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Synthesis of 2-aryl-1,1-difluoro-1,3-enynes via consecutive cross-coupling reactions of 2,2-difluoro-1-iodoethenyl *p*-toluenesulfonate

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ABSTRACT

Alkynylation reaction of 2,2-difluoro-1-iodoethenyl *p*-toluenesulfonate **1** with alkynyltributylstannanes in the presence of 10 mol% $Pd(PPh_3)_4$ and 10 mol% CuI in THF at reflux temperature for 3 h provided the corresponding 1,1-difluoro-1,3-enynyl tosylates **2** in 65–85% yields. The further arylation reaction of **2** with aryltributylstannanes in the presence of 10 mol% $Pd(PPh_3)_2Cl_2$ and 3 equiv. of LiBr in THF at reflux temperature for 8 h afforded the coupled products **3** in 32–83% yields.

1. Introduction

1,3-Enynes have received much attention because they are valuable synthetic intermediates for the formation of multifunctional molecules [1–4] and natural products [5,6] in organic synthesis. Especially, fluorinated 1,3-enynes would be important building blocks for the synthesis of fluorinated compounds having unique biological and physical properties [7–9]. Although various methods for the preparation of nonfluorinated 1,3-enynes have been well documented in the previous literatures [10], the preparation of fluorinated 1,3-enynes has been quite limited and most of them related to the synthesis of monofluorinated or 1,2-difluorinated 1,3-enynes. An efficient approach to fluorinated 1,3-enynes is the palladium-catalyzed coupling reaction of fluorinated vinyl iodides (bromides) with terminal alkyl- and phenyl-substituted alkynes in the presence of cuprous iodides and base. Burton et al. prepared 1,2-difluoro-1,3-enynes in good yields from the direct coupling of substituted fluorinated vinyl iodides with 1-alkynes via this method [11,12]. Monofluorinated 1,3-enynes were also prepared in a similar manner [13–16]. Highly stereoselective synthesis of monofluorinated conjugated enynes was achieved from the coupling reaction of (*Z*)-2-fluoroalkenyliodonium salts with 1-alkynes in the presence of Pd catalyst [17]. Hammond et al. prepared monofluorinated conjugated enynes in high yields via Wadsworth–Horner–Emmons olefination of a fluorine-containing building block TIPS-fluoropropargylphosphonate with aldehydes and ketones [18]. In contrast to the synthesis of monofluorinated or 1,2-difluorinated 1,3-enynes, the synthesis of 1,1-difluoro-1,3-enyne derivatives has been quite limited and thus only several methods were reported. Burton et al. reported that 1,1-difluoro-2-phenyl-1,3-enynes were synthesized in low yield via the hydrolysis of the trifluoromethylated allenic phosphonium salt [19]. 1,1-Difluoro-1,3-enynes were also prepared from the direct coupling reactions of 1,1-difluorovinyl iodides with alkynylzinc chloride in the presence of Pd catalyst [20]. Ichikawa et al. synthesized 2-alkylated 1,1-difluoro-1,3-enynes via the coupling reaction of 1-alkyl-2,2-difluorovinylboranes with 1-halo-1-alkynes in the presence of cuprous iodides, but 2-phenylated 1,1-difluoro-1,3-enynes can't be prepared from this method [21]. Recently, we reported an efficient method for the preparation of 2-phenyl-1,1-difluoro-1,3-enynes from the cross-coupling reaction of 2,2-difluoro-1-phenylethenylstannane with alkynyl iodides in the presence of catalytic amount of $Pd(PPh_3)_4$ and CuI [22]. However, the previous methods still have some limitations such as tedius procedure for the synthesis of starting material and lack of generality. Herein, we wish to report a general

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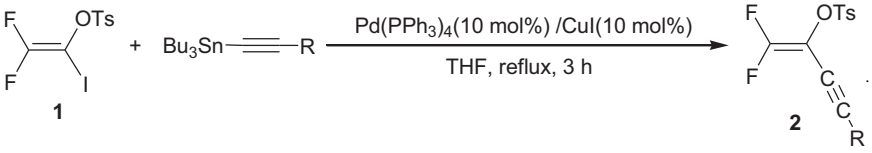
and straightforward preparation of 2-aryl-1,1-difluoro-1,3-enynes via the consecutive coupling reactions of 2,2-difluoro-1-iodoethenyl *p*-toluenesulfonate **1**, which can be easily prepared from the 2,2,2-trifluoroethyl *p*-toluenesulfonate, with alkynyl iodides and arylstannanes in the presence of Pd catalysis. Recently, we prepared the starting material **1** in 80 yield from the reaction of commercially available 2,2,2-trifluoroethyl *p*-toluenesulfonate with 2 equiv. of LDA followed by treatment with iodine at low temperature [23].

