% yield (Method B, 2.0 equiv of LiCl was used as an additive). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 2H), 7.76 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.9 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.52 (dt, J = 21.2, 3.0 Hz, 1H), 3.80 (s, 3H), 3.24 (d, J = 3.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.05 (d, J = 237.2 Hz), −119.30 (dd, J = 237.2, 21.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 135.5, 132.8, 130.6, 129.4, 129.3, 125.7, 120.3 (dd, J = 298.3, 288.4 Hz), 113.9, 70.9 (dd, J = 26.5, 19.8 Hz), 55.3. MS (EI, m/z): 328 (M^+, 3.43), 137 (100.00), 77 (11.96), 109 (10.49), 138 (8.29), 139 (6.14), 94 (5.2), 51 (3.3).

4-(2,2-Difluoro-1-hydroxy-2-(phenylsulfonyl)ethyl)benzonitrile (**4d**)



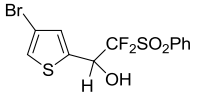
88% yield (Method A). White solid. m.p.: 132–134 °C. IR (KBr): 3396.7, 3097.4, 2237.0, 1607.4, 1583.8, 1505.0, 1448.7, 1404.7, 1348.8, 1337.0, 1314.9, 1298.0, 1245.6, 1200.5, 1177.2, 1158.3, 1104.6, 1091.6, 1008.5, 863.4, 829.3, 791.2, 755.2,6, 742.0, 700.2, 681.7, 617.9, 590.4, 564.3, 552.8, 481.4, 457.0, 428.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.5 Hz, 2H), 7.83–7.77 (m, 1H), 7.72–7.58 (m, 6H), 5.65 (dt, J = 20.5, 3.0 Hz, 1H), 3.63 (d, J = 3.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.31 (d, J = 238.5 Hz), −118.95 (dd, J = 238.4, 20.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 136.0, 132.4, 132.2, 130.8, 129.6, 129.0, 119.8 (dd, J = 299.1, 289.9 Hz), 118.4, 113.3, 70.6 (dd, J = 26.0, 20.1 Hz). MS (EI, m/z): 323 (M^+, 0.66), 132 (100.00), 77 (26.65), 134 (14.9), 104 (14.49), 78 (14.31), 143 (14.06), 51 (9.37), 133 (9.01). HRMS (EI): m/z calcd. For $C_{15}H_{11}NO_3F_2S$ (M^+) 323.0428, found 323.0421.

2,2-Difluoro-1-(3-iodophenyl)-2-(phenylsulfonyl)ethan-1-ol (**4e**)



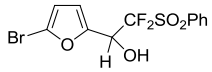
90% yield (Method A). White solid. m.p.: 117–118 °C. IR (KBr): 3535.3, 3067.8, 1810.5, 1683.8, 1591.0, 1581.5, 1567.0, 1540.6, 1469.8, 1448.1, 1424.3, 1394.2, 1333.1, 1311.3, 1179.0, 1155.2, 1107.8, 1087.4, 1074.3, 1060.7, 1025.1, 1007.7, 996.6, 914.5, 903.4, 845.9, 814.8, 767.0, 756.6, 717.9, 683.6, 658.2, 637.4, 616.6, 586.2, 541.6, 518.1, 476.3, 455.0, 440.2, 420.6. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.4 Hz, 2H), 7.84 (s, 1H), 7.83–7.73 (m, 1H), 7.75–7.67 (m, 1H), 7.68–7.59 (m, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 5.52 (d, J = 21.3 Hz, 1H), 3.42 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.79 (d, J = 238.3 Hz), −119.38 (dd, J = 238.0, 21.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 137.0, 135.9, 135.8, 132.5, 130.8, 130.2, 129.5, 127.5, 119.9 (dd, J = 299.2, 289.5 Hz), 94.2, 70.5 (dd, J = 26.4, 20.0 Hz). MS (EI, m/z): 424 (M^+, 8.93), 233 (100.00), 78 (35.41), 77 (27.05), 91 (26.03), 203 (19.38), 144 (18.16), 127 (11.78), 51 (10.92). HRMS (EI): m/z calcd. For $C_{14}H_{11}O_3F_2SI$ (M^+) 423.9442, found 423.9948.

