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Synthesis of 2,2-diaryl-1,1-difluoroethenes via Pd-catalyzed dehydrosulfonylative cross-coupling of α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates with arylboronic acids

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Dedicated to the memory of Sir Derek Barton for the 100th anniversary (1918–2018) of his birth.

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ABSTRACT

By using $PhSO_2CF_2H$ as the difluoromethylidene equivalent, a novel method for connecting aromatic aldehydes and arylboronic acids via consecutive reactions was developed to obtain structurally diverse 2,2-diaryl-1,1-difluoroethenes. The key step is the palladium-catalyzed dehydrosulfonylative cross-coupling of tosylates that are prepared from $PhSO_2CF_2H$, aromatic aldehydes and tosyl chloride. Mechanistic investigations showed that the reaction proceeds mainly through base-mediated dehydrosulfonylation followed by palladium-catalyzed $C(sp^2)$-$C(sp^2)$ cross-coupling reaction.

1. Introduction

1,1-Difluoroalkenes have attracted much attention in organic synthesis[1,2] as well as in pharmaceutical and agrochemical research[3,4] due to their unique chemical and biological properties.[5] On one hand, 1,1-difluoroalkenes have been used as versatile building blocks to deliver structurally diverse functionalized molecules, most of which are otherwise difficult to efficiently prepare. On the other hand, the difluoromethylidene group ($=CF_2$) is regarded as the bioisostere of carbonyl group and has been applied in the improvement of enzyme inhibitors.[6] In these contexts, many methods, including the difluoromethylidenation reactions, have been developed to synthesize 1,1-difluoroalkenes.[1] However, the methods that can deliver 1,1-diaryl-2,2-difluoroethenes are rare and usually suffer from limitations. The Wittig-type *gem*-difluoroolefination of diaryl ketones[7] and Barton–Kellogg-type *gem*-difluoroolefination diaryl thioketones[8] are of low efficiency and were demonstrated with only very few examples. The Julia-Kocienski-type *gem*-difluoroolefination of diaryl ketones[9] and *gem*-difluoroolefination of diaryl diazo compounds[10] are synthetically useful, but the availability of the diaryl compounds can impose restriction on their wide application. The metal-catalyzed cross-coupling reactions of 2,2-difluoro-1-arylvinylstannane reagents,[11] 2,2-difluoro-1-arylvinylzinc reagents,[12] α-halo-β,β-difluorostyrenes[12] and 2,2-difluoro-1-arylvinyl tosylates,[13] also involve the use of not readily-available coupling partners. Furthermore, the recently disclosed Rh(I)-catalyzed defluorinative cross-coupling of trifluoromethylketone *N*-tosylhydrazones and arylboronates affords 1,1-diaryl-2,2-difluoroethenes in moderate yields.[14]

In the past decade, a series of fluorinated sulfones have been developed as general fluoroalkylation reagents and widely used for the incorporation of various fluoroalkyl groups into organic molecules by us and others.[8,15,16] Difluoromethyl sulfones are among the most versatile fluorinated sulfones and are capable of incorporating difluoromethyl ($-CF_2H$), difluoromethylene ($-CF_2-$), difluoromethylidene group ($=CF_2$), as well as difluoro(sulfinato)methyl ($-CF_2SO_2M$) groups.[15b,e] The reaction of two molecules with

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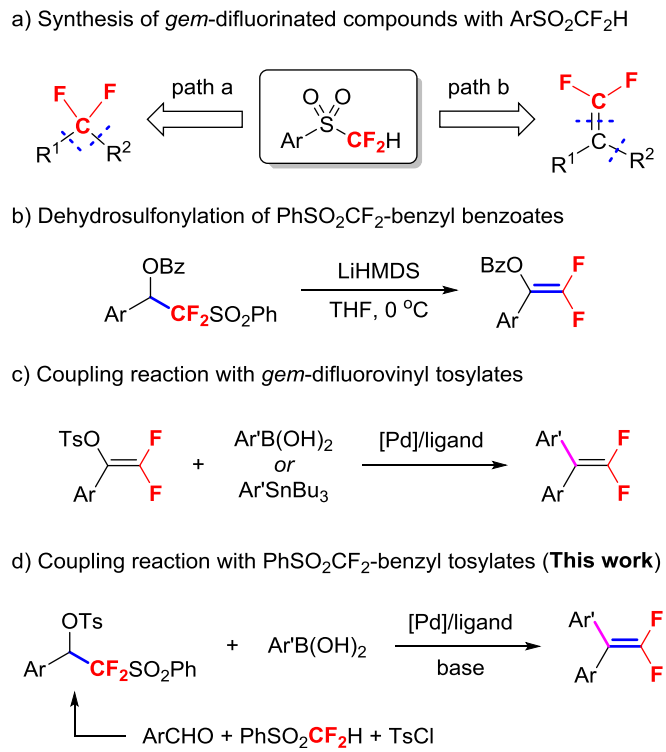
difluoromethyl sulfones via consecutive reactions is a unique synthetic method, which allows easy access to many unsymmetrical *gem*-difluorinated compounds (Scheme 1a). This strategy has been used for the synthesis of difluoromethylene-containing compounds (Scheme 1a, path a)[15]; however, the synthesis of difluoromethylidiene-containing compounds, namely, 1,1-difluoroalkenes, by using similar strategy is still underdeveloped (Scheme 1a, path b).

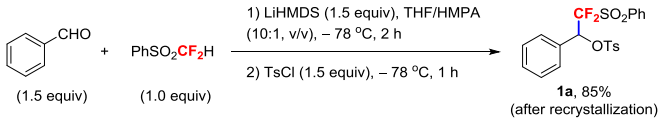
Inspired by our previous work on the preparation of 2,2-difluoro-1-arylvinyl benzoates from α-[difluoro(phenylsulfonyl)methyl]benzyl benzoates (Scheme 1b)[17] and Jeong's work on the Suzuki- and Stille-type cross-coupling reactions of 2,2-difluoro-1-arylvinyl tosylates (Scheme 1c),[13] we envisioned that α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates could be used as alternative precursors of 2,2-difluoro-1-arylvinyl tosylates to prepare 2,2-diaryl-1,1-difluoroethenes. Herein, we report a palladium-catalyzed dehydrosulfonylative cross-coupling reaction of readily available α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates with arylboronic acids (Scheme 1d). Since the base-mediated dehydrosulfonylative elimination reaction and the subsequent palladium-catalyzed cross-coupling can proceed smoothly in one pot without the isolation of the 2,2-difluoro-1-arylvinyl tosylate intermediates, this synthetic method provides a very convenient approach to obtain structurally diverse 2,2-diaryl-1,1-difluoroethenes.

2. Results and discussion

Our investigation began with the preparation of α-[difluoro(phenylsulfonyl)methyl]benzyl tosylate (**1a**) by an aldol-type reaction of commercially available $PhSO_2CF_2H$ and benzaldehyde followed by treatment with tosyl chloride (Scheme 2). As previously described,[18] the addition of $PhSO_2CF_2H$ to benzaldehyde could readily take place in THF in the presence of lithium



Scheme 1. The transformation of difluoromethyl sulfones and the synthesis of 1,1-difluoroalkenes.