2. Results and discussion

First, we tried the carbon-carbon bond formation between iodo site of **1** and alkynylstannane reagents in the presence of catalyst to afford 1,1-difluoro-1,3-enynyl tosylate **2**. The use of $Pd(PPh_3)_4$ and CuI co-catalyst afforded the high yield of the coupled product **2**. Therefore, the reaction of **1** with phenylethynylstannane reagent in the presence of 10 mol% $Pd(PPh_3)_4$ and 10 mol% CuI in THF at reflux for 3 h provided the enynyl tosylate **2a** in 83% yield. The coupled product between tosylate site of **1** and alkynylstannane reagent was not observed at all. The reactions of **1** with a variety of arylethynylstannanes such as phenylethynylstannane having electron-withdrawing group as well as electron-donating group on the benzene ring, alkylethynylstannane and trialkylsilylethynylstannane under the same reaction condition gave the corresponding 1,3-enynyl tosylate **2b**–**2i** in 65–85% yields. The results of the coupling reaction between **1** and alkynylstannane reagents were summarized in Table 1. The use of either $Pd(PPh_3)_4$ or CuI in this reaction did not proceed at all. We also performed the Sonogashira reaction of **1** with phenylethyne in the presence of $Pd(PPh_3)_2Cl_2$, CuI and triethylamine in DMF at 80 °C for 3 h, but the desired product **2a** was obtained in 42% yield.

Since we developed the method for the preparation of 1,1-diaryl-2,2-difluoroethenes via the cross-coupling reaction of 2,2-difluoro-1-arylethenyl tosylate with arylstannane reagents in recent years [24], we investigated the coupling reaction of 1,3-enynyl tosylates **2** with arylstannane reagents. When **2a** was treated with phenyltributylstannane (1.5 equiv.) in the presence of $Pd(PPh_3)_4$ (10 mol%) and LiBr (3 equiv.) in DMF at 80 °C for 5 h, the coupled product **3a** was not obtained, which result is different from the coupling reaction of 2,2-difluoro-1-arylethenyl tosylate with phenyltributylstannane. However, the use of THF as a solvent in this reaction caused the formation of the desired product. Therefore, **2a** was reacted with phenyltributyl-stannane in the presence of 10 mol% $Pd(PPh_3)_4$ and 3 equiv. LiBr in THF at reflux for 7 h to afford the coupled product **3a** in 30% yield. The longer reaction time in this reaction resulted in the formation of **3a** in lower yield. A couple of catalysts was examined to improve the yield of **3a**. The use of $Pd(CH_3CN)_2Cl_2$ decreased the yield of **3a**, but the coupling reaction was activated by using $Pd(PPh_3)_2Cl_2$, in which **3a** was obtained in 72% yield. Addition of X-Phos ligand did not cause to increase the yield of **3a**. The results of the optimization for the reaction of **2a** with phenyltributylstannane were summarized in Table 2. We also performed the Sonogashira reaction of **2a**

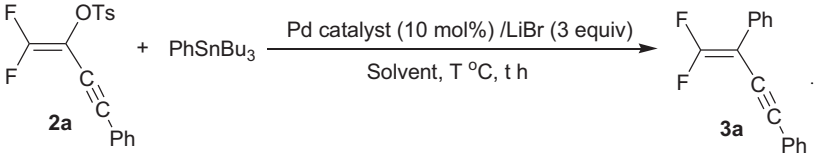
Table 1
The coupling reaction of **1** with alkynylstannane reagents.



Compound	R	Yield (%)[a]
2a	C_6H_5	83
2b	*p*-$CH_3C_6H_4$	72
2c	3,5-$(CF_3)_3C_6H_3$	65
2d	*p*-$CH_3OC_6H_4$	70
2e	*o*-$CH_3OC_6H_4$	65
2f	*n*-C_4H_9	79
2g	*n*-C_6H_{13}	73
2h	TIPS	80
2i	TMS	85

[a] Isolated yield.