1-(4-Bromothiophen-2-yl)-2,2-difluoro-2-(phenylsulfonyl)ethan-1-ol (**4f**)



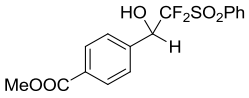
88% yield (Method A); 79% yield (Method B). White solid. m.p.: 122–124 °C. IR (KBr): 3853.2, 3648.8, 3447.0, 3117.9, 3088.4, 3064.5, 2905.4, 1583.5, 1525.6, 1478.7, 1450.8, 1427.2, 1389.4, 1355.3, 1324.5, 1314.1, 1288.6, 1203.4, 1182.4, 1153.2, 1122.0, 1081.6, 1024.8, 988.7, 872.2, 856.5, 825.4, 798.5, 771.9, 746.9, 728.3, 683.4, 621.8, 596.6, 582.0, 556.9, 518.0, 453.4, 427.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.8 Hz, 2H), 7.84–7.75 (m, 1H), 7.67–7.61 (m, 2H), 7.28 (d, J = 1.5 Hz, 1H), 7.09 (s, 1H), 5.79 (d, J = 19.9 Hz, 1H), 3.51 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.53 (dd, J = 237.0, 2.5 Hz), −119.18 (dd, J = 237.0, 20.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.3, 135.9, 132.5, 130.8, 130.3, 129.6, 124.7, 119.3 (dd, J = 299.3, 289.7 Hz), 109.7, 67.8 (dd, J = 27.3, 20.9 Hz). MS (EI, m/z): 382 (M^+, 4.16), 191 (100.00), 193 (97.5), 84 (31.41), 77 (30.37), 51 (14.34), 78 (10.79), 242 (10.76), 240 (10.09). HRMS (EI): m/z calcd. For $C_{12}H_9O_3F_2S_2Br$ (M^+) 381.9145, found 381.9143.

1-(5-Bromofuran-2-yl)-2,2-difluoro-2-(phenylsulfonyl)ethan-1-ol (**4g**)



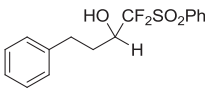
84% yield (Method A, 1.0 equiv of LiCl was used as an additive). White solid. m.p.: 96–97 °C. IR (KBr): 3466.7, 3137.6, 3118.2, 3058.8, 1583.4, 1497.9, 1478.0, 1448.7, 1408.3, 1364.2, 1336.8, 1312.4, 1275.5, 1227.7, 1198.3, 1178.5, 1157.9, 1108.8, 1087.2, 1074.9, 1017.5, 1000.0, 943.8, 924.8, 799.9, 768.3, 751.8, 710.3, 682.9, 605.3, 582.0, 532.3, 494.6, 438.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.4 Hz, 2H), 7.78 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 7.8 Hz, 2H), 6.53 (d, J = 3.4 Hz, 1H), 6.32 (d, J = 3.4 Hz, 1H), 5.53 (dt, J = 18.6, 4.7 Hz, 1H), 3.23 (d, J = 4.9 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −105.91 (dd, J = 237.8, 4.3 Hz), −116.43 (dd, J = 237.8, 18.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9, 135.8, 132.7, 130.8, 129.5, 123.7, 119.6 (dd, J = 298.2, 291.3 Hz), 113.9, 112.7, 66.0 (dd, J = 26.7, 21.4 Hz). MS (EI, m/z): 366 (M^+, 4.41), 175 (100.00), 177 (96.71), 77 (18.64), 51 (10.3), 224 (10.12), 226 (9.89), 178 (5.96), 101 (5.79). HRMS (EI): m/z calcd. For $C_{12}H_9O_4F_2SBr$ (M^+) 365.9373, found 365.9385.

