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[3,3]-Sigmatropic rearrangement of allyl (or propargyl) fluorovinyl ethers. Synthesis of α-trifluoromethyl unsaturated acids and derivatives

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Abstract—A one pot synthesis of α-trifluoromethyl unsaturated acids and derivatives via a [3,3]-sigmatropic rearrangement of allyl (or propargyl) fluorovinyl ethers is described.

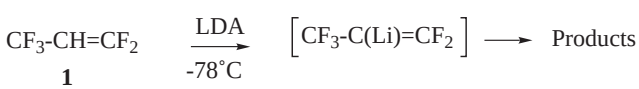
The trifluoromethyl group with its strong electronegativity, lipophilicity and stability induces considerable changes in the properties of the fluorine-substituted molecules.[1] Many reliable methods are now available to introduce the trifluoromethyl moiety into organic substrates.[2] Among these methods, the enzymatic hydrolysis of esters[3] (mainly leading to chiral compounds) and the [3,3]-sigmatropic rearrangement,[4] allow particularly access to chemical structures described in this paper. During the course of our studies on the preparation of stereoselectively fluorinated molecules, we have already emphasized the potential of this sigmatropic rearrangement.[5]

Herein, we report the reaction of the 1,1,3,3,3-pentafluoropropene **1**[6] with potassium alkoxides in THF which straightforwardly leads to α-trifluoromethyl unsaturated acids and derivatives **4** and **5**. These compounds bearing a trifluoromethyl group represent an attractive approach for the construction of more elaborate molecules.

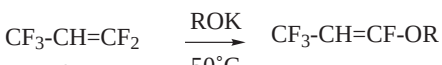
Burton has used **1**, as starting material, to introduce a trifluoromethyl moiety. Thus, he has firstly optimized the preparation of CF_3-C(Li)=CF_2 by treatment of **1** at −78°C with either LDA or *t*-BuLi in diethylether and pentane, and then has used this fluorinated intermediate in additional functionalization reactions[7] (Scheme 1).

In contrast to LDA which exhibits more of its basic character in a metalation reaction, the potassium alkoxide shows more of its nucleophilic character and reacts according to an addition-elimination process. Hence, the first step involves a selective fluorine substitution at low temperature (Scheme 2).

With a saturated alkoxide (*n*-HeptOK), the vinyl ether **2** obtained, which is stable, can be isolated and its geometry determined by NMR spectroscopy ($Z/E \approx 2/1$).[8]



Scheme 1. Metalation reaction with LDA in an aprotic medium.



Scheme 2. Substitution reaction with ROK in THF.

Keywords: 1,1,3,3,3-pentafluoropropene; [3,3]-sigmatropic rearrangement; α-trifluoromethyl unsaturated acids.

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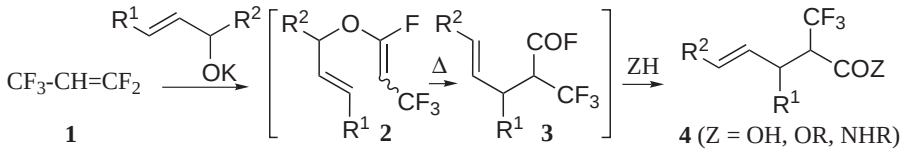
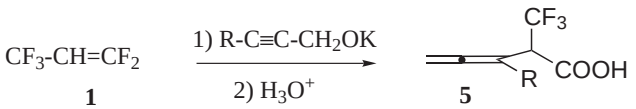
Table 1. Synthesis of α-trifluoromethyl γ-ethylenic acids and derivatives **4**



	R^1	R^2	ZH	Yield[a] (%)	^{19}F NMR-δ (ppm)/$CFCl_3$
1	H	H	H_2O	70	−68.6
2	Me	H	H_2O	80	−64.9 and −65.1 (major)[b]
3	H	Me	H_2O	82	−68.5[c]
4	H	Ph	H_2O	21	−68.2[c]
5	H	Me	EtOH	71	−68.7[c]
6	H	Me	t-$BuNH_2$	64	−68.7[c]
7		$-(CH_2)_3-$	MeOH	57	−64.5 and −65.4 (major)[d]
8	Ph	H	t-$BuNH_2$	50	−62.7 and −62.8 (major)[e]

[a] Overall yields based on the starting pentafluoropropene **1**.
[b] (dr = 64/36), Diastereomer ratio determined by ^1H NMR.
[c] Only *E* isomer.
[d] (dr = 61/39).
[e] (dr = 62/38).

Table 2. Synthesis of α-trifluoromethyl β-allenic acids **5**



	R	Yield[a] (%)	^{19}F NMR-δ (ppm)/$CFCl_3$
9	H	55	−69.2
10	Me	58	−67.1

[a] Overall yields based on the starting pentafluoropropene **1**.

In the case of allyl potassium alkoxides, the substitution reaction leads to allyl fluorovinyl ethers **2** which quickly undergo a [3,3]-sigmatropic rearrangement by increasing the temperature to about −30°C, giving the corresponding acid fluorides **3**. In previous publications,[5] we have already shown that the fluorine atom in the α position to the oxygen atom made easier the rearrangement of allyl vinyl ethers. By hydrolysis, the acid fluorides give acids **4**. Moreover, it is interesting to note that our method also allows to obtain an ester or an amide if an alcohol or an amine is added instead of water.[9] The results of this one pot synthesis are summarized in Table 1.

In the same way, propargyl potassium alkoxides lead via a [3,3]-sigmatropic rearrangement of intermediate propargyl fluorovinyl ethers to α-trifluoromethyl allenic acids **5**[9] (Table 2).

In conclusion, we have described a [3,3]-sigmatropic rearrangement of several allyl (or propargyl) fluorovinyl ethers. Good yields have been obtained for the synthesis of α-trifluoromethyl γ-ethylenic and β-allenic acids and derivatives which constitute useful precursors for synthesizing more complex fluorinated molecules.

Acknowledgements

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6. Compound **1** was purchased from PCR-Lancaster.
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8. ^{1}H NMR (*n*-heptO-CF=CH-CF_3): *E* isomer: $\delta = 3.86$ (t, 2H, $J = 6.4$ Hz), 4.17 (qd, 1H, $J = 6.7$ and 2.0 Hz) ppm; *Z* isomer: $\delta = 4.10$ (t, 2H, $J = 6.6$ Hz), 4.48 (qd, 1H, $J = 6.9$ and 3.9 Hz) ppm.
9. Typical procedure: allylic or propargylic alcohol (15 mmol) was added to KH (15 mmol) in 20 ml of THF. After 30 min at +20°C, this solution was added at −90°C, to a solution of pentafluoropropene **1** (10 mmol) in 20 ml of THF (stirring was continued for 3 h at −50°C). Then, the mixture was treated either with H_2SO_4 (10%) (entries 1, 2, 3, 4, 9 and 10), alcohol (EtOH or MeOH) (5 or 7) or *t*-$BuNH_2$ (6 and 8) and the temperature was allowed to rise to room temperature. After 30 min, the mixture was hydrolysed with H_2SO_4 (10%) and extracted with Et_2O.