

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

Rui Zhang, Chuanfa Ni, Yanchuan Zhao, Jinbo Hu*

Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 345 Ling-Ling Road, Shanghai 200032, China

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ABSTRACT

By using $\text{PhSO}_2\text{CF}_2\text{H}$ 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 $\text{PhSO}_2\text{CF}_2\text{H}$, aromatic aldehydes and tosyl chloride. Mechanistic investigations showed that the reaction proceeds mainly through base-mediated dehydrosulfonylation followed by palladium-catalyzed $\text{C}(\text{sp}^2)\text{-C}(\text{sp}^2)$ cross-coupling reaction.

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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 ($=\text{CF}_2$) 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 difluoromethylenation 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 ($-\text{CF}_2\text{H}$), difluoromethylene ($-\text{CF}_2-$), difluoromethylidene group ($=\text{CF}_2$), as well as difluoro(sulfinato)

* Corresponding author.

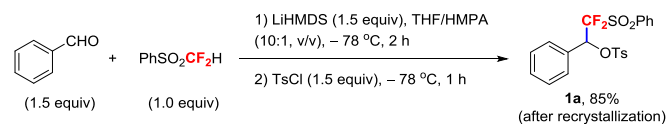
E-mail address: jinbohu@sioc.ac.cn (J. Hu).

methyl (-CF₂SO₂M) groups [15b,e]. The reaction of two molecules with 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 difluoromethylidene-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-arylviny 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-arylviny tosylates (Scheme 1c) [13], we envisioned that α -[difluoro(phenylsulfonyl)methyl]benzyl tosylates could be used as alternative precursors of 2,2-difluoro-1-arylviny 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-arylviny 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 PhSO₂CF₂H and benzaldehyde followed by treatment with tosyl chloride (Scheme 2). As previously described [18], the addition of PhSO₂CF₂H to benzaldehyde



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

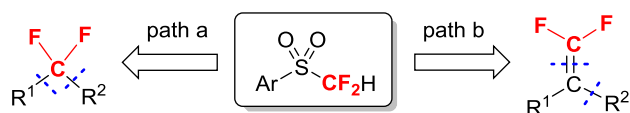
could readily take place in THF in the presence of lithium hexamethyldisilazide (LiHMDS) as the base and hexamethylphosphoric triamide (HMPA) as an additive at $-78\text{ }^{\circ}\text{C}$. We found that the further addition of tosyl chloride to the reaction mixture at the same temperature could afford 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% Pd₂(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 Cs₂CO₃ was used as the base and Pd₂(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 ¹⁹F NMR). Screening of solvents showed that other solvents are inferior to DME (Table 1, entries 2–5). The base effect is also significant: K₂CO₃ and *t*-BuOLi were found to be less effective due to their weaker basicity than Cs₂CO₃, 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 Cs₂CO₃, 4 mol% Pd₂(dba)₃ catalyst, 8 mol% P(*o*-tol)₃ ligand, DME solvent, 80 °C reaction temperature, and 8 h reaction time under N₂ atmosphere (Table 1, entry 12).

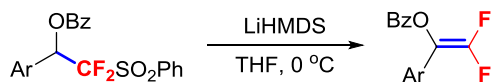
With the optimized conditions in hand, we first examined the substrate scope by reacting tosylate **1a** with different arylboronic acids **2** (Table 3). For ease of isolation of the desired product, all reactions were performed on 0.5-mmol scale. Generally, both electron-rich and electron-deficient 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 Cs₂CO₃ in DME.

We then examined the reactions of various tosylates **1b–1i** with

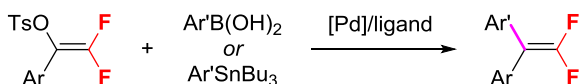
a) Synthesis of *gem*-difluorinated compounds with ArSO₂CF₂H



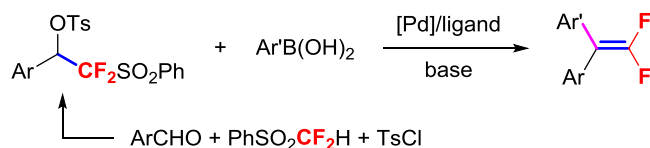
b) Dehydrosulfonylation of PhSO₂CF₂-benzyl benzoates