Methyl 4-(2,2-difluoro-1-hydroxy-2-(phenylsulfonyl)ethyl)benzoate (**4h**)



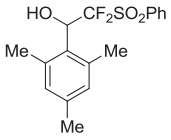
95% yield (Method A); 84% yield (Method B). White solid. m.p.: 117–119 °C. IR (KBr): 3503.9, 3066.1, 2955.8, 1731.3, 1717.9, 1610.2, 1477.6, 1449.3, 1437.4, 1416.4, 1335.8, 1313.1, 1281.1, 1192.9, 1178.3, 1157.9, 1108.9, 1087.6, 1017.9, 1003.6, 962.5, 872.8, 842.4, 812.1, 763.3, 750.2, 718.0, 698.1, 684.3, 623.2, 587.2, 555.8, 535.3, 491.3, 440.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 2H), 8.00 (d, J = 7.3 Hz, 2H), 7.78 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 7.9 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 5.65 (dt, J = 21.4, 2.9 Hz, 1H), 3.91 (s, 3H), 3.54 (d, J = 3.9 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.01 (d, J = 238.6 Hz), −119.10 (dd, J = 238.1, 21.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 138.6, 135.8, 132.7, 131.2, 130.8, 129.7, 129.5, 128.2, 120.1 (dd, J = 299.2, 289.5 Hz), 71.0 (dd, J = 26.1, 20.1 Hz), 52.4. MS (EI, m/z): 356 (M^+, 0.34), 165 (100.00), 77 (17.22), 166 (10.57), 59 (9.57), 78 (7.98), 105 (6.54), 214 (5.84), 167 (5.38). HRMS (EI): m/z calcd. For $C_{16}H_{14}O_5F_2S$ (M^+) 356.0530, found 356.0536. Anal. Calcd for $C_{16}H_{14}F_2O_5S$: C, 53.93; H, 3.96. Found: C, 53.75; H, 3.96.

1,1-Difluoro-4-phenyl-1-(phenylsulfonyl)butan-2-ol (**4i**) [17b]



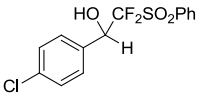
78% yield (Method A); 72% yield (Method B). Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.7 Hz, 2H), 7.80–7.75 (m, 1H), 7.66–7.60 (m, 2H), 7.34–7.28 (m, 2H), 7.25–7.19 (m, 3H), 4.50–4.37 (m, 1H), 3.03–2.91 (m, 1H), 2.83–2.75 (m, 1H), 2.73 (d, J = 5.1 Hz, 1H), 2.19–1.94 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.26 (dd, J = 236.7, 5.6 Hz), −116.81 (dd, J = 236.5, 18.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 135.6, 132.9, 130.7, 129.5, 128.7, 128.6, 126.3, 121.4 (dd, J = 294.8, 291.8 Hz), 68.8 (dd, J = 24.5, 21.1 Hz), 31.1, 31.0. MS (EI, m/z): 326 (M^+, 1.3), 91 (100.00), 144 (41.77), 104 (41.16), 143 (39.25), 77 (18.79), 147 (18.03), 105 (14.65).

2,2-Difluoro-1-mesityl-2-(phenylsulfonyl)ethan-1-ol (**4j**)



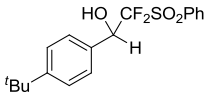
93% yield (Method A, 1.0 equiv of LiCl was used as an additive). White solid. m.p.: 87–88 °C. IR (KBr): 3749.4, 3647.6, 3522.4, 3095.6, 2970.8, 2922.5, 2334.1, 2245.5, 1611.7, 1582.4, 1557.7, 1540.2, 1506.5, 1477.9, 1409.5, 1384.9, 1325.8, 1311.0, 1195.3, 1179.2, 1157.5, 1140.3, 1119.3, 1080.6, 1028.7, 987.4, 959.7, 929.7, 907.2, 849.5, 814.0, 776.7, 756.4, 731.9, 707.8, 682.9, 650.5, 625.7, 596.0, 569.3, 552.2, 540.0, 520.7, 493.9, 444.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.7 Hz, 2H), 7.82–7.73 (m, 1H), 7.63 (t, J = 7.9 Hz, 2H), 6.85 (s, 2H), 6.14 (dd, J = 26.8, 4.5 Hz, 1H), 3.09 (d, J = 4.4 Hz, 1H), 2.50 (s, br., 3H), 2.33 (s, br., 3H), 2.25 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −102.65 (d, J = 236.4 Hz), −114.42 (dd, J = 236.5, 26.7 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3, 138.7, 137.9, 135.6, 132.7, 131.7, 130.8, 129.5, 129.2, 127.0, 121.8 (dd, J = 302.8, 288.0 Hz), 68.2 (dd, J = 27.5, 19.7 Hz), 20.9. MS (EI, m/z): 340 (M^+, 3.83), 149 (100.00), 84 (41.09), 86 (28.14), 121 (13.16), 150 (12.67), 77 (9.02), 105 (8.16), 147 (6.83). HRMS (EI): m/z calcd. For $C_{17}H_{18}O_3F_2S$ (M^+) 340.0945, found 340.0941.