Scheme 2. Development of one-pot procedures for the synthesis of α-[difluoro(phenylsulfonyl)methyl]benzyl tosylate **1a**.

hexamethyldisilazide (LiHMDS) as the base and hexamethylphosphoric triamide (HMPA) as an additive at −78 °C. We found that the further addition of tosyl chloride to the reaction mixture at the same temperature could afford the desired benzyl tosylate **1a** in 85% yield. The same procedures are also applicable for the preparation of other tosylates (**1b**-**1i**) from the corresponding aromatic aldehydes in good to excellent isolated yields (Table 1). The electronic nature and steric hindrance of the aryl substituent possess little influence on the reaction. Note that all the so-obtained tosylates are crystalline solids and thus can be easily isolated and purified by recrystallization. Compared with our previous observation that the reaction of α-[fluorobis(phenylsulfonyl)methyl]benzyl alcoholates with tosyl chloride failed to give the desired tosylates,[19] the ready tosylation of α-[difluoro(phenylsulfonyl)methyl]benzyl alcoholates by tosyl chloride should be attributed to their lower steric hindrance and higher thermal stability.

With α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates **1** in hand, we investigated their dehydrosulfonylative cross-coupling reaction with arylboronic acids under palladium catalysis to prepare 2,2-diaryl-1,1-difluoroethenes. The reaction between tosylate **1a** and phenylboronic acid (**2a**) was chosen as a model reaction to test and then optimize the coupling reaction (Table 2). Typically, the reaction was carried out with a loading of 4 mol% $Pd_2(dba)_3$ at 80 °C for 8 h, a base was added to promote the formation of the intermediate, 2,2-difluoro-1-phenylvinyl tosylate, and the molar ratio of **1a**, **2a**, and the base was 1.5/1.0/3.0. When Cs_2CO_3 was used as the base and $Pd_2(dba)_3$ was used as the catalyst, the reaction conducted in 1,2-dimethoxyethane (DME) afforded the desired coupling product **3a** in 68% yield (by ^{19}F NMR). Screening of solvents showed that other solvents are inferior to DME (Table 1, entries 2–5). The base effect is also significant: K_2CO_3 and *t*-BuOLi were found to be less effective due to their weaker basicity than Cs_2CO_3, thus retarding the dehydrosulfonylative elimination of **1a** (Table 1, entries 6 and 7). The reaction temperature also showed some influence on the reaction: the yield of **3a** was decreased to some extent when running the reaction at 100 °C or 60 °C (Table 1, entries 8 and 9). Importantly, it was found that the use of a phosphine ligand could further improve the reaction, with P(*o*-tol)$_3$ giving **3a** in the highest yield (75%) (Table 1, entries 10 and 11). Eventually, screening of the reactant ratio and catalyst loading established the optimal reaction conditions as follows: 1.2 equiv of **1a**, 1.0 equiv of **2a**, 3.0 equiv of Cs_2CO_3, 4 mol% $Pd_2(dba)_3$ catalyst, 8 mol% P(*o*-tol)$_3$ ligand, DME solvent, 80 °C reaction temperature, and 8 h reaction time under N_2 atmosphere (Table 1, entry 12).

With the optimized conditions in hand, we first examined the substrate scope by reacting tosylate **1a** with different arylboronic acids **2** (Table 3). For ease of isolation of the desired product, all reactions were performed on 0.5-mmol scale. Generally, both electron-rich and electron-deficient arylboronic acids reacted smoothly to give *gem*-difluoroolefins **3a**-**3i** in moderate to good isolated yields (50–76%). The oxidative homo-coupling was the major side reaction of arylboronic acids. Besides, it was found that vigorous stirring was needed to promote the formation of products **3** due to the low solubility of Cs_2CO_3 in DME.

We then examined the reactions of various tosylates **1b-1i** with phenylboronic acid (**2a**). As shown in Table 4, the reaction is

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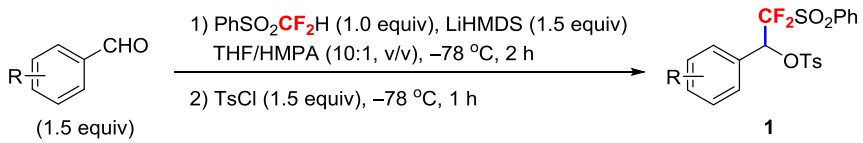
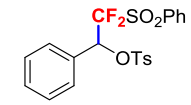
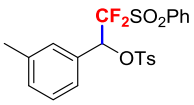
Table 1
Preparation of α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates **1**[a].

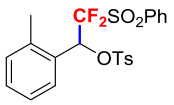




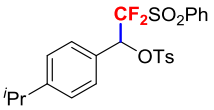
1a, 85%



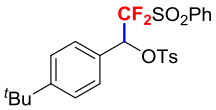
1b, 82%



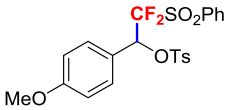
1c, 91%



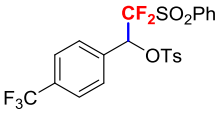
1d, 86%



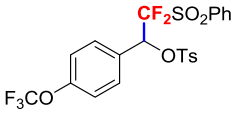
1e, 83%



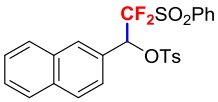
1f, 87%



1g, 74%



1h, 83%

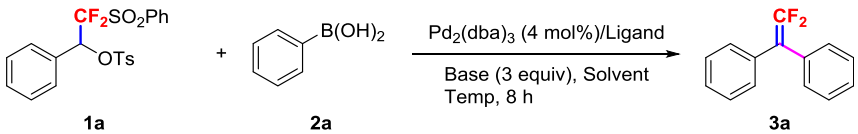


1i, 83%

[a] Isolated yields after recrystallization.

compatible with simple alkyl groups, such as methyl, isopropyl, and *tert*-butyl, trifluoromethyl group, trifluoromethoxy group, even 2-naphthyl substituent. However, both the arene substitution pattern and the electron-donating ability of the substituent could significantly influence the formation of the coupling products. In the cases of alkyl-substituted benzyl tosylates, the *meta*- and *para*-substituted ones could smoothly undergo the reaction to afford the coupling products in moderate yields (Table 4, **3c**, **3k**, and **3l**), while the *ortho*-substituted ones failed to participate in the reaction due to the difficulty in dehydrosulfonylation caused by the steric

Table 2
Screening of cross-coupling conditions[a].