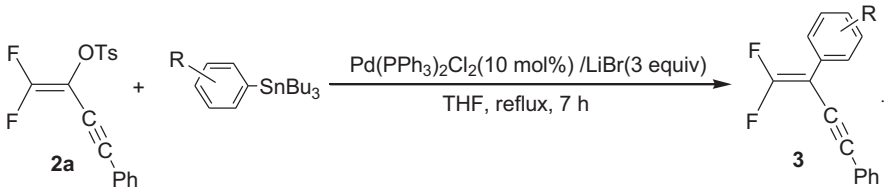
Table 2
The optimization for the coupling reaction of **2a** with phenyltributylstannane.



Entry	Pd Catalyst	Solvent	*T* (°C)	*t* (h)	Yield (%)[a]
1	$Pd(PPh_3)_4$	DMF	60	5	0
2	$Pd(PPh_3)_4$	DMF	80	5	0
3	$Pd(PPh_3)_4$	THF	reflux	7	30
4	$Pd(PPh_3)_4$	THF	reflux	17	10
5	$Pd(PPh_3)_2Cl_2$	THF	reflux	7	72
6	$Pd(PPh_3)_2Cl_2$[b]	THF	reflux	7	55
7	$Pd(CH_3CN)_2Cl_2$	THF	reflux	7	20

[a] Isolated yield.
[b] X-Phos (20 mol%) as a ligand was added.

Table 3
The coupling reaction of **2a** with aryltributylstannane.



Compound	R	Yield (%)[a]
3a	H	72
3b	*p*-CH_3	52
3c	*m*-CH_3	47
3d	*p*-Cl	83
3e	*m*-Cl	81
3f	*m*-OCH_3	33
3g	*p*-F	73
3h	*m*-F	67
3i	*p*-CF_3	75
3j	*m*-CF_3	69

[a] Isolated yield.

with phenylethyne in the presence of $Pd(PPh_3)_2Cl_2$, CuI and triethylamine in DMF at 80 °C for 3 h, but the desired product **3a** was not obtained. The Suzuki-Miyaura reaction of **2a** with phenylboronic acid in the presence of $Pd(OAc)_2$, $Pd(PPh_3)_2Cl_2$ or $Pd(CH_3CN)_2Cl_2$, and base such as K_2CO_3, Na_2CO_3, Cs_2CO_3, or K_3PO_4 provided the homo-coupled product of phenylboronic acid instead of **3a**.

Optimized reaction condition was applied to prepare a variety of the coupled products **3**. Therefore, reactions of **2a** with phenyltributylstannanes substituted with the methyl, chloro, methoxy, fluoro and trifluoromethyl group at ortho-, meta- or para-position of the benzene ring in the presence of 10 mol% $Pd(PPh_3)_2Cl_2$ and 3 equiv. LiBr in THF at reflux for 7 h resulted in the formation of **3b**–**3k** in 32–83% yields. The coupling reaction with phenyltributylstannanes having the methyl or methoxy group at meta- or para position of the benzene ring gave relatively lower yields. However, phenyltributylstannanes having electron-withdrawing group such as fluoro or trifluoromethyl group provided the coupled product in high yields in this reaction. The results of these reactions are summarized in Table 3.

3. Conclusion

In summary, we have developed a general method for the preparation 2,2-difluoro-1-alkynylethenyl tosylate **2** via the Stille coupling reaction between 2,2-difluoro-1-iodoethenyl tosylate **1** with alkynylstannane reagents. Further direct coupling reaction at the tosylate site of **2** with arylstannane reagents via the Stille type reaction afforded the 2-aryl-1,1-difluoro-1,3-enynes **3** in good yields. This method provided an efficient and straightforward preparation of 2-aryl-1,1-difluoro-1,3-enynes via the consecutive Stille cross-coupling reaction at two iodo and tosyl elecrophilic sites of **1**. The coupled products **3** are potentially reactive species toward the nucleophiles to give monofluorinated enynes and also toward the electrophiles to give fluorinated enones. The further synthetic utilities of **3** will be described in the future paper.

4. Experimental

^1H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker AVANCEII^{++} NMR spectrometer with tetramethylsilane (TMS) as an internal standard and ^{19}F NMR spectra were also recorded on a 400 MHz Bruker AVANCEII^{++} NMR spectrometer with $C_6H_5CF_3$ (−63.72 ppm from $CFCl_3$) as an internal standard and the upfield as negative. All chemical shifts (δ) are expressed in parts per million and coupling constant (J) are given in Hertz. Mass spectra were obtained by using Agilent Technologies 6890N GC/5973 Network MSD (EI, 70 eV). Elemental analysis data were obtained by using EA1110 elemental analyzer. Melting points were determined in open capillary tubes and are uncorrected.