1-(4-Chlorophenyl)-2,2-difluoro-2-(phenylsulfonyl)ethan-1-ol (**4k**) [17b]



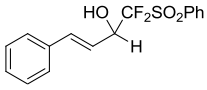
88% yield (Method B). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.5 Hz, 2H), 7.82–7.75 (m, 1H), 7.63 (t, J = 7.9 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 5.56 (dt, J = 21.0, 3.0 Hz, 1H), 3.41 (d, J = 3.7 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −104.17 (dd, J = 238.0, 2.5 Hz), −119.38 (dd, J = 237.9, 20.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 135.6, 132.6, 132.2, 130.7, 129.5, 129.5, 128.8, 120.0 (dd, J = 298.7, 289.2 Hz), 70.7 (dd, J = 26.2, 20.0 Hz). MS (EI, m/z): 332 (M^+, 2.53), 141 (100.00), 143 (45.53), 77 (34.7), 78 (11.21), 142 (8.98), 51 (8.8), 113 (7.6), 40 (6.23).

1-(4-(tert-Butyl)phenyl)-2,2-difluoro-2-(phenylsulfonyl)ethan-1-ol (**4l**) [17b]



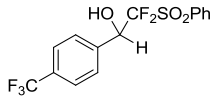
68% yield (Method B). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.8 Hz, 2H), 7.76 (t, J = 7.7 Hz, 1H), 7.61 (t, J = 7.8 Hz, 2H), 7.40 (s, 4H), 5.55 (dt, J = 21.5, 3.2 Hz, 1H), 3.20 (d, J = 3.9 Hz, 1H), 1.30 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.65 (dd, J = 237.8, 2.5 Hz), −119.31 (dd, J = 237.7, 21.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.6, 135.5, 132.9, 130.6, 129.3, 127.8, 125.4, 120.3 (dd, J = 298.6, 288.6 Hz), 71.1 (dd, J = 26.7, 19.6 Hz), 34.7, 31.2. MS (EI, m/z): 354 (M^+, 1.83), 163 (100.00), 164 (12.26), 57 (11.82), 197 (8.85), 77 (8.75), 91 (5.25), 133 (4.19), 148 (3.67).

(E)-1,1-Difluoro-4-phenyl-1-(phenylsulfonyl)but-3-en-2-ol (**4m**) [17b]



80% yield (Method B). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.5 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 7.9 Hz, 2H), 7.44–7.39 (m, 2H), 7.39–7.25 (m, 3H), 6.89 (d, J = 15.9 Hz, 1H), 6.25 (dd, J = 15.9, 6.6 Hz, 1H), 5.20–5.09 (m, 1H), 3.00 (d, J = 5.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −106.58 (dd, J = 237.3, 5.1 Hz), −116.22 (dd, J = 237.2, 17.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 135.7, 133.1, 130.8, 129.5, 128.8, 128.7, 127.1, 120.6 (dd, J = 296.5, 292.3 Hz), 120.6, 71.0 (dd, J = 25.3, 21.4 Hz). MS (EI, m/z): 324 (M^+, 3.56), 133 (100.00), 115 (17.01), 134 (14.37), 77 (12.84), 182 (8.63), 55 (7.33), 103 (4.76), 78 (4.36).