Entry	Ligand (mol%)	Base	Solvent	Temp. (°C)	Yield (%)
1	–	Cs_2CO_3	DME	80	68
2	–	Cs_2CO_3	DMF	80	34
3	–	Cs_2CO_3	DMSO	80	—[b]
4	–	Cs_2CO_3	1,4-dioxane	80	16
5	–	Cs_2CO_3	NMP	80	19
6	–	K_2CO_3	DME	80	8
7	–	*t*-BuOLi	DME	80	0
8	–	Cs_2CO_3	DME	100	60
9	–	Cs_2CO_3	DME	60	48
10	P(*o*-tol)$_3$ (18)	Cs_2CO_3	DME	80	75
11	sPhos (18)	Cs_2CO_3	DME	80	70
12[c]	P(*o*-tol)$_3$ (8)	Cs_2CO_3	DME	80	75 (72)

[a] Unless otherwise noted, all reactions were conducted according to the following conditions: **1a** (0.3 mmol), **2a** (0.2 mmol), base (0.6 mmol), $Pd_2(dba)_3$ (0.008 mmol), ligand (0.036 mmol) in solvent (2.0 mL) at 60, 80, or 100 °C for 8 h. Yields were determined by ^{19}F NMR spectroscopy analysis with $PhSO_2CF_2H$ as an internal standard. Isolated yield was given in the parentheses.
[b] Intractable mixture.
[c] **1a** (0.24 mmol) and P(*o*-tol)$_3$ (0.016 mmol) were used.

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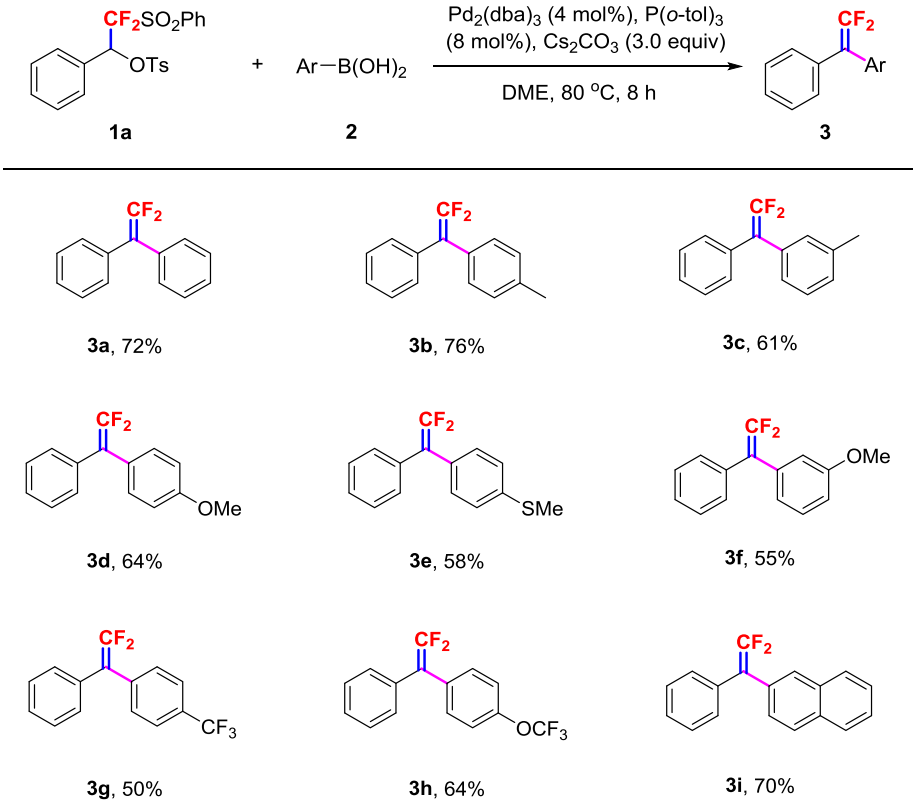
Table 3
Scope of arylboronic acids[a].



[a] Reaction conditions: **1a** (0.6 mmol), **2** (0.5 mmol), Cs_2CO_3 (1.5 mmol), $Pd_2(dba)_3$ (0.02 mmol), P(*o*-tol)$_3$ (0.04 mmol) in DME (5.0 mL) at 80 °C for 8 h. Isolated yields.

hindrance (Table 4, **3j**). In the case where methoxy-substituted benzyl tosylate was used, the cross-coupling reaction was unsuccessful (Table 4, **3d**). The failure of this reaction presumably arises from the strong electron-donating destabilization of the carbanion of benzyl tosylate **1f**, which renders the deprotonation of **1f** much more difficult.

To gain further insights into this palladium-catalyzed dehydrosulfonylative cross-coupling reaction, we conducted the control experiment in the absence of the palladium and monitored the progress of the reactions after 1 h with ^{19}F NMR spectroscopy (Scheme 3). In the absence of $Pd_2(dba)_3$/P(*o*-tol)$_3$, the consumption of tosylate **1a** led to the formation 2,2-difluoro-1-phenylvinyl tosylate (**4a**) as the major product (Scheme 3a); whereas in the presence of $Pd_2(dba)_3$/P(*o*-tol)$_3$, in addition to the coupling product **3a**, the intermediate **4a** was also observed in substantial amount (Scheme 3b). Theses results suggested that **4a** is a possible intermediate for the generation of **3a**. Moreover, tosylate **1a** was consumed at the similar rate with or without the catalyst, indicating that the dehydrosulfonylation of **1a** to form **4a** should be a major pathway. In combination with previously reported coupling reaction of isolated 2,2-difluoro-1-arylvinyl tosylates **4** with arylboronic acids,[13b] a proposed mechanism of our present reaction is given in Scheme 3c, path a. First, Cs_2CO_3-promoted dehydrosulfonylation of tosylate **1** gave 2,2-difluoro-1-arylvinyl tosylate **4**. Second, the palladium-catalyzed cross-coupling of **4** with arylboronic acids affords 2,2-diaryl-1,1-difluoroethenes **3**. Although the involvement of palladium-catalyzed C(sp^3)-C(sp^2) coupling[20] of **1** with arylboronic acids **2** to give intermediate **5** followed by dehydrosulfonylation (Scheme 3c, path b) cannot be fully ruled out at this stage, this pathway should not be the major one, if any, as we observed that the dehydrosulfonylation of **1a** was faster than the formation of **3a**.

3. Conclusions

In summary, we report a new *gem*-difluoroolefination protocol for the synthesis of 2,2-diaryl-1,1-difluoroethenes from readily available $PhSO_2CF_2H$, aromatic aldehydes, and arylboronic acids. The key step is the palladium-catalyzed dehydrosulfonylative cross-coupling of α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates that are derived from $PhSO_2CF_2H$, aromatic aldehydes, and tosyl chloride. The dehydrosulfonylation and coupling reaction are operated in one pot without the separation of the intermediates, 2,2-difluoro-1-arylvinyl tosylates. This protocol not only represents a novel synthetic application of $PhSO_2CF_2H$,[15] it also provides an efficient approach to prepare a series of 2,2-diaryl-1,1-difluoroethenes with varying structures from simple starting materials.