Commercially available reagents were purchased from Aldrich, Lancaster, Tokyo Kasei and Fluorochem. All solvents were dried by general purification method. Flash chromatography was performed on 40–60 μm silica gel (230–400 mesh).

4.1. General procedure for the preparation of 1,1-difluoro-1,3-enyn-2-yl p-toluenesulfonates *2*

A 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with $Pd(PPh_3)_4$ (10 mol%), CuI (10 mol%) and 3 mL of THF. The solution of 2,2-difluoro-1-iodoethenyl *p*-toluenesulfonate (0.300 g, 0.833 mmol) and alkynyltributylstannane (1.0 mmol) dissolved in 3 mL of THF was added into the reaction mixture. After the reaction mixture was refluxed for 3 h and then cooled to room temperature, the mixture was quenched with water. The reaction mixture was extracted with ether twice, dried over anhydrous $MgSO_4$ and chromatographed on SiO_2 column. Elution with *n*-hexane and ethyl acetate (4:1) provided 1,1-difluoro-1,3-enyn-2-yl *p*-toluenesulfonates **2**.

4.1.1. 1,1-Difluoro-4-phenylbut-1-en-3-yn-2-yl p-toluenesulfonate (*2a*)

2a was prepared in 83% yield (0.231 g) according to the general procedure. **2a**: yellow solid; mp 70–72 °C; ^1H NMR ($CDCl_3$) δ 7.90 (d, J = 8.4 Hz, 2H), 7.35–7.20 (m, 5H), 7.18 (d, J = 8.4 Hz, 2H), 2.38 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −81.79 (d, J = 11.3 Hz, 1F), −94.54 (d, J = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.3 (dd, J = 303, 295 Hz), 146.0, 132.5, 131.3, 129.8, 129.5, 128.8, 128.3, 120.9, 100.4–99.6 (m), 74.6 (dd, J = 9, 3 Hz), 21.6; MS, m/z (relative intensity) 334 (M^+, 2), 155 (25), 139 (6), 129 (100), 101 (11), 91 (53), 75 (16), 65 (20), 51 (6). Anal. Calcd for $C_{17}H_{12}F_2O_3S$: C, 61.07; H, 3.62. Found: C, 59.89; H, 3.60.

4.1.2. 1,1-Difluoro-4-p-tolylbut-1-en-3-yn-2-yl p-toluenesulfonate (*2b*)

2b was prepared in 72% yield (0.209 g) according to the general procedure. **2b**: yellow oil; ^1H NMR ($CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H),

7.31 (d, J = 8.4 Hz, 2H), 7.10–7.03 (m, 4H), 2.37 (s, 3H), 2.33 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −82.53 (d, J = 11.3 Hz, 1F), −95.13 (d, J = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.3 (dd, J = 303, 295 Hz), 146.1, 140.0, 132.6, 131.3, 129.9, 129.1, 128.9, 128.3, 117.8, 100.7–99.8 (m), 74.0 (dd, J = 9, 3 Hz), 21.6, 21.5; MS, m/z (relative intensity) 348 (M^+, 5), 155 (26), 143 (100), 115 (8), 91 (55), 65 (13). Anal. Calcd for $C_{18}H_{14}F_2O_3S$: C, 62.06; H, 4.05. Found: C, 61.79; H, 4.01.

4.1.3. 4-(3,5-Bis(trifluoromethyl)phenyl)-1,1-difluorobut-1-en-3-yn-2-yl p-*toluenesulfonate (**2c**)*

2c was prepared in 65% yield (0.254 g) according to the general procedure. **2c**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.84 (s, 1H), 7.62 (s, 2H), 7.38 (d, J = 8.2 Hz, 2H), 2.41 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −64.16 (s, 6F), −78.63 (d, J = 7.5 Hz, 1F), −91.90 (d, J = 7.5 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 161.1 (dd, J = 303, 295 Hz), 146.7, 132.7, 132.5, 132.2, 131.3, 130.1, 129.2, 122.5 (q, J = 290 Hz), 100.6–99.5 (m), 78.3 (dd, J = 9, 3 Hz), 21.7; MS, m/z (relative intensity) 470 (M^+, 1), 451 (4), 265 (83), 218 (10), 187 (12), 168 (8), 155 (90), 139 (15), 91 (100), 65 (21). Anal. Calcd for $C_{19}H_{10}F_8O_3S$: C, 48.52; H, 2.14. Found: C, 48.46; H, 2.12.

