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A Novel Synthesis of Disubstituted 1,1-Difluoro-1-alkenes by Using 2,2,2-Trifluoroethyl *p*-Toluenesulfonate as a Difluorovinylidene Unit

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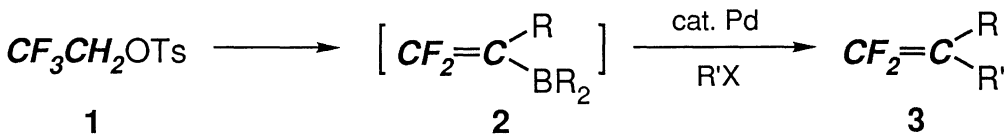
2,2,2-Trifluoroethyl *p*-toluenesulfonate is treated with lithium diisopropylamide and trialkylboranes successively to generate 1-alkyl-2,2-difluorovinylboranes, which in turn couple with aryl iodides in the presence of palladium catalyst and tetrabutylammonium fluoride to afford disubstituted 1,1-difluoro-1-alkenes in good yields.

Fluoroolefins are an unique class with a reactive carbon-carbon double bond toward both nucleophiles and radical species.1) Because of their versatility for introducing fluorinated carbon units, the synthesis of fluoroolefins by a general method is a highly desirable goal. Recently we have reported the synthesis of monosubstituted 1,1-difluoro-1-alkenes from 2,2,2-trifluoroethyl *p*-toluenesulfonate (**1**) by the introduction of an alkyl group at a 2,2-difluorovinylic position using trialkylboranes.2) This reaction proceeds *via* intermediary 1-alkyl-2,2-difluorovinylboranes **2**, which prompted us to investigate the further introduction of a carbon substituent onto the vinylic carbon bearing a boryl group by a palladium-catalyzed coupling reaction.3) As illustrated below, this scheme affords disubstituted 1,1-difluoro-1-alkenes (**3**)4) and might be a general method for preparing a wide variety of **3**. The feature of this method is that two different carbon substituents (R and R') can be selected independently and attached to a difluorovinylidene unit successively, that is, the carbon framework of **3** could be constructed at will in this process.



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Isolated dibutyl(1-butyl-2,2-difluorovinyl)borane (**2a**, R=^{n}Bu) prepared from **1** was treated with iodobenzene in the presence of a catalytic amount of dichlorobis(triphenylphosphine)palladium(II) and sodium methoxide in refluxing tetrahydrofurane (THF),[3a] which resulted in the coupling of both the alkenyl and the alkyl moieties on boron atom with iodobenzene to give the desired difluoroalkene **3a** (R=^{n}Bu) and butylbenzene, respectively in a 2:1 ratio. In examining several bases other than sodium methoxide, we found that

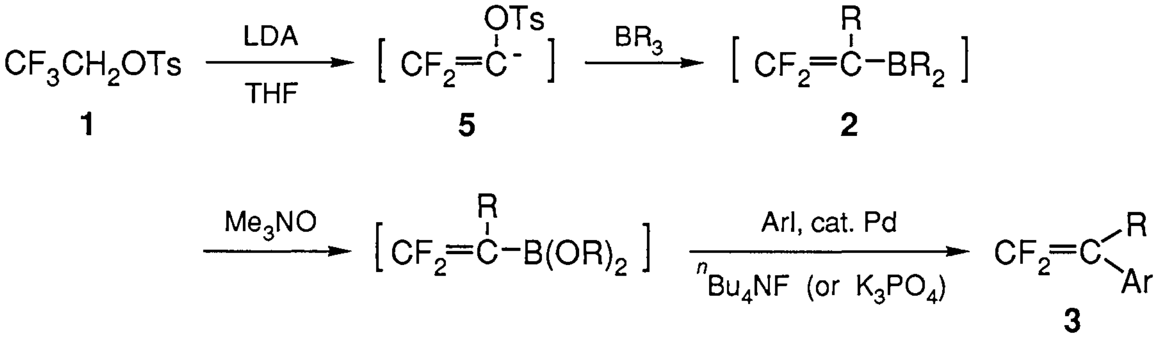


Table 1. One-pot Synthesis of Disubstituted 1,1-Difluoro-1-alkenes[a]

Entry	R	Ar	Additive	Yield of **3**/%[b]
1	^{n}Bu	C_6H_5	^{n}Bu$_4$NF	86
2		*p*-MeC$_6$H$_4$	^{n}Bu$_4$NF	64
3		*p*-MeOC$_6$H$_4$	^{n}Bu$_4$NF	71
4		*p*-NH$_2$C$_6$H$_4$	^{n}Bu$_4$NF	73
5		*o*-NH$_2$C$_6$H$_4$	^{n}Bu$_4$NF	63
6		*p*-NO$_2$C$_6$H$_4$	K$_3$PO$_4$[c]	75[d]
7		1-C$_{10}$H$_7$	^{n}Bu$_4$NF	83[d]
8	^{sec}Bu	C_6H_5	^{n}Bu$_4$NF	63[d]

a) Unless otherwise noted, all reactions were carried out under the conditions described in the text. Molar ratio of **1** : ArI : Additive = 1.3 : 1 : 4.

b) Isolated yield. All compounds were fully characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, IR, and Mass spectra.

