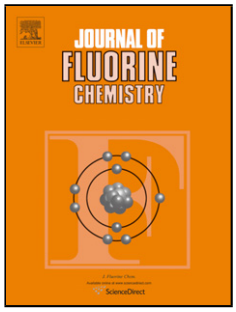

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Cross-coupling of 1,1-difluoro-1-en-3-yn-2-yl tosylates with arylboronic acids: A new approach to 2-aryl-1,1-difluoro-1,3-enynes

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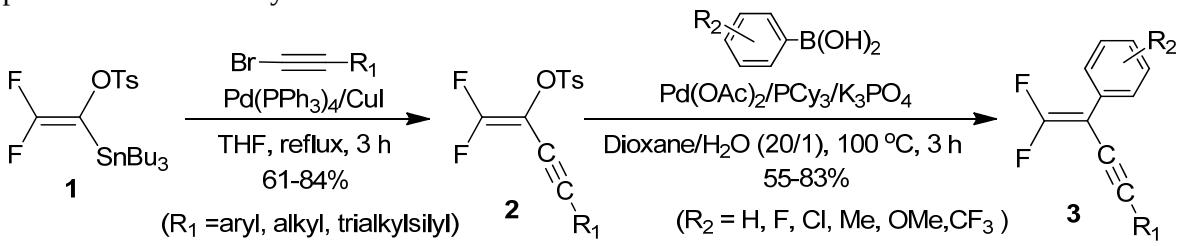
Graphical abstract

Alkynylation reaction of 2,2-difluoro-1-tributylstannylethenyl *p*-toluenesulfonate **1** with alkynyl bromides 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 61-84% yields. The further arylation reaction of **2** with arylboronic acids in the presence of 2 mol% $Pd(OAc)_2$, 4 mol% PCy_3, K_3PO_4 (1.7 equiv) in dioxane /H_2O (20/1) at 100 °C for 3 h afforded the coupled products **3** in 55-83% yields.



Highlights

1. Cross-coupling of 2,2-difluoro-1-tributylstannylethenyl *p*-toluenesulfonate with alkynyl bromides
2. Arylation of 1,1-difluoro-1,3-enynyl tosylates with arylboronic acids
3. Use of less toxic arylboronic acids for the cross-coupling of 1,1-difluoro-1-en-3-yn-2-yl tosylates
4. Efficient and straightforward preparation of 2-aryl-1,1-difluoro-1,3-enynes

Abstract

The palladium-catalyzed direct alkynylation of 2,2-difluoro-1-tributylstannylethenyl *p*-toluenesulfonate **1** with alkynyl bromides provided the corresponding 1,1-difluoro-1,3-enynyl tosylates **2** in good yields. The Suzuki-Miyaura arylation reaction of **2** with arylboronic acids afforded the cross-coupled products , 2-aryl-1,1-difluoro-1,3-enynes **3**, in good yields.

Keywords : 2,2-difluoro-1-tributylstannylethenyl *p*-toluenesulfonate, alkynyl bromides, 1,1-difluoro-1,3-enynyl tosylates, arylboronic acids

1. Introduction

1,3-Enyne functional group is an important structural frame in many natural products[1-3] and pharmaceuticals,[4-6] and also was transformed to useful functional group in the multifunctional molecules and material sciences.[7-10] Of particular interests in 1,3-enynes are fluorine-containing conjugated enynes which would be important building blocks for the synthesis of fluorinated compounds having unique biological and physical properties.[11-13] Especially, pharmaceutical application of fluorine-containing compounds have been well reviewed in recent years.[14,15] Although various methods for the preparation of nonfluorinated 1,3-enynes have been well established in the previous literatures,[16] there are only limited reports on the synthesis of fluorinated 1,3-enynes and most of them described the synthesis of 1,2-difluorinated[17,18] or monofluorinated 1,3-enynes.[19-22] Especially, the synthesis of 1,1-difluoro-1,3-enyne derivatives which have high reactivity at *gem*-difluorinated vinyl carbon was scarcely 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.[23] Transition-metal catalyzed cross-coupling reactions between 2,2-difluoroethenyl building blocks and alkynyl coupling partners are straightforward process to give 1,1-difluoro-1,3-enynes. For example, 1,1-difluoro-1,3-enynes were prepared from the cross-coupling of 1,1-difluorovinyl iodides with alkynylzinc chloride[24] or terminal alkynes[25,26] in the presence of Pd catalyst. Ichikawa et al. synthesized 2-alkylated 1,1-difluoro-1,3-enynes via the cross-coupling of 1-alkyl-2,2-difluorovinylboranes with 1-halo-1-alkynes in the presence of cuprous iodides.[27] Hammond et al. reported that the Pd-catalyzed reaction of *gem*-difluorohomoallenyl bromide with terminal alkynes provided the