4. Experimental section

4.1. General

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. The solvents MeCN and DMF were distilled over CaH_2. The solvents THF and

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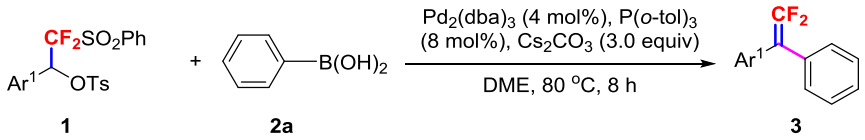
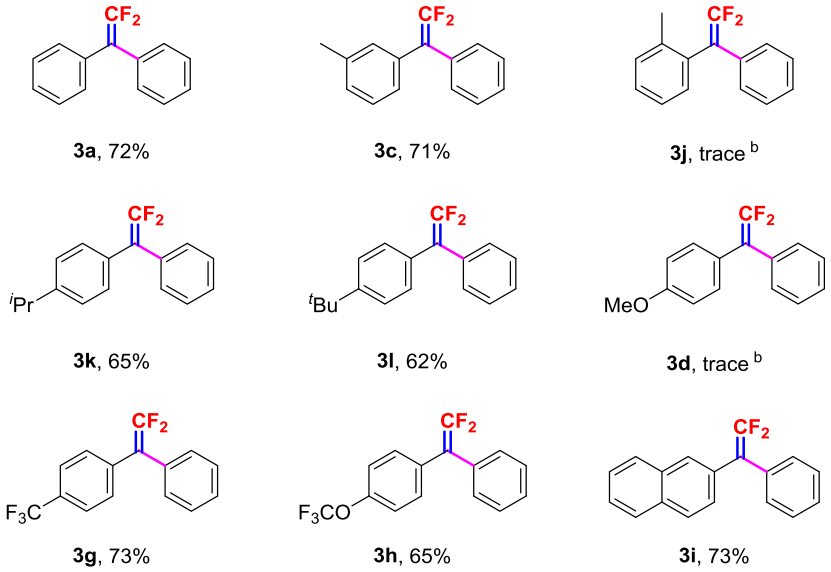
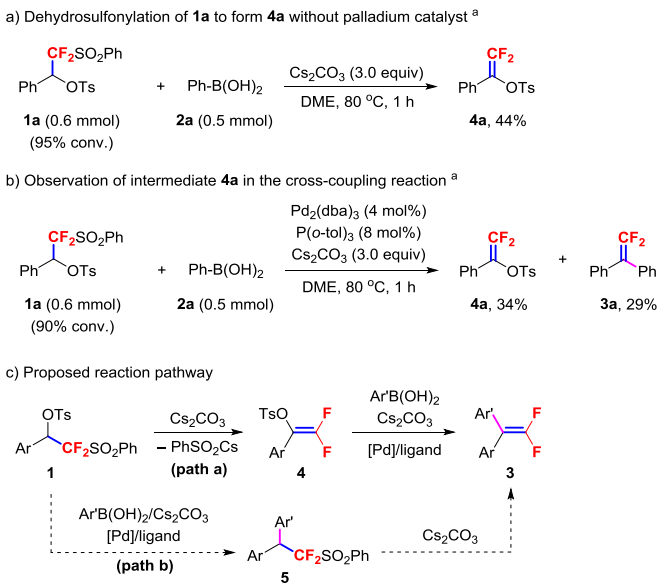
Table 4
Scope of α-[difluoro(phenylsulfonyl)methyl]benzyl tosylates.





[a] Reaction conditions: **1** (0.6 mmol), **2a** (0.5 mmol), Cs_2CO_3 (1.5 mmol), $Pd_2(dba)_3$ (0.02 mmol), P(*o*-tol)$_3$ (0.04 mmol) in DME (5.0 mL) at 80 °C for 8 h. Isolated yields. [b] Yields were determined by ^{19}F NMR spectroscopy analysis with $PhOCF_3$ as an internal standard.

toluene were distilled over sodium. Difluoromethyl phenyl sulfone ($PhSO_2CF_2H$) was either prepared according to reported procedures[21] or purchased from J&K Scientific. All the melting points were uncorrected. ^1H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker AM-300 NMR, VarianMercury-300, or Agilent MR-400 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 $CDCl_3$ at δ 7.26. ^{19}F NMR chemical shifts were determined relative to external $CFCl_3$ at δ 0.0. MS (EI-MS) were obtained on an Agilent 5975C gas chromatography and HP5989A mass spectrometer. MS (ESI) were obtained on an AGILENT1100 mass spectrometer. High-resolution mass data were recorded on a Thermo Scientific LTQ FTICR mass spectrometer in the ESI mode.



Scheme 3. Mechanism considerations. [a] Conversions and yields were determined by ^{19}F NMR spectroscopy analysis with $PhOCF_3$ as an internal standard.

4.2. *Typical experimental procedures for the synthesis of*α-*[difluoro(phenylsulfonyl)methyl]benzyl tosylates* ***1a*–*1i***

Into a 250-mL three-necked round bottom flask equipped with a magnetic stir bar were added benzaldehyde (7.959 g, 75.0 mmol, 1.5 equiv), difluoromethyl phenyl sulfone (9.61 g, 50.0 mmol, 1.0 equiv), hexamethylphosphoramide (HMPA) (12.0 mL), and THF (120.0 mL). The mixture was cooled to −78 °C with a dry ice-acetone cold bath, and stirred at this temperature for 10 min. A solution of lithium bis(trimethylsilyl)amide (1.0 M in THF, 75.0 mL, 75.0 mmol, 1.5 equiv) was added dropwise at −78 °C. The mixture was stirred at −78 °C for 2 h, after which *p*-toluenesulfonyl chloride (14.3 g, 75.0 mmol, 1.5 equiv) was added and then the mixture was stirred at −78 °C for another 1 h. The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (40 mL). Ethyl acetate (EtOAc) (50 mL) were added to the reaction and the organic phase was separated. The aqueous phase was extracted with EtOAc

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(2 × 50 mL) and the combined organic phases were dried with $MgSO_4$, filtered, and evaporated under vacuum. The residue was purified by recrystallization from petroleum ether (PE)/EtOAc to afford the desired product **1a** as a white solid (19.194 g, 85% yield).

4.2.1. 2,2-Difluoro-1-phenyl-2-(phenylsulfonyl)ethyl 4-methylbenzenesulfonate (*1a*)

Performed on 50-mmol scale, 19.194 g, 85% yield. White solid, m.p. 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.8 Hz, 2H), 7.72 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.56 (t, J = 7.8 Hz, 2H), 7.34–7.32 (m, 3H), 7.27–7.23 (m, 3H), 7.16 (d, J = 8.1 Hz, 2H), 6.17 (dd, J = 14.1, 9.5 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.16 (s), 135.53 (s), 133.20 (s), 132.94 (s), 130.78 (s), 130.27 (s), 129.51 (s), 129.29 (s), 129.01 (s), 128.46 (s), 128.18 (s), 119.01 (dd, J = 298.8, 290.0 Hz), 77.37 (d, J = 20.2 Hz), 77.47–77.20 (m), 77.24 (d, J = 7.3 Hz), 21.62 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.54 (dd, J = 240.9, 9.4 Hz, 1 F), −110.38 (dd, J = 240.9, 14.1 Hz, 1 F); MS (ESI, m/z, %): 474.90 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{21}H_{18}F_2O_5S_2Na^+$: 475.0456; Found: 475.0452.