4.1.4. 1,1-Difluoro-4-(4-methoxyphenyl)but-1-en-3-yn-2-yl p-*toluenesulfonate (**2d**)*

2d was prepared in 70% yield (0.212 g) according to the general procedure. **2d**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 2.39 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −82.65 (d, J = 11.3 Hz, 1F), −95.29 (d, J = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.4 (dd, J = 303, 295 Hz), 146.1, 135.5, 133.6, 133.1, 132.9, 130.2, 129.8, 129.1, 100.6–99.8 (m), 73.6 (dd, J = 9, 3 Hz), 55.8, 22.0; MS, m/z (relative intensity) 364 (M^+, 15), 159 (100), 139 (7), 116 (8), 91 (31), 65 (7). Anal. Calcd for $C_{18}H_{14}F_2O_4S$: C, 59.34; H, 3.87. Found: C, 59.21; H, 3.84.

4.1.5. 1,1-Difluoro-4-(2-methoxyphenyl)but-1-en-3-yn-2-yl p-*toluenesulfonate (**2e**)*

2e was prepared in 70% yield (0.197 g) according to the general procedure. **2e**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 2H), 7.38–7.26 (m, 3H), 7.08–7.06 (m, 1H), 6.88–6.83 (m, 2H), 3.83 (s, 3H), 2.36 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −82.53 (d, J = 11.3 Hz, 1F), −94.63 (d, J = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.3 (dd, J = 306, 295 Hz), 146.0, 133.6, 132.8, 131.3, 129.9, 129.1, 120.5, 110.9, 110.5, 100.8–99.5 (m), 78.5 (dd, J = 9, 3 Hz), 55.9, 21.8; MS, m/z (relative intensity) 364 (M^+, 15), 159 (100), 155 (30), 139 (17), 131 (27), 115 (38), 91 (94), 77 (28), 65 (15). Anal. Calcd for $C_{18}H_{14}F_2O_4S$: C, 59.34; H, 3.87. Found: C, 59.18; H, 3.82.

4.1.6. 1,1-Difluorooct-1-en-3-yn-2-yl p-*toluenesulfonate (**2f**)*

2f was prepared in 79% yield (0.207 g) according to the general procedure. **2f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.86 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 2.46 (s, 3H), 2.16 (t, J = 6.8 Hz, 2H), 1.43–1.26 (m, 4H), 0.87 (t, J = 6.8 Hz, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −84.14 (d, J = 18.8 Hz, 1F), −97.76 (d, J = 18.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.5 (dd, J = 300, 293 Hz), 145.8, 132.7, 130.1, 129.7, 128.7, 128.4, 102.8 (d, J = 9, 5 Hz), 100.0 (dd, J = 48, 39 Hz), 66.4 (dd, J = 9, 3 Hz), 29.8, 21.8, 21.6, 19.0, 13.4; MS, m/z (relative intensity) 314 (M^+, 1), 155 (70), 139 (17), 109 (40), 91 (100), 79 (10), 65 (20). Anal. Calcd for $C_{15}H_{16}F_2O_3S$: C, 57.31; H, 5.13. Found: C, 57.17; H, 5.08.

4.1.7. 1,1-Difluorodec-1-en-3-yn-2-yl p-*toluenesulfonate (**2g**)*

2g was prepared in 73% yield (0.208 g) according to the general procedure. **2g**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 1.65–1.57 (m, 3H), 1.41–1.33 (m, 5H), 0.92 (m, 5H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −84.10 (d, J = 18.8 Hz, 1F), −97.78 (d, J = 18.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.6 (dd, J = 301, 293 Hz), 145.9, 133.0, 129.9, 128.9, 102.8 (d, J = 9, 5 Hz), 100.2 (dd, J = 48, 39 Hz), 66.7 (dd, J = 9, 3 Hz), 31.4, 28.5, 27.9, 22.6, 21.8, 19.5, 14.1; MS, m/z (relative intensity) 342 (M^+, 1), 155 (100), 139 (20), 137 (23), 91 (85), 79 (3), 65 (8). Anal. Calcd for $C_{17}H_{20}F_2O_3S$: C, 59.63; H, 5.89. Found: C, 59.45; H, 5.85.