corresponding 1,1-difluoro-1,3-enynes.[28] We also prepared 1,1-difluoro-2-phenyl-1,3-enynes from the cross-coupling of 2,2-difluoro-1-phenylethenylstannane with alkynyl iodides in the presence of catalytic amount of $Pd(PPh_3)_4$ and CuI.[29] We reported that 2-arylated 1,1-difluoro-1,3-enynes were prepared from the palladium-catalyzed cross-coupling of 1,1-difluoro-1-en-3-yn-2-yl tosylates with arylstannane reagents.[30] Wang et al. carried out the Cu(I)-catalyzed cross-coupling of terminal alkynes with trifluoromethyl ketone *N*-tosylhydrazones to afford 1,1-difluoro-1,3-enynes.[31] However, the previous methods still have several limitations such as low yield preparation of the products, use of unstable vinylmetal reagents, lack of generality, use of toxic stannyl group and tedius procedure for the synthesis of starting material. Herein, we wish to report the preparation of 2-aryl-1,1-difluoro-1,3-enynes via the cross-coupling of 1,1-difluoro-1-en-3-yn-2-yl tosylates **2** with relatively less toxic arylboronic acids in the presence of Pd catalyst and base.

2. Results and discussion

Although 1,1-difluoro-1-en-3-yn-2-yl tosylates can be prepared from the Pd-catalyzed cross-coupling of 2,2-difluoro-1-iodoethenyl tosylate with alkynylstannanes,[30] we performed the Pd-catalyzed cross-coupling of 2,2-difluoro-1-tributylstannylethenyl tosylate **1**[32] with alkynyl bromides because the latter method would be efficient and high yield preparation of **2**. Thus, the reaction of **1** with phenylethynyl bromide in the presence of 10 mol% $Pd(PPh_3)_4$ and 10 mol% CuI in THF provided the corresponding 1,1-difluoro-1,3-enynes **2** in 61-84% yields. The results for the preparation of **2** were summarized in Table 1. The use of alkynyl iodides in this cross-coupling reaction resulted in the formation of homocoupled diynes as a major product. This result is speculated that transmetallation process in catalytic cycle is relatively slower than self-dimerization after oxidative insertion of alkynyl iodides with Pd catalyst.

Although a couple of cross-coupling reactions of fluorinated alkenyl tosylate with arylboronic acids in the presence of Pd catalyst have been previously reported,[33,34] we recently developed the cross-coupling of 2,2-difluoro-1-iodoethenyl tosylate with arylboronic acids in the presence of Pd catalyst to give 2,2-difluoro-1-arylethenyl tosylates or 2,2-difluoro-1,1-diarylethenes.[35] In the course of our studies on the cross-coupling of *gem*-difluorinated alkene, we extended to examine the reactivity of cross-coupling of 1,1-difluoro-1,3-enynyl tosylates **2** with arylboronic acids. When **2a** was treated with phenylboronic acid (1.2 equiv) in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol%) and Cs_2CO_3 (1.7 equiv) in MeOH at room temperature for 12 hours, the desired product **3a** was not observed at all. A couple of catalysts was examined to promote the cross-coupling of **2a** with phenylboronic acid. The use of Pd catalysts such as $Pd(OAc)_2$ or $Pd_2(dba)_3$ in the same reaction also did not provide the coupled product, either. We also screened the effect of bases such as Na_2CO_3 or K_3PO_4, but no coupled product was formed. However, when **2a** was reacted with phenylboronic acid (1.2 equiv) in the presence of $Pd(OAc)_2$ (2 mol%), PCy_3 (4 mol%) and K_3PO_4(1.7 equiv) in dioxane at 100 ^oC for 14 hours, the coupled product **3a**, along with homocoupled product of phenylboronic acid, was obtained in only 28% yield based on the conversion of starting material. According to this result, it is