4.2.2. 2,2-Difluoro-2-(phenylsulfonyl)-1-(m-tolyl)ethyl 4-methylbenzenesulfonate (*1b*)

Performed on 50-mmol scale, 19.246 g, 82% yield. White solid, m.p. 115–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.9 Hz, 2H), 7.72 (t, J = 7.9 Hz, 1H), 7.61–7.54 (m, 4H), 7.16–7.11 (m, 5H), 7.04 (s, 1H), 6.12 (dd, J = 14.6, 9.1 Hz, 1H), 2.37 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.20 (s), 138.21 (s), 135.64 (s), 133.26 (s), 132.94 (s), 131.06 (s), 130.70 (s), 129.50 (s), 129.46 (s), 129.34 (s), 129.18 (s), 128.39 (s), 128.09 (s), 126.28 (s), 119.10 (dd, J = 298.7, 289.6 Hz), 77.52 (dd, J = 28.0, 20.3 Hz). 21.53 (s), 21.10 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.28 (dd, J = 241.3, 9.1 Hz, 1 F), −110.66 (dd, J = 241.3, 14.6 Hz, 1 F); MS (ESI, m/z, %): 488.90 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{22}H_{10}F_2O_5S_2Na^+$: 489.0612; Found: 489.0619.

4.2.3. 2,2-Difluoro-2-(phenylsulfonyl)-1-(o-tolyl)ethyl 4-methylbenzenesulfonate (*1c*)

Performed on 50-mmol scale, 21.255 g, 91% yield. White solid, m.p. 138–139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.9 Hz, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.9 Hz, 4H), 7.25 (d, J = 6.6 Hz, 1H), 7.21–7.10 (m, 4H), 6.99 (t, J = 7.6 Hz, 1H), 6.53 (dd, J = 16.5, 6.9 Hz, 1H), 2.44 (s, 2H), 2.36 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.17 (s), 137.42 (s), 135.63 (s), 133.24 (s), 132.85 (s), 130.79 (s), 130.54 (s), 130.06 (s), 129.48 (s), 129.36 (s), 129.01 (s), 128.09 (s), 127.98 (s), 126.20 (s), 119.36 (dd, J = 299.9, 287.5 Hz), 73.12 (dd, J = 24.6, 15.1 Hz), 21.59 (s), 19.28 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −106.89 (d, J = 247.2 Hz, 1 F), −111.72 (d, J = 244.1 Hz, 1 F); MS (ESI, m/z, %): 488.95 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{22}H_{10}F_2O_5S_2Na^+$: 489.0612; Found: 489.0617.

4.2.4. 2,2-Difluoro-1-(4-isopropylphenyl)-2-(phenylsulfonyl)ethyl 4-methylbenzenesulfonate (*1d*)

Performed on 20-mmol scale, 8.482 g, 86% yield. White solid, m.p. 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.7 Hz, 2H), 7.71 (dd, J = 10.7, 4.3 Hz, 1H), 7.55 (t, J = 8.0 Hz, 4H), 7.19 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.3 Hz, 2H), 7.05 (d, J = 8.2 Hz, 2H), 6.14 (dd, J = 14.6, 9.3 Hz, 1H), 2.84 (hept, J = 7.0 Hz, 1H), 2.34 (s, 3H), 1.19 (d, J = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.29 (s), 144.94 (s), 135.58 (s), 133.38 (s), 133.00 (s), 130.70 (s), 129.42 (s), 129.31 (s), 129.11 (s), 128.07 (s), 126.51 (s), 119.16 (dd, J = 298.8, 289.5 Hz), 77.8–77.32 (m), 33.87 (s), 23.81 (s), 23.78 (s), 21.55 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.31 (dd, J = 241.3, 9.3 Hz, 1 F), −110.64 (dd, J = 241.4, 14.5 Hz, 1 F); MS (ESI, m/z, %): 516.95 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{24}H_{24}F_2O_5S_2Na^+$: 517.0925; Found: 517.0920.

4.2.5. 1-(4-(tert-Butyl)phenyl)-2,2-difluoro-2-(phenylsulfonyl)ethyl 4-methylbenzenesulfonate (*1e*)

Performed on 20-mmol scale, 8.397 g, 83% yield. White solid, m.p. 151–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.73–7.69 (m, 1H), 7.57–7.53 (m, 4H), 7.19 (s, 4H), 7.10 (d, J = 8.1 Hz, 2H), 6.14 (dd, J = 14.8, 9.1 Hz, 1H), 2.34 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.51 (s), 144.85 (s), 135.55 (s), 133.42 (s), 133.03 (s), 130.72 (s), 129.39 (s), 129.30 (s), 128.83 (s), 128.08 (s), 125.35 (s), 119.16 (dd, J = 298.8, 289.2 Hz), 77.77–77.29 (m), 34.67 (s), 31.17 (s), 21.57 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.12 (dd, J = 241.6, 9.1 Hz, 1 F), −110.82 (dd, J = 241.7, 14.8 Hz, 1 F); MS (ESI, m/z, %): 530.95 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{25}H_{26}F_2O_5S_2Na^+$: 531.1082; Found: 531.1079.

4.2.6. 2,2-Difluoro-1-(4-methoxyphenyl)-2-(phenylsulfonyl)ethyl 4-methylbenzenesulfonate (*1f*)

Performed on 20-mmol scale, 8.403 g, 87% yield. White solid, m.p. 95–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.7 Hz, 2H), 7.72–7.70 (m, 1H), 7.66–7.64 (m, 2H), 7.59–7.55 (m, 2H), 7.31–7.24 (m, 2H), 7.15 (d, J = 8.1 Hz, 2H), 6.83–6.77 (m, 3H), 3.83 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.06 (s), 135.45 (s), 133.19 (s), 133.03 (s), 131.40 (s), 130.83 (s), 129.63 (s), 129.33 (s), 129.25 (s), 128.22 (s), 120.62 (s), 119.22 (dd, J = 298.8, 288.6 Hz), 118.38 (s), 110.70 (s), 70.29 (dd, J = 29.8, 20.2 Hz), 55.83 (s), 21.59 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.09 (dd, J = 243.2, 7.3 Hz, 1 F), −111.54 (dd, J = 243.2, 16.1 Hz, 1 F); MS (ESI, m/z, %): 504.95 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{22}H_{20}F_2O_6S_2Na^+$: 505.0562; Found: 505.0526.

4.2.7. 2,2-Difluoro-2-(phenylsulfonyl)-1-(4-(trifluoromethyl)phenyl)ethyl 4-methylbenzenesulfonate (*1g*)

Performed on 20-mmol scale, 7.721 g, 74% yield. White solid, m.p. 140–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.77–7.73 (m, 1H), 7.62–7.57 (m, 4H), 7.48 (q, J = 8.4 Hz, 4H), 7.16 (d, J = 8.1 Hz, 2H), 6.21 (dd, J = 13.7, 9.4 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.63 (s), 135.78 (s), 133.55 (s), 132.86 (s), 132.83 (q, J = 32.89 Hz), 132.61 (s), 130.80 (s), 129.62 (s), 129.47 (s), 129.41 (s), 128.18 (s), 125.39 (q, J = 3.7 Hz), 123.56 (q, J = 272.4 Hz), 118.75 (dd, J = 299.3, 290.3 Hz), 76.39 (dd, J = 27.6, 20.9 Hz), 21.53 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.06 (s, 3 F), −107.85 (dd, J = 241.7, 9.4 Hz, 1 F), −110.39 (dd, J = 241.7, 13.7 Hz, 1 F); MS (ESI, m/z, %): 542.90 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{22}H_{17}F_5O_5S_2Na^+$: 543.0330; Found: 543.0342.

