CFC- or HFC-Free Approach to α-Substituted β,γ,γ-Trifluoroallyl Alcohols by the Reaction of β-Fluoro-β-trifluoromethylated Enol Tosylate with Grignard Reagents

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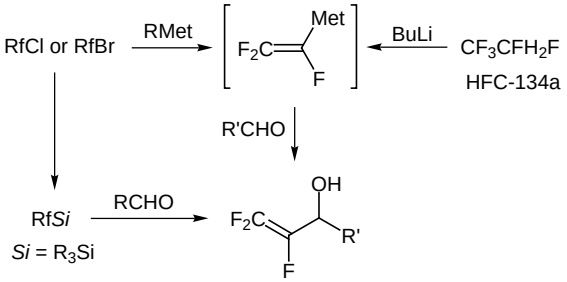
Abstract: The reaction of β-fluoro-β-trifluoromethylated enol tosylate with Grignard reagents giving the corresponding β,γ,γ-trifluoroallyl alcohols as well as heteropoly acid-mediated ethanolysis of the allyl alcohols affording (*Z*)-β-substituted α-fluoro-α,β-unsaturated esters is described.

Key words: fluorine, trifluoromethyl, Grignard reaction, sulfonates, cleavage, nucleophilic additions, alcohols, esters

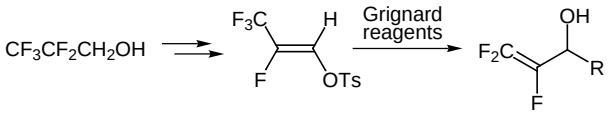
Trifluoroallyl alcohols are one of the most useful intermediate in organofluorine chemistry.[1] Although there are several accesses to these compounds, previous methods suffer from the use of chlorofluorocarbon (CFC)[2] or bromofluorocarbon[3] as starting substrates, which will not be able to be used in the future according to the protocol of Montreaol. Fluoroalkylsilanes are also usable for the synthesis of title products. But bromofluoroalkylcarbons are essential for the preparations of the silanes.[4] Recently, Burdon had found that 1,1,1,2-tetrafluoroethane (HFC-134a) can be employed as a precursor of tetrafluorovinyllithium spieces,[5] and Burdon and Percy have extended its synthetic utilizations for the synthesis of aliphatic organofluorine compounds (Scheme 1).[6]



Scheme 1 Previous Methods for the Preparations of α-Substituted β,γ,γ-Trifluoroallyl Alcohols

However low boiling point (-26.5 °C) of HFC-134a seems to cause handling problem at ambient temperature. Therefore, more convenient and CFC- or HFC-free approaches to these compounds are still required.

We report here a new expedient entry to α-substituted β,γ,γ-trifluoroallyl alcohols using the reaction of β-fluoro-β-*trifluoromethylated* enol tosylate,[7] readily prepared from commercially available polyfluoroalcohol, with Grignard reagents (Scheme 2).



Scheme 2

β-fluoro-β-trifluoromethylated enol tosylate can be prepared according to the our previous report.[7c]

To a THF solution of phenylmagnesium bromide (PhMgBr) (1.05 M THF solution, 2.9 mL, 3 mmol) was slowly added a THF (1 mL) solution of 3,3,3,4-tetrafluoro-1-propenyl tosylate (**1**) (1 mmol) at ambient temperature under argon. After being stirred at reflux temperature for 3 h, the reaction mixture was quenched with a cold saturated NH_4Cl solution (50 mL), followed by extraction with diethyl ether (30 mL × 3). The oraganic layer was washed with a $NaHCO_3$ solution (20 mL × 2) and brine (20 mL × 2), dried over Na_2SO_4, and concentrated in vacuo to give the residue, which was chromatographed on silica gel using chloroform to obtain the corresponding 2,3,3-trifluoro-1-phenyl-2-propen-1-ol (**2a**) in 75% yield (Table 1, entry 3). Conducting the reaction at 50 °C or at room temperature provided the less yield of **2a** with recovery of **1a** (entries 1 and 2). Two equivalents of PhMgBr was not enough to obtain good yield of **2a** (entry 4).

Other Grignard reagents carrying 4-methylphenyl, 4-chlorophenyl, or 2-napthyl group, participated well in the reaction to give the corresponding β,γ,γ-trifluoroallyl alcohols **2b**–**d** in 57–80% yields (entries 5–8). However the reaction of **1** with 2-methyphenylmagnesium bromide was very sluggish to give the corresponding allyl alcohol **2e** in only 25% yield, due to the steric factor of the methyl group at 2-position on the phenyl group (entry 9). The reaction with hydrocinnamylmagnesium bromide also did not proceed effectively, producing the corresponding alcohol **2f** in only 14% yield (entry 10).