speculated that the use of bulky ligand such as PCy_3 has an effect on the reaction process. However, the use of other ligands such as X-Phos, S-Phos or dppp did not provide the coupled product **3a**. The increase of amount of catalyst and ligand resulted in the decrease of yield of the coupled product **3a**. Addition of small amount of water into dioxane (dioxane : water = 20 :1) to resolve K_3PO_4 and phenylboronic acid in the same reaction dramatically caused not only to increase the yield of **3a** up to 70%, but also decrease the reaction time to 3 hours. However, the use of quite excess of water (dioxane : water = 3:1) in this reaction, the desired product **3a** was not formed at all, but homocoupled product of phenylboronic acid was formed as a major product. Reaction temperature was also important to the yield of **3a**. Therefore, when the reaction was performed at 50 ^oC under the same reaction conditions, **3a** was obtained in only 24% yield. The results of the optimization for the formation of the coupled product **3a** were summarized in Table 2.

Optimized reaction condition was applied to prepare a variety of the coupled products **3**. Therefore, the reactions of **2a** with a variety of arylboronic acids having electron-withdrawing group such as fluoro, chloro or trifluoromethyl as well as electron-donating group such as methyl or methoxy on the *meta*- or *para*-position of benzene ring under the same reaction conditions gave the corresponding 2-arylated 1,1-difluoro-1,3-enynes **3b-3k** in 55-83% yields. However, the reaction of **2a** with *ortho*-substituted arylboronic acids such as *ortho*-methylphenylboronic acid afforded the trace amount of product **3l**. The results of the coupling reaction between **2a** and arylboronic acids were summarized in Table 3.

3. Conclusion

In summary, we have developed a general and efficient method for the preparation of 1,1-difluoro-1-en-3-yn-2-yl tosylates **2** which were prepared in high yields from the palladium-catalyzed cross-coupling of 2,2-difluoro-1-tributylstannylethenyl tosylate with alkynyl bromides. The use of alkynyl iodides in this reaction resulted in the formation of dimerized product of alkynyl iodides. Further Suzuki-Miyaura cross-coupling of **2** with less toxic arylboronic acids in the presence of $Pd(OAc)_2$ catalyst, PCy_3 ligand, and K_3PO_4 salt afforded the corresponding 2-aryl-1,1-difluoro-1,3-enynes in good yields. This latter reaction is the first example of Suzuki-Miyaura cross-coupling in the 1,1-difluoro-1,3-enynyl tosylate system.

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 constants (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-tributylstannylethenyl *p*-toluenesulfonate (0.200 g, 0.382 mmol) and alkynyl bromide (0.450 mmol) dissolved in 3 mL of THF was added into the reaction mixture. After the reaction mixture was refluxed for 3 hours 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**.

The characterization data (^1H and ^{13}C NMR, Mass) for compounds **2a-e** and **2h-k** have been previously reported.[30]

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

2a was prepared in 78% yield (0.100 g) according to the general procedure. Anal. Calcd for $C_{17}H_{12}F_2O_3S$: C, 61.07; H, 3.62. Found: C, 60.81; H, 3.57.

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

2b was prepared in 68% yield (0.090 g) according to the general procedure. Anal. Calcd for $C_{18}H_{14}F_2O_3S$: C, 62.06; H, 4.05. Found: C, 61.83; H, 3.98.

*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 84% yield (0.151 g) according to the general procedure. Anal. Calcd for $C_{19}H_{10}F_8O_3S$: C, 48.52; H, 2.14. Found: C, 48.43; H, 2.09.

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

2d was prepared in 62% yield (0.086 g) according to the general procedure. Anal. Calcd for $C_{18}H_{14}F_2O_4S$: C, 59.34; H, 3.87. Found: C, 59.11; H, 3.81.

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

2e was prepared in 61% yield (0.085 g) according to the general procedure. Anal. Calcd for $C_{18}H_{14}F_2O_4S$: C, 59.34; H, 3.87. Found: C, 59.11; H, 3.82.