4.2.8. 2,2-Difluoro-2-(phenylsulfonyl)-1-(4-(trifluoromethoxy)phenyl)ethyl 4-methylbenzenesulfonate (*1h*)

Performed on 20-mmol scale, 8.797 g, 83% yield. White solid, m.p. 105–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.75 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 8.1 Hz, 4H), 7.36 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.1 Hz, 2H), 6.18 (dd, J = 13.6, 9.7 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.48 (s), 145.55 (s), 135.73 (s), 133.05 (s), 132.71 (s), 130.78 (s), 130.71 (s), 129.57 (s), 129.38 (s), 128.23 (d, J = 2.1 Hz), 128.11 (s), 120.74 (s), 120.26 (q, J = 258.0 Hz), 118.82 (dd, J = 298.6, 290.5 Hz), 76.42 (dd, J = 27.5, 20.7 Hz), 21.50 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −58.34 (s, 3 F), −108.54 (dd, J = 241.2, 9.6 Hz, 1 F), −110.88 (dd, J = 241.4, 13.6 Hz, 1 F); MS (ESI, m/z, %): 558.90 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{22}H_{17}F_5O_6S_2Na^+$: 559.0279; Found: 559.0264.

4.2.9. 2,2-Difluoro-1-(naphthalen-2-yl)-2-(phenylsulfonyl)ethyl 4-methylbenzenesulfonate (*1i*)

Performed on 20-mmol scale, 8.332 g, 83% yield. White solid, m.p. 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.5 Hz, 2H), 7.80–7.64 (m, 5H), 7.60–7.46 (m, 6H), 7.37 (d, J = 8.6 Hz, 1H), 6.99 (d, J = 8.2 Hz, 2H), 6.32 (dd, J = 14.1, 9.6 Hz, 1H), 2.18 (s, 3H); ^{13}C

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NMR (101 MHz, $CDCl_3$) δ 145.24 (s), 135.56 (s), 133.89 (s), 133.21 (s), 132.91 (s), 132.47 (s), 130.76 (s), 129.87 (s), 129.38 (s), 129.28 (s), 128.48 (s), 128.35 (s), 128.10 (s), 127.64 (s), 127.42 (s), 126.64 (s), 125.01 (s), 119.23 (dd, J = 298.8, 290.2 Hz), 77.68 (d, J = 20.4, 7.2 Hz), 21.39 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.51 (dd, J = 241.2, 9.6 Hz, 1 F), −110.19 (dd, J = 241.2, 14.1 Hz, 1 F); MS (ESI, *m/z*, %): 524.90 ($M+Na^+$, 100.00); HRMS (ESI): Calcd. For $C_{25}H_{10}F_2O_5S_2Na^+$: 525.0612; Found: 525.0603.

4.3. Typical experimental procedures for the synthesis of 2,2-diaryl-1,1-difluoroethenes **3a**–**3l**

Under the N_2 atmosphere, DME (5.0 mL) was added into an oven-dried 20-mL Schlenk tube containing tosylate **1a** (270.2 mg, 0.6 mmol, 1.0 equiv), phenylboronic acid (**2a**) (60.9 mg, 0.5 mmol, 1.0 equiv), tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$) (18.4 mg, 0.02 mmol, 4 mol%), tri(*o*-tolyl)phosphine (12.2 mg, 0.04 mmol, 8 mol%), Cs_2CO_3 (489.0 mg, 1.5 mmol, 3.0 equiv) and a magnetic stir bar. The mixture were heated to 80 °C and stirred vigorously for 8 h. After the addition of petroleum ether (PE) (10 mL), the mixture was filtered through Celite layer. The filtrate was concentrated under vacuum and purified by flash column chromatography (silica gel; petroleum ether) to give the desired product **3a** as colorless oil (77.6 mg, 72% yield).

4.3.1. (2,2-Difluoroethene-1,1-diyl)dibenzene (**3a**)

Prepared from **1a** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 77.6 mg, 72% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.26 (m, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −87.80 (s, 2 F); MS (ESI, *m/z*, %): 238.95 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[14]

4.3.2. 1-(2,2-Difluoro-1-phenylvinyl)-4-methylbenzene (**3b**)

Prepared from **1a** (0.6 mmol) and *p*-tolylboronic acid (**2b**) (0.5 mmol), 74.5 mg, 76% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.22 (m, 9H), 7.15 (s, 4H), 2.36 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −88.10 (d, J = 34.0 Hz, 1 F), −88.30 (d, J = 34.1 Hz, 1 F); MS (ESI, *m/z*, %): 253.00 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[14]

4.3.3. 1-(2,2-Difluoro-1-phenylvinyl)-3-methylbenzene (**3c**)

Method A, prepared from **1a** (0.6 mmol) and *m*-tolylboronic acid (**2c**) (0.5 mmol), 53.7 mg, 61% yield; Method B, prepared from **1b** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 62.5 mg, 71% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.19 (m, 6H), 7.15–7.03 (m, 3H), 2.33 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −87.79 (d, J = 32.9 Hz, 1 F), −88.14 (d, J = 32.8 Hz, 1 F); MS (ESI, *m/z*, %): 253.0 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[14]

4.3.4. 1-(2,2-Difluoro-1-phenylvinyl)-4-methoxybenzene (**3d**)

Prepared from **1a** (0.6 mmol) and 4-methoxyphenylboronic acid (**2d**) (0.5 mmol), 67.8 mg, 64% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.22 (m, 5H), 7.18 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 3.81 (s, 1H), 3.81 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −88.73 (d, J = 34.9 Hz, 1 F), −88.91 (d, J = 34.9 Hz, 1 F); MS (ESI, *m/z*, %): 269.0 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[14]

4.3.5. (4-(2,2-Difluoro-1-phenylvinyl)phenyl)(methyl)sulfane (**3e**)

Prepared from **1a** (0.6 mmol) and 4-(methylthio)phenylboronic acid (**2e**) (0.5 mmol), 66.1 mg, 58% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.21 (m, 7H), 7.17 (d, J = 8.4 Hz, 2H), 2.48 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −87.67 (d, J = 32.4 Hz, 1 F), −87.77 (d, J = 32.4 Hz, 1 F); MS (ESI, *m/z*, %): 284.95 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[8b]

4.3.6. 1-(2,2-Difluoro-1-phenylvinyl)-3-methoxybenzene (**3f**)

Prepared from **1a** (0.6 mmol) and 3-methoxyphenylboronic acid (**2f**) (0.5 mmol), 58.3 mg, 55% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 6H), 6.86–6.81 (m, 3H), 3.77 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −87.09 (d, J = 31.8 Hz, 1 F), −87.56 (d, J = 31.7 Hz, 1 F); MS (ESI, *m/z*, %): 268.95 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[8b]

4.3.7. 1-(2,2-Difluoro-1-phenylvinyl)-4-(trifluoromethyl)benzene (**3g**)