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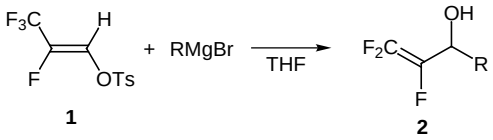
Table 1 Preparation of α-Substituted β,γ,γ-Trifluroallyl Alcohol **2**



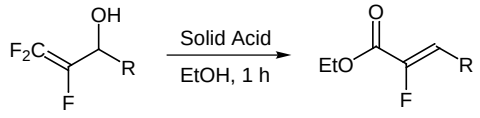
1 **2**

Entry[a]	RMgBr (equiv)	Temp.	Product	Yield (%)[b]
1	PhMgBr (3)	r.t.	**2a**	53 (10)
2	PhMgBr (3)	50 °C	**2a**	71 (6)
3	PhMgBr (3)	reflux	**2a**	75[c]
4	PhMgBr (2)	reflux	**2a**	59 (12)
5	4-MeC_6H_4MgBr (3)	reflux	**2b**	85[c]
6	4-ClC_6H_4MgBr (3)	reflux	**2c**	57[c]
7	4-ClC_6H_4MgBr (5)	reflux	**2c**	72[c]
8	2-NapMgBr (3)	reflux	**2d**	70[c]
9	2-MeC_6H_4MgBr (5)	reflux	**2e**	25 (trace)
10	$PhCH_2CH_2MgBr$ (5)	reflux	**2f**	14 (trace)

[a] The reaction was performed with tosylate **1** (1 mmol) in THF (4 mL).
[b] ^{19}F NMR yields. Values in parentheses stand for the recovery of **1**.
[c] Yields of isolated products.

As described in Table 2, moreover, α-substituted β,γ,γ-trifluoroallyl alcohols **2** can be converted to the corresponding β-substituted α-fluoro-α,β-unsaturated carboxylic acid esters **3** without the use of an excess amount of concd H_2SO_4[8] or iodine.[9]

Table 2 Preparation of (*Z*)-β-Substituted α-Fluoro-α,β-unsaturated Carboxylic Acid Esters **3**



2 **3**

Entry[a]	R	Solic Acid (g/mmol of **2**)	Temp.	Product	Yield (%)[b]
1	Ph	M K10 (0.2)	reflux	**3a**	7 (70)
2	Ph	$H_4SiW_{12}O_{40}$ (0.2)	reflux	**3a**	69 (18)
3	Ph	$H_4SiW_{12}O_{40}$ (1.0)	reflux	**3a**	85
4	Ph	$H_4SiW_{12}O_{40}$ (1.0)	r.t.	**3a**	0 (95)
5	4-MeC_6H_4	$H_4SiW_{12}O_{40}$ (1.0)	reflux	**3b**	87

[a] The reaction was performed with alcohol **2** (1 mmol) in EtOH (4 mL) for 1 h.
[b] Yields of isolated products. Values in parentheses stand for the recovery of **2**.

Although the optimization of the ethanolysis conditions was not carried out, some results can be described. Using a catalytic or small amount of tungstosilicic acid ($H_4SiW_{12}O_{40}$)[10] (0.2–1.0 g/1 mmol of **2**), which has remarkable advantages such as ease of handle and non-corrosiveness, at reflux temperature afforded (*Z*)-α-fluoro-α,β-unsaturated carboxylic acid esters **3a**,**b** exclusively in good yields, (entries 2–5). The ethanolysis at room temperature did not occur, the alcohol **2a** being recovered in quantitative yield (entry 4). Montmorillonite K 10 (Clay, MK10) is not effective for the ethanolysis of the allyl alcohol **2a** (Table 2, entry 1) at all.[11] It should be noted that only (*Z*)-isomer was obtained in the all cases.

In short, we describe herein the first reaction of β-fluoro-β-trifluoromethylated enol tosylate with Grignard reagents providing a new entry to α-substituted β,γ,γ-trifluoroallyl alcohols as well as $H_4SiW_{12}O_{40}$-mediated ethanolysis of the alcohols affording (*Z*)-β-substituted α-fluoro-α,β-unsaturated carboxylic acid esters **3**, exclusively.

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