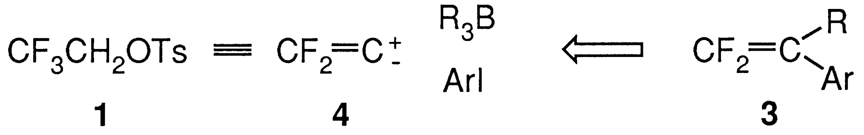
c) When ^{n}Bu$_4$NF was employed instead of K$_3$PO$_4$, the addition of fluoride ion to the desired alkene **3** occurred to yield 1,1,1-trifluoro-2-*p*-nitrophenylhexane.

d) Yield by ^{19}F NMR relative to an internal $C_6H_5CF_3$ standard.

tetrabutylammonium fluoride[5)] and potasium phosphate[6)] were effective for the coupling reaction, and tetrabutylammonium fluoride suppressed the formation of butylbenzene to a favorable extent.

Furthermore, the selective oxidation of alkyl-boron bond in **2** was tried in order to avoid the participation of alkyl moiety in the coupling reaction. Treatment of **2a** with trimethylamine oxide [7)] prior to the coupling reaction caused no formation of buthylbenzene to give **3a** selectively in a good yield. Then, the procedure thus obtained was applied to the synthesis of **3a** from **1** in a one-pot operation. The generation of **2a** from **1** and tributylborane[2)] followed by the successive oxidation and coupling reaction afforded **3a** in 86% isolated yield.

In a similar manner, several other disubstituted 1,1-difluoro-1-alkenes were synthesized from **1** in good yields as summarized in Table 1. This sequence of reactions provides a general method for the introduction of two different carbon substituents, each one of alkyl and aryl groups, onto difluorovinylidene unit in different polarities, and **1** turns out to function as a difluorovinylidene synthon **4**.



A typical reaction procedure is described for the synthesis of 1,1-difluoro-2-phenyl-1-hexene (**3a**); **1** (160 mg, 0.63 mmol) in THF (1 ml) was added dropwise to a THF solution (2 ml) of lithium diisopropylamide (LDA, 1.32 mmol) at -78 °C under an argon atomosphere. The reaction mixture was stirred for 30 min at -78 °C to generate 2,2-difluoro-1-tosyloxyvinyllithium (**5**),[8)] and then treated with tributylborane (0.69 ml, 1.0 M in THF, 0.69 mmol) at -78 °C. After being stirred for 1 h at -78 °C, the mixture was brought to room temperature and stirred for an additional 3 h. The vinylborane solution thus obtained was treated with solid trimethylamine oxide (117 mg, 1.56 mmol) at 0 °C and stirred for 1 h at that temperature. To the resulting solution were added the palladium catalyst generated from dichlorobis(triphenylphosphine)palladium(II) (44 mg, 0.063 mmol) and butylithium (0.077 ml, 1.63 M in hexane, 0.126 mmol) in THF (1 ml), iodobenzene (53 µl, 0.47 mmol), and tetrabutylammonium fluoride (1.89 ml, 1.0M in THF, 1.89 mmol) successively at room temperature. After stirring for 12 h at 50 °C, the reaction mixture was quenched with water. Usual workup followed by thin-layer chromatography on silica gel (hexane) gave **3a** (80 mg, 86%).[9)]

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9) **3a**: IR (neat) 1725, 1230, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=0.87$ (3H, m), 1.08-1.46 (4H, m), 2.20-2.49 (2H, m), and 7.31 (5H, br s); ^{19}F NMR ($CDCl_3/C_6F_6$) 69.7 ppm (2F, t, $J_{FH}=2$ Hz); ^{13}C NMR ($CDCl_3$) $\delta=13.8$, 22.1, 27.4, 29.9 (t, $J_{CF}=2$ Hz), 92.5 (t, $J_{CF}=18$ Hz), 127.2, 128.3 (t, $J_{CF}=3$ Hz), 128.4, 133.9 and 153.6 (t, $J_{CF}=288$ Hz); MS (75 ev) *m/z* (rel intensity) 196 (M^+; 41), 154 (100), 153 (24), 133 (15), 127 (12), and 103 (27); Found: *m/z* 196.1062. Calcd for $C_{12}H_{14}F_2$: M, 196.1063.

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