*4.1.6. 1,1-Difluoro-4-(4-chlorophenyl)but-1-en-3-yn-2-yl p-toluenesulfonate (**2f**)*

2f was prepared in 72% yield (0.101 g) according to the general procedure. **2f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.37-7.22 (m, 4H), 7.11-7.07 (m, 2H), 2.42 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ -80.57 (d, *J* = 7.5 Hz, 1F), -93.51 (d, *J* = 7.5 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.7 (dd, *J* = 302, 301 Hz), 146.4, 134.4, 132.7, 131.4, 130.3, 129.9, 129.6, 129.1, 128.6, 122.8, 100.4, 98.8 (dd, J = 9, 7 Hz), 75.9 (dd, *J* = 9, 3 Hz), 21.9; MS, m/z (relative intensity) 368 (M^+, 2), 163 (64), 139 (10), 91 (100), 75 (6), 65 (26). Anal. Calcd for $C_{17}H_{11}ClF_2O_3S$: C, 55.37; H, 3.01. Found: C, 55.15; H, 3.05.

*4.1.7. 1,1-Difluoro-4-(4-trifluoromethylphenyl)but-1-en-3-yn-2-yl p-toluenesulfonate (**2g**)*

2g was prepared in 79% yield (0.121 g) according to the general procedure. **2g**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.36-7.31 (m, 4H), 2.40 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ -79.87 (d, *J* = 11.3 Hz, 1F), -79.87 (s, 3F), -92.77 (d, *J* = 11.3 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 160.7 (dd, *J* = 302, 296 Hz), 146.3, 132.5, 131.4, 130.2, 129.1, 128.6, 125.4, 122.4, 101.2 (dd, J = 59, 50 Hz), 99.4, 30.4, 21.8; MS, m/z (relative intensity) 402 (M^+, 1), 383 (6), 197 (77), 155 (41), 139 (10), 91 (100), 65 (31). Anal. Calcd for $C_{18}H_{11}F_5O_3S$: C, 53.74; H, 2.76. Found: C, 53.61; H, 2.74.

*4.1.8. 1,1-Difluorooct-1-en-3-yn-2-yl p-toluenesulfonate (**2h**)*

2h was prepared in 75% yield (0.090 g) according to the general procedure. Anal. Calcd for $C_{15}H_{16}F_2O_3S$: C, 57.31; H, 5.13. Found: C, 57.07; H, 5.06.

*4.1.9. 1,1-Difluorodec-1-en-3-yn-2-yl p-toluenesulfonate (**2i**)*

2i was prepared in 71% yield (0.093 g) according to the general procedure. Anal. Calcd for $C_{17}H_{20}F_2O_3S$: C, 59.63; H, 5.89. Found: C, 59.47; H, 5.83.

*4.1.10. 1,1-Difluoro-4-(triisopropylsilyl)but-1-en-3-yn-2-yl p-toluenesulfonate (**2j**)*

2j was prepared in 74% yield (0.117 g) according to the general procedure. Anal. Calcd for $C_{20}H_{28}F_2O_3SSi$: C, 57.94; H, 6.81. Found: C, 57.59; H, 6.72.

*4.1.11. 1,1-Difluoro-4-(trimethylsilyl)but-1-en-3-yn-2-yl p-toluenesulfonate (**2k**)*

2k was prepared in 76% yield (0.096 g) according to the general procedure. Anal. Calcd for $C_{14}H_{16}F_2O_3SSi$: C, 50.89; H, 4.88. Found: C, 50.68; H, 4.83.

*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 $Pd(OAc)_2$ (2 mol%), PCy_3 (4 mol%), K_3PO_4 (0.51 mmol) and 1 mL of dioxane/H_2O (20/1). The solution of **2a** (0.100 g, 0.30 mmol) and arylboronic acid (0.36 mmol) dissolved in 2 mL of dioxane/H_2O (20/1) was added into the reaction mixture. After the reaction mixture was heated at 100 ^oC for 3 hours 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**.

The characterization data (^1H and ^{13}C NMR, Mass) for compounds **3a-e** and **3g-k** have been previously reported.[30]

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

3a was prepared in 70% yield (0.050 g) according to the general procedure. Anal. Calcd for $C_{16}H_{10}F_2$: C, 79.99; H, 4.20. Found: C, 79.71; H, 4.14.

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

3b was prepared in 61% yield (0.046 g) according to the general procedure. Anal. Calcd for $C_{17}H_{12}F_2$: C, 80.30; H, 4.76. Found: C, 80.01; H, 4.70.