c) Coupling reaction with *gem*-difluorovinyl tosylates

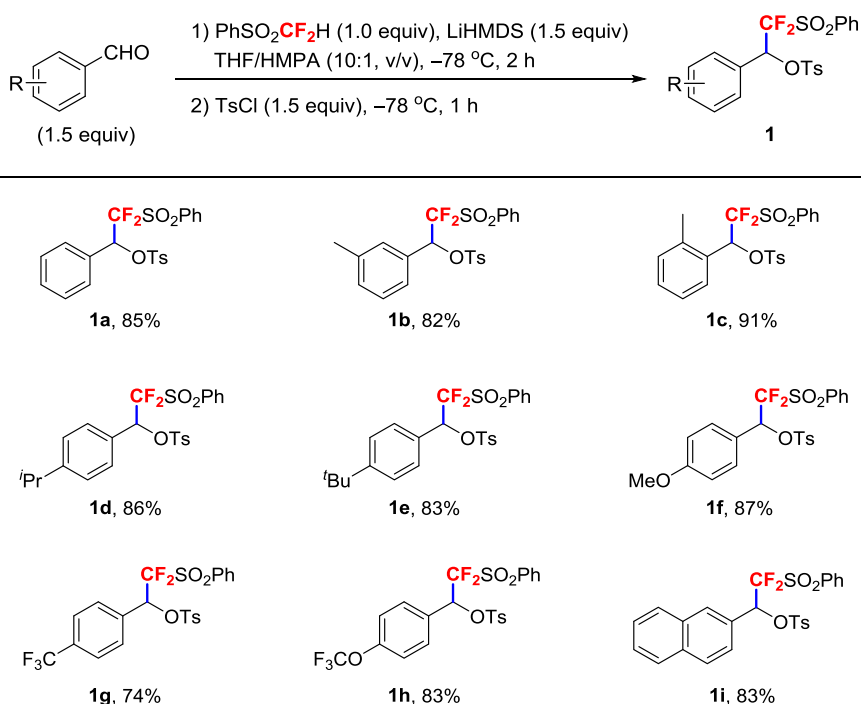


d) Coupling reaction with PhSO₂CF₂-benzyl tosylates (This work)



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

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

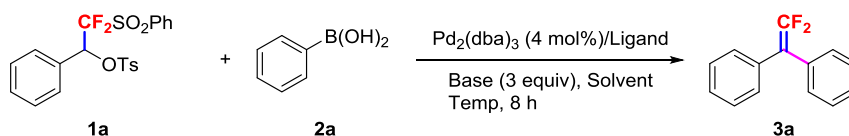


^a Isolated yields after recrystallization.

phenylboronic acid (**2a**). As shown in Table 4, the reaction is 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

Table 2
Screening of cross-coupling conditions^a.



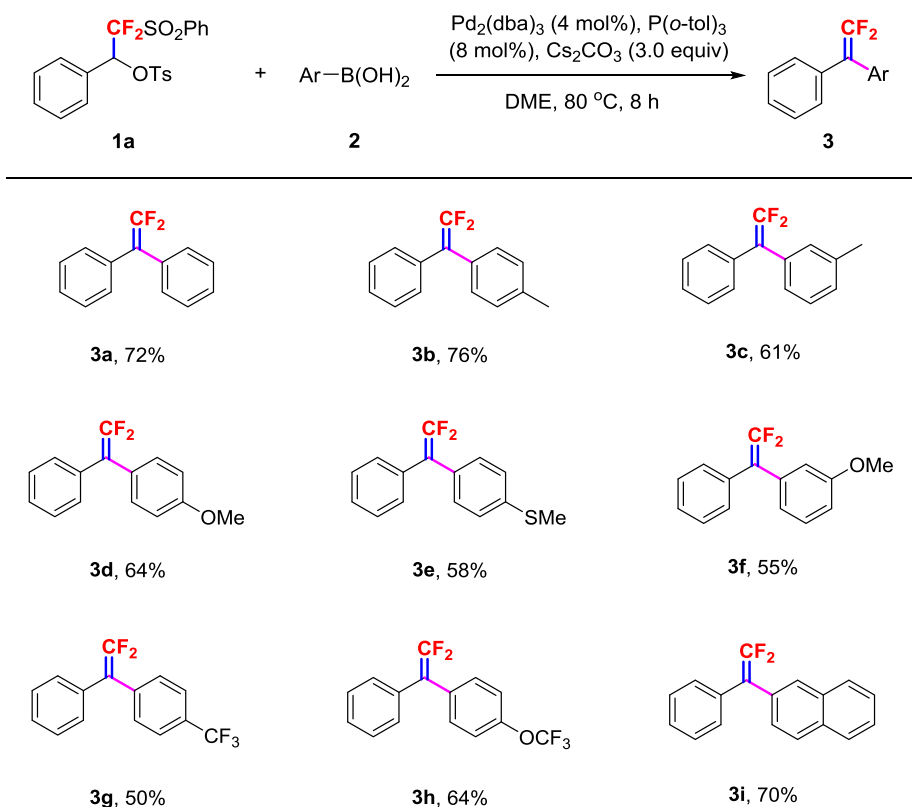
Entry	Ligand (mol%)	Base	Solvent	Temp. ($^\circ\text{C}$)	Yield (%)
1	—	Cs_2CO_3	DME	80	68
2	—	Cs_2CO_3	DMF	80	34
3	—	Cs_2CO_3	DMSO	80	— ^b
4	—	Cs_2CO_3	1,4-dioxane	80	16
5	—	Cs_2CO_3	NMP	80	19
6	—	K_2CO_3	DME	80	8
7	—	<i>t</i> -BuOLi	DME	80	0
8	—	Cs_2CO_3	DME	100	60
9	—	Cs_2CO_3	DME	60	48
10	$\text{P}(o\text{-tol})_3$ (18)	Cs_2CO_3	DME	80	75
11	sPhos (18)	Cs_2CO_3	DME	80	70
12 ^c	$\text{P}(o\text{-tol})_3$ (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), $\text{Pd}_2(\text{dba})_3$ (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 $\text{PhSO}_2\text{CF}_2\text{H}$ as an internal standard. Isolated yield was given in the parentheses.