Method A, prepared from **1a** (0.6 mmol) and 4-(trifluoromethyl) phenylboronic acid (**2g**) (0.5 mmol), 62.4 mg, 50% yield; Method B, prepared from **1g** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 91.1 mg, 73% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.1 Hz, 2H), 7.38–7.29 (m, 5H),7.23 (dd, J = 8.1, 7.0 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.74 (s, 3 F), −85.74 (d, J = 28.1 Hz, 1 F), −86.47 (d, J = 28.1 Hz, 1 F); MS (ESI, *m/z*, %): 322.95 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[9a]

4.3.8. 1-(2,2-Difluoro-1-phenylvinyl)-4-(trifluoromethoxy)benzene (**3h**)

Method A, prepared from **1a** (0.6 mmol) and 4-(trifluoromethoxy)phenylboronic acid (**2h**) (0.5 mmol), 85.1 mg, 64% yield; Method B, prepared from **1h** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 86.2 mg, 65% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.24 (m, 7H), 7.19 (d, J = 8.1 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −57.86 (s), −86.88 (d, J = 30.7 Hz, 1 F), −87.33 (d, J = 30.7 Hz, 1 F); MS (ESI, *m/z*, %): 322.95 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[9a]

4.3.9. 2-(2,2-Difluoro-1-phenylvinyl)naphthalene (**3i**)

Method A, prepared from **1a** (0.6 mmol) and 2-naphthylboronic acid (**2i**) (0.5 mmol), 81.2 mg, 70% yield; Method B, prepared from **1i** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 84.7 mg, 73% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.72 (m, 4H), 7.48–7.46 (m, 2H), 7.34–7.29 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −87.35 (d, J = 31.5 Hz, 1 F), −87.56 (d, J = 31.5 Hz, 1 F); MS (ESI, *m/z*, %): 289.0 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[9a]

4.3.10. 1-(2,2-Difluoro-1-phenylvinyl)-4-isopropylbenzene (**3k**)

Prepared from **1d** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 83.8 mg, 65% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5H), 7.21–7.16 (m, 4H), 2.91 (hept, J = 6.9 Hz, 1H), 1.26 (d, J = 6.9 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −88.23 (d, J = 2.8 Hz, 2 F); MS (ESI, *m/z*, %): 281.0 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[9a]

4.3.11. 1-(tert-Butyl)-4-(2,2-difluoro-1-phenylvinyl)benzene (**3l**)

Prepared from **1e** (0.6 mmol) and phenylboronic acid (**2a**) (0.5 mmol), 84.3 mg, 62% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.32 (m, 4H), 7.30–7.26 (m, 3H), 7.19 (d, J = 8.1 Hz, 2H), 1.32 (s, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −88.02 (d, J = 33.4 Hz, 1 F), −88.20 (d, J = 33.4 Hz, 1 F); MS (ESI, *m/z*, %): 295.0 ($M+Na^+$, 100.00). The characterization data are in consistence with previous report.[14]

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.tet.2018.04.054.