2,2-Difluoro-2-(phenylsulfonyl)-1-(4-(trifluoromethyl)phenyl) ethan-1-ol (**4n**)



86% yield (Method B). White solid. m.p.: 78–80 °C. IR (KBr): 3529.8, 3064.3, 2949.6, 1940.7, 1823.0, 1708.4, 1622.1, 1583.1, 1478.1, 1449.3, 1419.8, 1399.4, 1332.7, 1165.3, 1129.5, 1114.0, 1089.6, 1068.7, 1020.1, 1008.8, 861.2, 829.2, 796.1, 763.4, 728.6, 710.3, 684.0, 658.3, 635.9, 623.8, 603.7, 584.5, 535.0, 473.9, 442.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.8 Hz, 2H), 7.79 (t, J = 7.5 Hz, 1H), 7.69–7.56 (m, 6H), 5.66 (d, J = 20.9 Hz, 1H), 3.51 (d, J = 3.1 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.85, −104.13 (d, J = 238.4 Hz), −119.23 (dd, J = 238.4, 20.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 135.9, 132.5, 131.7 (q, J = 32.5 Hz), 130.8, 129.6, 128.6, 125.5 (q, J = 3.8 Hz), 124.0 (d, J = 272.3 Hz), 120.0 (dd, J = 299.1, 289.7 Hz), 70.8 (dd, J = 26.1, 20.1 Hz). MS (EI, m/z): 366 (M^+, 0.37), 175 (100.00), 127 (23.49), 77 (18.87), 177 (16.19), 78 (13.51), 143 (12.55), 176 (9.26), 51 (6.41). HRMS (EI): m/z calcd. For $C_{15}H_{11}O_3F_5$(M^+) 366.0349, found 366.0363.

Acknowledgements

Support of our work by the National Basic Research Program of China (2015CB931900), the National Natural Science Foundation of China (21632009, 21421002 and 21372246), the Chinese Academy of Sciences, Shanghai Academic Research Leader Program (15XD1504400), and the Youth Innovation Promotion Association CAS (2014231) is gratefully acknowledged.