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

3c was prepared in 59% yield (0.045 g) according to the general procedure. Anal. Calcd for $C_{17}H_{12}F_2$: C, 80.30; H, 4.76. Found: C, 80.05; H, 4.71.

*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. Anal. Calcd for $C_{16}H_9ClF_2$: C, 69.96; H, 3.30. Found: C, 69.65; H, 3.25.

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

3e was prepared in 80% yield (0.066 g) according to the general procedure. Anal. Calcd for $C_{16}H_9ClF_2$: C, 69.96; H, 3.30. Found: C, 69.57; H, 3.34.

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

3f was prepared in 64% yield (0.052 g) according to the general procedure. **3f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.54-7.49 (m, 3H), 7.38-7.33 (m, 3H), 7.27-7.25 (m, 1H), 6.94-6.90 (m, 2H), 3.83 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $C_6H_5CF_3$) δ -77.56 (d, *J* = 7.5 Hz, 1F), -81.90 (d, *J* = 7.5 Hz, 1F); ^{13}C NMR ($CDCl_3$) δ 159.5 (dd, *J* = 300, 296 Hz), 134.4, 131.7, 130.1, 129.3, 128.9, 128.7, 128.6, 123.1, 114.4, 114.3, 94.4 (dd, *J* = 8, 4 Hz), 82.5 (dd, *J* = 28, 20 Hz), 80.6 (dd, *J* = 8, 4 Hz), 55.6; MS, m/z (relative intensity) 270 (M^+, 100), 255 (5), 225 (7), 207 (16), 176 (11), 151 (10), 135 (9), 110 (15). Anal. Calcd for $C_{17}H_{12}F_2O$: C, 75.55; H, 4.48. Found: C, 75.21; H, 4.43.

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

3g was prepared in 55% yield (0.045 g) according to the general procedure. Anal. Calcd for $C_{17}H_{12}F_2O$: C, 75.55; H, 4.48. Found: C, 75.18; H, 4.42.

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

3h was prepared in 82% yield (0.063 g) according to the general procedure. Anal. Calcd for $C_{16}H_9F_3$: C, 74.42; H, 3.51. Found: C, 74.15; H, 3.46.

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

3i was prepared in 77% yield (0.060 g) according to the general procedure. Anal. Calcd for $C_{16}H_9F_3$: C,

74.42; H, 3.51. Found: C, 74.18; H, 3.46.

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

3j was prepared in 76% yield (0.070 g) according to the general procedure. Anal. Calcd for $C_{17}H_9F_5$: C, 66.24; H, 2.94. Found: C, 65.92; H, 2.89.

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

3k was prepared in 70% yield (0.065 g) according to the general procedure. Anal. Calcd for $C_{17}H_9F_5$: C, 66.24; H, 2.94. Found: C, 65.98; H, 2.91.

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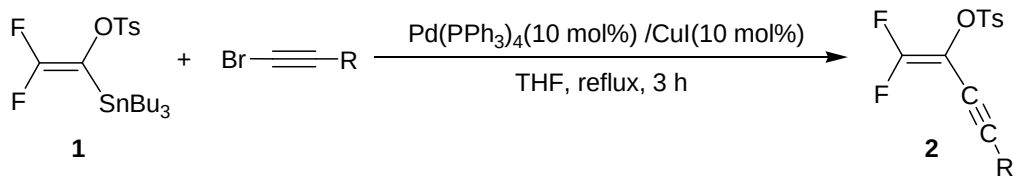
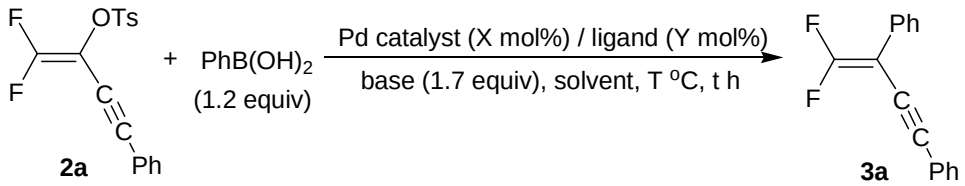
Table 1. The preparation of 1,1-difluoro-1-en-3-yn-2-yl tosylates **2**



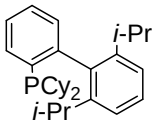
Compound	R	Yield (%)[a]
2a	C_6H_5	78
2b	*p*-$CH_3C_6H_4$	68
2c	3,5-$(CF_3)_2C_6H_3$	84
2d	*p*-$CH_3OC_6H_4$	62
2e	*o*-$CH_3OC_6H_4$	61
2f	*p*-ClC_6H_4	72
2g	*p*-$CF_3OC_6H_4$	79
2h	*n*-C_4H_9	75
2i	*n*-C_6H_{13}	71
2j	(*i*-Pr)$_3$Si	74
2k	Me_3Si	76

[a]Isolated yield.