References

1. For recent reviews on the synthetic applications of 1,1-difluoroalkenes, see: (a) Chelucci G. *Chem Rev*. 2012;112:1344;
(b) Liu Y, Deng M, Zhang Z, Ding X, Dai Z, Guan J. *You Ji Hua Xue*. 2012;32:661;
(c) Zhang X, Cao S. *Tetrahedron Lett*. 2017;58:375.
2. For selected recent examples on the synthetic applications of 1,1-difluoroalkenes, see: (a) Hu M, Ni C, Li L, Han Y, Hu J. *J Am Chem Soc*. 2015;137:14496. and references therein;;
(b) Gao B, Zhao Y, Ni C, Hu J. *Org Lett*. 2014;16:102;
(c) Gao B, Zhao Y, Hu J. *Angew Chem Int Ed*. 2015;54:638;
(d) Tian P, Wang C-Q, Cai S-H, et al. *J Am Chem Soc*. 2016;138:15869;
(e) Tang H-J, Lin L-Z, Feng C, Loh T-P. *Angew Chem Int Ed*. 2017;56:9872;
(f) Dai W, Shi H, Zhao X, Cao S. *Org Lett*. 2016;18:4284;
(g) Kong L, Zhou X, Li X. *Org Lett*. 2016;18:6320;
(h) Dai W, Zhang X, Zhang J, Lin Y, Cao S. *Adv Synth Catal*. 2016;358:183;
(i) Xie J, Yu J, Rudolph M, Rominger F, Hashmi ASK. *Angew Chem Int Ed*. 2016;55:9416;
(j) Thornbury RT, Toste FD. *Angew Chem Int Ed*. 2016;55:11629;
(k) Zell D, Dhawa U, Müller V, Bursch M, Grimme S, Ackermann L. *ACS Catal*. 2017;7:4209;
(l) Zhang J, Dai W, Liu Q, Cao S. *Org Lett*. 2017;19:3283;
(m) Hu J, Han X, Yuan Y, Shi Z. *Angew Chem Int Ed*. 2017;56:13342;
(n) Kojima R, Kubota K, Ito H. *Chem Commun*. 2017;53:10688;
(o) Kong L, Liu B, Zhou X, Wang F, Li X. *Chem Commun*. 2017;53:10326;
(p) Zell D, Meller V, Dhawa U, et al. *Chem Eur J*. 2017;23:12145;
(q) Lu X, Wang Y, Zhang B, et al. *J Am Chem Soc*. 2017;139:12632;
(r) Sakaguchi H, Uetake Y, Ohashi M, Niwa T, Ogoshi S, Hosoya T. *J Am Chem Soc*. 2017;139:12855;
(s) Li J, Lefebvre Q, Yang H, Zhao Y, Fu H. *Chem Commun*. 2017;53:10299;
(t) Fujita T, Kinoshita R, Takanohashi T, Suzuki N, Ichikawa J. *Beilstein J Org Chem*. 2017;13:2682;
(u) Fuchibe K, Shigeno K, Zhao N, et al. *J Fluorine Chem*. 2017;203:173;
(v) Li J, Xu C, Wei N, Wang M. *J Org Chem*. 2017;82:11348;
(w) Zhang B, Zhang X, Hao J, Yang C. *Org Lett*. 2017;19:1780;
(x) Fang Z, Hu W-L, Liu D-Y, Yu C-Y, Hu X-G. *Green Chem*. 2017;19:1299.
3. (a) . In: Ojima I, ed. *Fluorine in Medicinal Chemistry and Chemical Biology*. West Sussex: Wiley-Blackwell; 2009;
(b) . In: Gouverneur V, Müller K, eds. *Fluorine in Pharmaceutical and Medicinal Chemistry: from Biophysical Aspects to Clinical Applications*. London: Imperial College Press; 2012.
4. (a) Welch JT, Lin J, Boros LG, DeCorte B, Bergmann K, Gimi R. In: *Biomedical Frontiers of Fluorine Chemistry*. Washington: ACS; 1996:129;
(b) Zhao K, Lim DS, Funaki T, Welch JT. *Bioorg Med Chem*. 2003;11:207;
(c) Boros LG, De Corte B, Gimi RH, Welch JT, Wu Y, Handschumacher RE. *Tetrahedron Lett*. 1994;35:6033;
(d) Khrimian AP, DeMilo AB, Waters RM, Liquido NJ, Nicholson JM. *J Org Chem*. 1994;59:8034;
(e) Lin J, Welch JT. *Tetrahedron Lett*. 1998;39:9613.
5. (a) Chambers RD. *Fluorine in Organic Chemistry*. Oxford: Blackwell; 2004;
(b) Kirsch P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*. second ed. Weinheim: Wiley-VCH; 2013.
6. For examples, see: (a) McDonald IA, Lacoste JM, Bey P, Palfreyman MG, Zreika M. *J Med Chem*. 1985;28:186;
(b) Bobek M, Kavai I, De Clercq E. *J Med Chem*. 1987;30:1494;
(c) Moore WR, Schatzman GL, Jarvi ET, Gross RS, McCarthy JR. *J Am Chem Soc*. 1992;114:360;
(d) Berry CN, Lassalle G, Lunven C, et al. *J Pharmacol Exp Ther*. 2002;303:1189;
(e) Weintraub PM, Holland AK, Gates CA, et al. *Bioorg Med Chem*. 2003;11:427;
(f) Altenburger JM, Lassalle GY, Matrougui M, et al. *Bioorg Med Chem*. 2004;12:1713;
(g) Pan Y, Qiu J, Silverman RB. *J Med Chem*. 2003;46:5292;
(h) Rogawski MA. *Epilepsy Res*. 2006;69:273;
(i) Juncosa JI, Takaya K, Le HV, et al. *J Am Chem Soc*. 2018;140:2151.
7. (a) Nowak I, Robins MJ. *Org Lett*. 2005;7:721;
(b) Krishnamoorthy S, Kothandaraman J, Saldana J, Prakash GKS. *Eur J Org Chem*. 2016;2016:4965.
8. (a) Mlostoń G, Prakash GKS, Olah GA, Heimgartner H. *Helv Chim Acta*. 2002;85:1644;
(b) Takayama R, Yamada A, Fuchibe K, Ichikawa J. *Org Lett*. 2017;19:5050.
9. (a) Zhao Y, Huang W, Zhu L, Hu J. *Org Lett*. 2010;12:1444;
(b) Gao B, Zhao Y, Hu M, Ni C, Hu J. *Chem Eur J*. 2014;20:7803;
(c) Gao B, Zhao Y, Hu J, Hu J. *Org Chem Front*. 2015;2:163;
(d) Gao B, Hu J, Zhao Y, Hu J. *Tetrahedron Lett*. 2015;56:4180.
10. (a) Hu M, He Z, Gao B, Li L, Ni C, Hu J. *J Am Chem Soc*. 2013;135:17302;
(b) See Ref. 2(a);. (c) Zheng J, Lin J-H, Yu L-Y, Wei Y, Zheng X, Xiao J-C. *Org Lett*. 2015;17:6150;
(d) Zhang Z, Yu W, Wu C, Wang C, Zhang Y, Wang J. *Angew Chem Int Ed*. 2016;55:273.
11. (a) Choi JH, Jeong IH. *Tetrahedron Lett*. 2008;49:952;
(b) Han SY, Lee HY, Jeon JH, Jeong IH. *Tetrahedron Lett*. 2012;53:1833.
12. (a) Raghavanpillai A, Burton DJ. *J Org Chem*. 2006;71:194;
(b) Fujita T, Suzuki N, Ichitsuka T, Ichikawa J. *J Fluorine Chem*. 2013;155:97.
13. (a) Han SY, Jeong IH. *Org Lett*. 2010;12:5518;
(b) Kim JH, Choi SJ, Jeong IH. *Beilstein J Org Chem*. 2013;9:2470.
14. Zhang Z, Yu W, Zhou Q, Li T, Zhang Y, Wang J. *Chin J Chem*. 2016;34:473.
15. For reviews, see: (a) Ni C, Hu J. *Chem Soc Rev*. 2016;45:5441;
(b) Ni C, Hu M, Hu J. *Chem Rev*. 2015;115:765;
(c) Zhang W, Ni C, Hu J. *Top Curr Chem*. 2012;308:25;
(d) Ni C, Hu J. *Synlett*. 2011:770;
(e) Hu J. *J Fluorine Chem*. 2009;130:1130;
(f) Hu J, Zhang W, Wang F. *Chem Commun*. 2009:7465;
(g) Prakash GKS, Hu J. *Acc Chem Res*. 2007;40:921;
(h) Liu Q, Ni C, Hu J. *Natl Sci Rev*. 2017;4:303.
16. For selected recent examples, see: (a) Rong J, Deng L, Tan P, Ni C, Gu Y, Hu J. *Angew Chem Int Ed*. 2016;55:2743;
(b) Rong J, Ni C, Wang Y, Kuang C, Gu Y, Hu J. *Acta Chim Sinica*. 2017;75:105;
(c) Miao W, Zhao Y, Ni C, Gao B, Zhang W, Hu J. *J Am Chem Soc*. 2018;140:880;
(d) Merchant RR, Edwards JT, Qin T, et al. *Science*. 2018;360:75;
(e) Miao W, Ni C, Zhao Y, Hu J. *Org Lett*. 2016;18:2766;
(f) Xiao P, Rong J, Ni C, et al. *Org Lett*. 2016;18:5912;
(g) Li X, Zhao J-W, Hu M, et al. *Chem Commun*. 2016;52:3657;
(h) Zhao Y, Jiang F, Hu J. *J Am Chem Soc*. 2015;137:5199;
(i) Zhao Y, Ni C, Jiang F, Gao B, Shen X, Hu J. *ACS Catal*. 2013;3:631;
(j) Zhao Y, Gao B, Ni C, Hu J. *Org Lett*. 2012;14:6080;
(k) Su Y-M, Feng G-S, Wang Z-Y, Lan Q, Wang X-S. *Angew Chem Int Ed*. 2015;54:6003;
(l) Zhao Y, Gao B, Hu J. *J Am Chem Soc*. 2012;134:5790;
(m) Prakash GKS, Ni C, Wang F, Hu J, Olah GA. *Angew Chem Int Ed*. 2011;50:2559;
(n) Prakash GKS, Ni C, Wang F, Zhang Z, Haiges R, Olah GA. *Angew Chem Int Ed*. 2013;52:10835;
(o) He Z, Luo T, Hu M, Cao Y, Hu J. *Angew Chem Int Ed*. 2012;51:3944;
(p) Shen X, Zhang L, Zhao Y, Zhu L, Li G, Hu J. *Angew Chem Int Ed*. 2011;50:2588.
17. Zhang L, Li Y, Hu J. *J Fluorine Chem*. 2007;128:755.
18. Prakash GKS, Hu J, Wang Y, Olah GA. *Eur J Org Chem*. 2005:2218.
19. Shen X, Ni C, Hu J. *Chin J Chem*. 2013;31:878.
20. Brambilla M, Tredwell M. *Angew Chem Int Ed*. 2017;56:11981.
21. (a) Hine J, Porter JJ. *J Am Chem Soc*. 1960;82:6178;
(b) Langlois BR. *J Fluorine Chem*. 1988;41:247;
(c) Wang X, Liu G, Xu X-H, Shibata N, Tokunaga E, Shibata N. *Angew Chem Int Ed*. 2014;53:1827.

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