4.1.8. 1,1-Difluoro-4-(triisopropylsilyl)but-1-en-3-yn-2-yl p-*toluenesulfonate (**2h**)*

2h was prepared in 80% yield (0.276 g) according to the general procedure. **2h**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.85 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 2.45 (s, 3H), 0.98 (d, J = 1.6 Hz, 18H), 0.95–0.90 (m, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −80.70 (d, J = 11.3 Hz, 1F), −94.49 (d, J = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 161.7 (dd, J = 302, 293 Hz), 146.0, 132.8, 130.1, 128.8, 105.0 (d, J = 9, 5 Hz), 100.1 (dd, J = 47, 28 Hz), 91.3 (dd, J = 9, 3 Hz), 21.9, 18.5, 11.1; MS, m/z (relative intensity) 414 (M^+, 1), 371 (100), 269 (45), 261 (18), 205 (14), 155 (15), 139 (19), 91 (28), 77 (5), 65 (3). Anal. Calcd for $C_{20}H_{28}F_2O_3SSi$: C, 57.94; H, 6.81. Found: C, 57.72; H, 6.77.

4.1.9. 1,1-Difluoro-4-(trimethylsilyl)but-1-en-3-yn-2-yl p-*toluenesulfonate (**2i**)*

2i was prepared in 85% yield (0.234 g) according to the general procedure. **2i**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.86 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 2.47 (s, 3H), 0.07 (s, 9H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −80.63 (d, J = 11.3 Hz, 1F), −94.00 (d, J = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 161.5 (dd, J = 302, 293 Hz), 146.1, 132.7, 130.0, 130.0, 107.9 (d, J = 9, 5 Hz), 100.1 (dd, J = 47, 28 Hz), 89.1 (dd, J = 9, 3 Hz), 21.8, −0.7; MS, m/z (relative intensity) 330 (M^+, 1), 155 (50), 139 (17), 125 (45), 91 (100), 73 (20), 65 (30). Anal. Calcd for $C_{14}H_{16}F_2O_3SSi$: C, 50.89; H, 4.88. Found: C, 50.78; H, 4.86.

*4.2. General procedure for the preparation of 2-aryl-1,1-difluoro-4-phenylbut-1-en-3-ynes **3***

A 10 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with $Pd(PPh_3)_2Cl_2$ (10 mol%), LiBr (0.078 g, 0.90 mmol) and 1 mL of THF. The solution of **2a** (0.100 g, 0.30 mmol) and aryltributylstannane (0.45 mmol) dissolved in 2 mL of THF was added into the reaction mixture. After the reaction mixture was refluxed for 7 h and then cooled to room temperature, the mixture was quenched with water. The reaction mixture was extracted with ether twice, dried over anhydrous $MgSO_4$ and chromatographed on SiO_2 column. Elution with n-hexane and ethyl acetate (20:1) provided 2-aryl-1,1-difluoro-4-phenylbut-1-en-3-ynes **3**.

*4.2.1. 1,1-Difluoro-2,4-diphenylbut-1-en-3-yne (**3a**)*

3a was prepared in 72% yield (0.052 g) according to the general procedure. **3a**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.62–7.58 (m, 4H), 7.52–7.38 (m, 3H), 7.35–7.29 (m, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −75.89 (d, J = 3.8 Hz, 1F), −80.47 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.1 (dd, J = 301, 296 Hz), 141.2, 131.5, 130.7, 128.6, 128.4, 127.9, 127.2, 122.7, 94.3 (dd, J = 8, 4 Hz), 82.4 (dd, J = 28, 20 Hz), 80.4 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 240 (M^+, 100), 220 (21), 189 (43), 163 (7), 150 (3), 87 (3), 63 (3), 51 (4). Anal. Calcd for $C_{16}H_{10}F_2$: C, 79.99; H, 4.20. Found: C, 79.83; H, 4.18.

*4.2.2. 1,1-Difluoro-4-phenyl-2-p-tolylbut-1-en-3-yne (**3b**)*

3b was prepared in 52% yield (0.040 g) according to the general procedure. **3b**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.50–7.48 (m, 4H),

7.35–7.32 (m, 3H), 7.21–7.19 (m, 2H), 2.36 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −76.66 (d, J = 3.8 Hz, 1F), −81.06 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.2 (dd, J = 300, 296 Hz), 138.0, 131.8, 129.5, 128.8, 128.6, 127.9, 127.8, 123.1, 94.4 (dd, J = 8, 4 Hz), 82.4 (dd, J = 28, 20 Hz), 80.9 (dd, J = 8, 4 Hz), 21.4; MS, m/z (relative intensity) 254 (M^+, 100), 238 (17), 233 (15), 202 (20), 189 (9), 101 (5), 91 (4). Anal. Calcd for $C_{17}H_{12}F_2$: C, 80.30; H, 4.76. Found: C, 80.02; H, 4.72.