^b Intractable mixture.

^c **1a** (0.24 mmol) and $\text{P}(o\text{-tol})_3$ (0.016 mmol) were used.

Table 3
Scope of arylboronic acids^a.



^a Reaction conditions: **1a** (0.6 mmol), **2** (0.5 mmol), Cs_2CO_3 (1.5 mmol), $\text{Pd}_2(\text{dba})_3$ (0.02 mmol), $\text{P}(o\text{-tol})_3$ (0.04 mmol) in DME (5.0 mL) at 80 °C for 8 h. Isolated yields.

to the difficulty in dehydrosulfonylation caused by the steric 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 ¹⁹F NMR spectroscopy (Scheme 3). In the absence of $\text{Pd}_2(\text{dba})_3/\text{P}(o\text{-tol})_3$, 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 $\text{Pd}_2(\text{dba})_3/\text{P}(o\text{-tol})_3$, in addition to the coupling product **3a**, the intermediate **4a** was also observed in substantial amount (Scheme 3b). These 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 $\text{C}(\text{sp}^3)\text{-C}(\text{sp}^2)$ 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

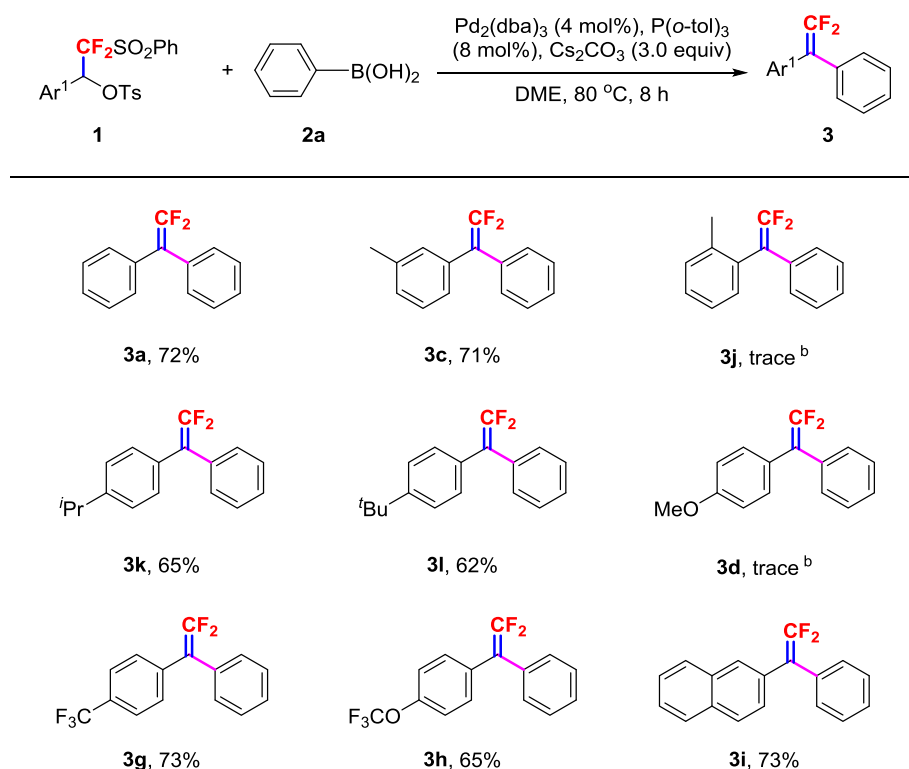
In summary, we report a new *gem*-difluoroolefination protocol for the synthesis of 2,2-diaryl-1,1-difluoroethenes from readily available $\text{PhSO}_2\text{CF}_2\text{H}$, aromatic aldehydes, and arylboronic acids. The key step is the palladium-catalyzed dehydrosulfonylative cross-coupling of α -[difluoro(phenylsulfonyl)methyl]benzyl tosylates that are derived from $\text{PhSO}_2\text{CF}_2\text{H}$, 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 $\text{PhSO}_2\text{CF}_2\text{H}$ [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