Table 2. Optimization for the formation of the coupled product **3a**



Entry	Pd Catalyst (X)	ligand (Y)	base	Solvent	*T* (°C)	*t* (h)	Yield (%)[a]
1	$Pd(PPh_3)_2Cl_2$ (5)	–	Cs_2CO_3	MeOH	25	12	0
2	$Pd_2(dba)_3$ (5)	–	Cs_2CO_3	MeOH	25	12	0
3	$Pd(OAc)_2$ (5)	–	Cs_2CO_3	MeOH	25	12	0
4	$Pd(OAc)_2$ (5)	–	Na_2CO_3	MeOH	25	12	0
5	$Pd(OAc)_2$ (5)	–	K_3PO_4	MeOH	25	12	0
6	$Pd(OAc)_2$ (2)	PCy_3 (4)	K_3PO_4	Dioxane	100	14	28
7	$Pd(OAc)_2$ (5)	PCy_3 (10)	K_3PO_4	Dioxane	100	14	21
8	$Pd(OAc)_2$ (10)	PCy_3 (20)	K_3PO_4	Dioxane	100	14	18
9	$Pd(OAc)_2$ (2)	X-Phos[b] (4)	K_3PO_4	Dioxane	100	14	0
10	$Pd(OAc)_2$ (2)	S-Phos[c] (4)	K_3PO_4	Dioxane	100	14	0
11	$Pd(OAc)_2$ (2)	dppp (4)	K_3PO_4	Dioxane	100	14	0
12	$Pd(OAc)_2$ (2)	PCy_3 (4)	K_3PO_4	Dioxane/H_2O (20/1)	100	3	70
13	$Pd(OAc)_2$ (2)	PCy_3 (4)	Na_2CO_3	Dioxane/H_2O (20/1)	100	3	45
14	$Pd(OAc)_2$ (2)	PCy_3 (4)	Cs_2CO_3	Dioxane/H_2O (20/1)	100	3	56
15	$Pd(OAc)_2$ (2)	PCy_3 (4)	K_3PO_4	Dioxane/H_2O (3/1)	100	3	0
16	$Pd(OAc)_2$ (2)	PCy_3 (4)	K_3PO_4	Dioxane/H_2O (20/1)	50	14	24

[a]Isolated yield. [b]X-Phos = 

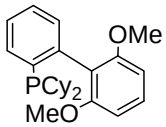
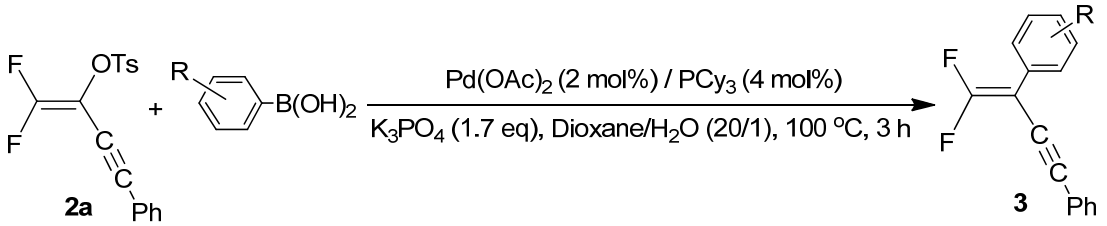
[c]S-Phos = 

Table 3. The coupling reaction of **2a** with arylboronic acids



Compound	R	Yield (%)[a]
3a	H	70
3b	*p*-CH_3	61
3c	*m*-CH_3	59
3d	*p*-Cl	83
3e	*m*-Cl	80
3f	*p*-OCH_3	64
3g	*m*-OCH_3	55
3h	*p*-F	82
3i	*m*-F	77
3j	*p*-CF_3	76
3k	*m*-CF_3	70

[a]Isolated yield.