*4.2.3. 1,1-Difluoro-4-phenyl-2-m-tolylbut-1-en-3-yne (**3c**)*

3c was prepared in 47% yield (0.036 g) according to the general procedure. **3c**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.51–7.50 (m, 3H), 7.41–7.27 (m, 4H), 7.14–7.12 (m, 2H), 2.39 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −76.06 (d, J = 3.8 Hz, 1F), −80.56 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.2 (dd, J = 300, 296 Hz), 141.5, 138.5, 131.7, 128.9, 128.7, 128.5, 128.2, 125.2, 124.5, 122.9, 94.5 (dd, J = 8, 4 Hz), 82.5 (dd, J = 28, 20 Hz), 80.8 (dd, J = 8, 4 Hz), 21.7; MS, m/z (relative intensity) 254 (M^+, 100), 238 (16), 233 (17), 202 (19), 189 (8), 101 (5). Anal. Calcd for $C_{17}H_{12}F_2$: C, 80.30; H, 4.76. Found: C, 80.11; H, 4.73.

*4.2.4. 2-(p-Chlorophenyl)-1,1-difluoro-4-phenylbut-1-en-3-yne (**3d**)*

3d was prepared in 83% yield (0.068 g) according to the general procedure. **3d**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.55–7.46 (m, 4H), 7.41–7.34 (m, 5H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −75.15 (d, J = 3.8 Hz, 1F), −79.74 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.3 (dd, J = 300, 296 Hz), 137.8, 134.0, 131.8, 129.3, 129.2, 129.0, 128.6, 122.7, 95.0 (dd, J = 8, 4 Hz), 82.0 (dd, J = 28, 20 Hz), 80.1 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 276 (M^+ + 2, 34), 274 (M^+, 100), 238 (37), 223 (11), 189 (40), 187 (30), 163 (10), 137 (9), 123 (9), 111 (10), 75 (11), 63 (8), 50 (9). Anal. Calcd for $C_{16}H_9ClF_2$: C, 69.96; H, 3.30. Found: C, 69.68; H, 3.27.

*4.2.5. 2-(m-Chlorophenyl)-1,1-difluoro-4-phenylbut-1-en-3-yne (**3e**)*

3e was prepared in 81% yield (0.067 g) according to the general procedure. **3e**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.52–7.50 (m, 1H), 7.48–7.41 (m, 3H), 7.36–7.28 (m, 5H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −74.38 (d, J = 3.8 Hz, 1F), −78.93 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.5 (dd, J = 300, 296 Hz), 134.8, 132.7, 131.8, 129.9, 129.0, 128.5, 128.3, 128.0, 126.1, 122.7, 95.1 (dd, J = 8, 4 Hz), 82.0 (dd, J = 28, 20 Hz), 79.8 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 276 (M^++2, 34), 274 (M^+, 100), 238 (50), 189 (26), 187 (13), 137 (5), 119 (5), 95 (5). Anal. Calcd for $C_{16}H_9ClF_2$: C, 69.96; H, 3.30. Found: C, 69.64; H, 3.26.

*4.2.6. 1,1-Difluoro-2-(m-methoxyphenyl)-4-phenylbut-1-en-3-yne (**3f**)*

3f was prepared in 33% yield (0.027 g) according to the general procedure. **3f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.56–7.54 (m, 2H), 7.39–7.33 (m, 4H), 7.26–7.21 (m, 2H), 6.92–6.90 (m, 1H), 3.87 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −75.50 (d, J = 3.8 Hz, 1F), −79.70 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.5 (dd, J = 300, 296 Hz), 132.2, 131.7, 129.8, 128.8, 128.6, 122.9, 120.4, 113.9, 113.8, 113.6, 94.5 (dd, J = 8, 4 Hz), 82.5 (dd, J = 28, 20 Hz), 80.6 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 270 (M^+, 100), 255 (7), 227 (14), 207 (14), 176 (12). Anal. Calcd for $C_{17}H_{12}F_2O$: C, 75.55; H, 4.48. Found: C, 75.28; H, 4.41.