References

[1] (a) P. Kirsch, Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications, 2nd, Wiley-VCH, Weinheim, 2013;
(b) W.B. Farnham, Chem. Rev. 96 (1996) 1633;
(c) G.K.S. Prakash, A.K. Yudin, Chem. Rev. 97 (1997) 757;
(d) G.K.S. Prakash, M. Mandal, J. Fluor. Chem. 112 (2001) 123;
(e) R.P. Singh, J.M. Shreeve, Tetrahedron 56 (2000) 7613;
(f) J.-A. Ma, D. Cahard, J. Fluor. Chem. 128 (2007) 975;
(g) M. Medebielle, W.R. Dolbier Jr., J. Fluor. Chem. 129 (2008) 930;
(h) A. Studer, Angew. Chem. Int. Ed. 51 (2012) 8950;
(i) T. Umemoto, Chem. Rev. 96 (1996) 1757;
(j) C. Ni, J. Hu, Chem. Soc. Rev. 45 (2016) 5441.
[2] (a) G.M. Blackburn, D.E. Kent, F. Kolkmann, J. Chem. Soc. Chem. Commun. (1981) 1188;
(b) G.M. Blackburn, D.E. Kent, F. Kolkmann, J. Chem. Soc. Perkin Trans. 1 (1984) 1119;
(c) W.B. Motherwell, M.J. Tozer, B.C. Ross, J. Chem. Soc. Chem. Commun. (1989) 1437;
(d) J. Rong, C. Ni, J. Hu, Asian J. Org. Chem. (2017), doi:http://dx.doi.org/10.1002/ajoc.201600509.
[3] (a) J.A. Erickson, J.I. McLoughlin, J. Org. Chem. 60 (1995) 1626;
(b) R. Sasson, A. Hagooly, S. Rozen, Org. Lett. 5 (2003) 769;
(c) Y. Li, J. Hu, Angew. Chem. Int. Ed. 44 (2005) 5882;
(d) G.K.S. Prakash, C. Weber, S. Chacko, G.A. Olah, Org. Lett. 9 (2007) 1863.
[4] (a) J. Hu, W. Zhang, F. Wang, Chem. Commun. (2009) 7465;
(b) M.-C. Belhomme, T. Besset, T. Poisson, X. Pannecoucke, Chem. Eur. J. 21 (2015) 12836;
(c) C. Ni, L. Zhu, J. Hu, Acta Chim. Sin. 73 (2015) 90.
[5] (a) G.K.S. Prakash, J. Hu, Acc. Chem. Res. 40 (2007) 921;
(b) J. Hu, J. Fluor. Chem. 130 (2009) 1130;
(c) C. Ni, J. Hu, Synlett (2011) 770;
(d) W. Zhang, C. Ni, J. Hu, Top. Cur. Chem. 308 (2012) 25;
(e) C. Ni, M. Hu, J. Hu, Chem. Rev. 115 (2015) 765.
[6] (a) Y. Zhao, W. Huang, J. Zheng, J. Hu, Org. Lett. 13 (2011) 5342;
(b) G.-F. Du, Y. Wang, C.-Z. Gu, B. Dai, L. He, RSC Adv. 5 (2015) 35421;
(c) O.M. Michurin, D.S. Radchenko, I.V. Komarov, Tetrahedron 72 (2016) 1351;
(d) D. Chen, C. Ni, Y. Zhao, X. Cai, X. Li, P. Xiao, J. Hu, Angew. Chem. Int. Ed. 55 (2016) 12632;
(e) J.-B. Han, H.-L. Qin, S.-H. Ye, L. Zhu, C.-P. Zhang, J. Org. Chem. 81 (2016) 2506.
[7] (a) R. Eujen, B. Hoge, D.J. Brauer, J. Organomet. Chem. 519 (1996) 7;
(b) D.J. Burton, G.A. Hartgraves, J. Fluor. Chem. 128 (2007) 119;
(c) Other work on fluorinated organozincs derived from difluorocarbene insertion is as below: V. V. Levin, A.A. Zemtsov, M.I. Struchkova and A.D. Dilman, Org. Lett. 15, 2013, 917.
[8] (a) G.K.S. Prakash, S.K. Ganesh, J.P. Jones, A. Kulkarni, K. Masood, J.K. Swabeck, G.A. Olah, Angew. Chem. Int. Ed. 51 (2012) 12090;
(b) P.S. Fier, J.F. Hartwig, J. Am. Chem. Soc. 134 (2012) 5524;
(c) X.-L. Jiang, Z.-H. Chen, X.-H. Xu, F.-L. Qing, Org. Chem. Front. 1 (2014) 774;
(d) C. Matheis, K. Jouvin, L.J. Goossen, Org. Lett. 16 (2014) 5984;
(e) B. Bayarmagnai, C. Matheis, K. Jouvin, L.J. Goossen, Angew. Chem. Int. Ed. 54 (2015) 5753;
(f) K. Jouvin, C. Matheis, L.J. Goossen, Chem. Eur. J. 21 (2015) 14324.
[9] Y. Gu, X. Leng, Q. Shen, Nat. Commun. 5 (2014) 5405.
[10] K. Aikawa, W. Toya, Y. Nakamura, K. Mikami, Org. Lett. 17 (2015) 4996.
[11] (a) H. Serizawa, K. Ishii, K. Aikawa, K. Mikami, Org. Lett. 18 (2016) 3686;
(b) K. Aikawa, H. Serizawa, K. Ishii, K. Mikami, Org. Lett. 18 (2016) 3690;
(c) L. Xu, D.A. Vicic, J. Am. Chem. Soc. 138 (2016) 2536.
[12] For a previous report on nucleophilic difluoromethylation of aldehydes using bromodifluoromethyl phenyl sulfone as the fluoroalkylation reagent and tetrakis(dimethylamino)ethylene (TDAE) as the electron-transfer agent, see: G. K. S. Prakash, Y. Wang, J. Hu, and G.A. Olah, J. Fluor. Chem. 126, 2005, 1361.
[13] J. Zhu, C. Ni, B. Gao, J. Hu, J. Fluor. Chem. 171 (2015) 139.
[14] D.J. Burton, D.M. Wiemers, J. Am. Chem. Soc. 107 (1985) 5015.
[15] G.A. Hartgraves, D.J. Burton, J. Fluor. Chem. 39 (1988) 425.
[16] D.J. Burton, R. Takei, S. Shin-Ya, J. Fluor. Chem. 18 (1981) 197.
[17] (a) G.K.S. Prakash, J. Hu, G.A. Olah, J. Org. Chem. 68 (2003) 4457;
(b) G.K.S. Prakash, Y. Wang, J. Hu, G.A. Olah, J. Fluor. Chem. 126 (2005) 1361;
(c) C. Ni, F. Wang, J. Hu, Beilstein J. Org. Chem. 4 (2008) 21.