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

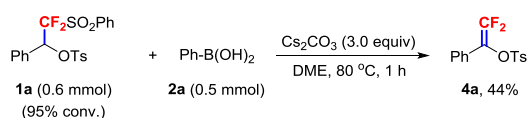


^a Reaction conditions: **1** (0.6 mmol), **2a** (0.5 mmol), Cs_2CO_3 (1.5 mmol), $\text{Pd}_2(\text{dba})_3$ (0.02 mmol), $\text{P}(o\text{-tol})_3$ (0.04 mmol) in DME (5.0 mL) at 80 °C for 8 h. Isolated yields. ^b Yields were determined by ^{19}F NMR spectroscopy analysis with PhOCF_3 as an internal standard.

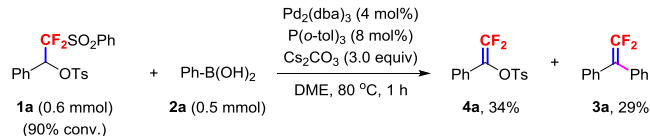
MeCN and DMF were distilled over CaH_2 . The solvents THF and toluene were distilled over sodium. Difluoromethyl phenyl sulfone ($\text{PhSO}_2\text{CF}_2\text{H}$) was either prepared according to reported procedures

[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 $(\text{CH}_3)_4\text{Si}$ (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.

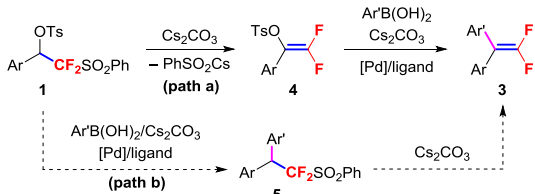
a) Dehydrosulfonylation of **1a** to form **4a** without palladium catalyst^a



b) Observation of intermediate **4a** in the cross-coupling reaction^a



c) Proposed reaction pathway



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 (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; ^1H 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, 1F), –110.38 (dd, $J = 240.9$, 14.1 Hz, 1F); MS (ESI, m/z , %): 474.90 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{21}\text{H}_{18}\text{F}_2\text{O}_5\text{S}_2\text{Na}^+$: 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; ^1H 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, 1F), –110.66 (dd, $J = 241.3$, 14.6 Hz, 1F); MS (ESI, m/z , %): 488.90 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{22}\text{H}_{10}\text{F}_2\text{O}_5\text{S}_2\text{Na}^+$: 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. ^1H 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, 1F), –111.72 (d, $J = 244.1$ Hz, 1F); MS (ESI, m/z , %): 488.95 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{22}\text{H}_{10}\text{F}_2\text{O}_5\text{S}_2\text{Na}^+$: 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; ^1H 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, 1F), –110.64 (dd, $J = 241.4$, 14.5 Hz, 1F); MS (ESI, m/z , %): 516.95 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{24}\text{H}_{24}\text{F}_2\text{O}_5\text{S}_2\text{Na}^+$: 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; ^1H 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, 1F), –110.82 (dd, $J = 241.7$, 14.8 Hz, 1F); MS (ESI, m/z , %): 530.95 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{25}\text{H}_{26}\text{F}_2\text{O}_5\text{S}_2\text{Na}^+$: 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; ^1H 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, 1F), –111.54 (dd, $J = 243.2$, 16.1 Hz, 1F); MS (ESI, m/z , %): 504.95 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{22}\text{H}_{20}\text{F}_2\text{O}_6\text{S}_2\text{Na}^+$: 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; ^1H 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, 3F), –107.85 (dd, $J = 241.7$, 9.4 Hz, 1F), –110.39 (dd, $J = 241.7$, 13.7 Hz, 1F); MS (ESI, m/z , %): 542.90 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{22}\text{H}_{17}\text{F}_5\text{O}_5\text{S}_2\text{Na}^+$: 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; ^1H 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, 3F), –108.54 (dd, $J = 241.2$, 9.6 Hz, 1F), –110.88 (dd, $J = 241.4$, 13.6 Hz, 1F); MS (ESI, m/z , %): 558.90 ($\text{M} + \text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{22}\text{H}_{17}\text{F}_5\text{O}_6\text{S}_2\text{Na}^+$: 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; ^1H 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 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 ($\text{M}+\text{Na}^+$, 100.00); HRMS (ESI): Calcd. For $\text{C}_{25}\text{H}_{10}\text{F}_2\text{O}_5\text{S}_2\text{Na}^+$: 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) ($\text{Pd}_2(\text{dba})_3$) (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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$, 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; ^1H 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 ($\text{M}+\text{Na}^+$,

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>.

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