*4.2.7. 1,1-Difluoro-2-(p-fluorophenyl)-4-phenylbut-1-en-3-yne (**3g**)*

3g was prepared in 73% yield (0.057 g) according to the general procedure. **3g**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.59–7.56 (m, 1H), 7.52–7.49 (m, 3H), 7.38–7.36 (m, 2H), 7.13–7.06 (m, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −76.29 (d, J = 3.8 Hz, 1F), −80.97 (d, J = 3.8 Hz, 1F), −114.55 (m, 1F); ^{13}C NMR ($CDCl_3$) δ 162.5 (d, J = 247 Hz), 159.2 (dd, J = 300, 296 Hz), 136.6, 131.8, 129.8, 128.7, 126.8, 122.8, 115.8, 94.8 (dd, J = 8, 4 Hz), 81.9 (dd, J = 28, 20 Hz), 80.4 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 258 (M^+, 100), 238 (19), 207 (76), 181 (13), 75 (10), 63 (10), 51 (12). Anal. Calcd for $C_{16}H_9F_3$: C, 74.42; H, 3.51. Found: C, 74.13; H, 3.45.

*4.2.8. 1,1-Difluoro-2-(m-fluorophenyl)-4-phenylbut-1-en-3-yne (**3h**)*

3h was prepared in 67% yield (0.052 g) according to the general procedure. **3h**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.52–7.50 (m, 2H), 7.45–7.36 (m, 5H), 7.08–6.99 (m, 2H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −74.43 (d, J = 3.8 Hz, 1F), −78.81 (d, J = 3.8 Hz, 1F), −113.54 (m, 1F); ^{13}C NMR ($CDCl_3$) δ 163.0 (d, J = 244 Hz), 159.5 (dd, J = 300, 296 Hz), 133.1, 131.8, 130.3, 128.6, 123.6, 122.9, 115.0, 114.9, 114.1, 95.0 (dd, J = 8, 4 Hz), 81.2 (dd, J = 28, 20 Hz), 79.9 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 258 (M^+, 100), 238 (21), 207 (50), 181 (5), 103 (4). Anal. Calcd for $C_{16}H_9F_3$: C, 74.42; H, 3.51. Found: C, 74.20; H, 3.47.

*4.2.9. 1,1-Difluoro-2-(p-trifluoromethyl)phenyl-4-phenylbut-1-en-3-yne (**3i**)*

3i was prepared in 75% yield (0.069 g) according to the general procedure. **3i**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.52–7.50 (m, 2H), 7.75–7.71 (m, 4H), 7.67–6.65 (m, 2H), 7.53–7.50 (m, 1H), 7.37–7.35 (m, 2H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −63.85 (s, 3F), −73.53 (d, J = 3.8 Hz, 1F), −78.57 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.7 (dd, J = 300, 296 Hz), 134.7, 132.2, 131.8, 130.3, 129.1, 128.7, 126.6, 122.8, 95.2 (dd, J = 8, 4 Hz), 82.0 (dd, J = 28, 20 Hz), 79.6 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 308 (M^+, 100), 289 (10), 257 (13), 238 (34), 189 (17), 119 (7). Anal. Calcd for $C_{17}H_9F_5$: C, 66.24; H, 2.94. Found: C, 66.02; H, 2.92.

*4.2.10. 1,1-Difluoro-2-(m-trifluoromethyl)phenyl-4-phenylbut-1-en-3-yne (**3j**)*

3j was prepared in 69% yield (0.064 g) according to the general procedure. **3j**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.87–7.78 (m, 3H), 7.65–7.41 (m, 4H), 7.37–7.34 (m, 2H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ −63.86 (s, 3F), −74.19 (d, J = 3.8 Hz, 1F), −79.16 (d, J = 3.8 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.6 (dd, J = 300, 296 Hz), 140.8, 131.8, 131.2, 130.7, 129.8, 129.3, 128.7, 125.0, 124.8, 122. 6, 95.4 (dd, J = 8, 4 Hz), 82.1 (dd, J = 28, 20 Hz), 79.7 (dd, J = 8, 4 Hz); MS, m/z (relative intensity) 308 (M^+, 100), 289 (7), 257 (12), 238 (30), 189 (19), 119 (7). Anal. Calcd for $C_{17}H_9F_5$: C, 66.24; H, 2.94. Found: C, 66.10; H, 2.93.

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