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A NOVEL SYNTHESIS OF 1,1-DIFLUOROOLEFINS FROM 1,1,1-TRIFLUOROETHYL *p*-TOLUENESULFONATE *VIA* BORON ATE-COMPLEX

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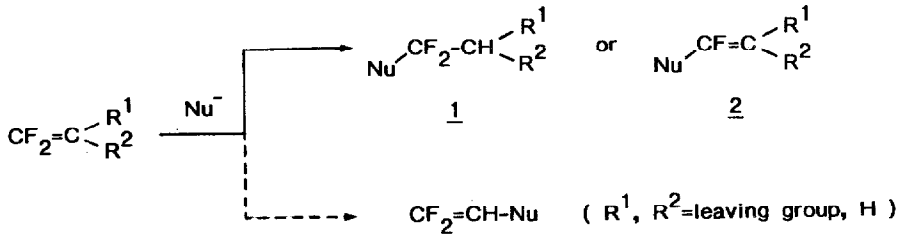
Summary: The nucleophilic substitution of *gem*-difluorovinylic tosyloxy group with alkyl groups is effected by treating 2,2-difluoro-1-tosyloxyvinyllithium with trialkylboranes to afford 1,1-difluoroolefins in good yields.

Fluoroolefins containing a terminal difluoromethylene group are a particularly versatile and useful class for further synthesis of fluorocarbon derivatives, because of their unique reactivities both in ionic and radical reactions.[1,2] Over the years, a number of examples have been reported on the preparation of 1,1-difluoroolefins, most of which are based on the *difluoromethylenation* of carbonyl moiety[2,3] or phosphine ylides.[4] On the other hand, there are few synthetic methods for *gem-difluorovinylation*,[5] especially by nucleophilic substitution of *gem* -difluorovinyl derivatives. This is probably due to the fact that 1,1-difluoroolefins readily undergo preferential attack of nucleophiles at the terminal difluoromethylene carbon to yield the addition products 1 or the substitution products 2 with loss of fluoride.[6] The selective substitution reaction at the vinylic carbon adjacent to difluoromethylene, therefore, opens a new way to 1,1-difluoroolefins (Scheme 1).

Among β-fluorine-stabilized carbanions there has been reported 2,2-difluoro-1-tosyloxyvinyllithium (4), which can be easily generated from 2,2,2-trifluoroethyl *p*-toluenesulfonate (3) and 2 equiv. of lithium diisopropylamide (LDA).[7] It occurred to us that this accessible vinyl anion 4



Scheme 1

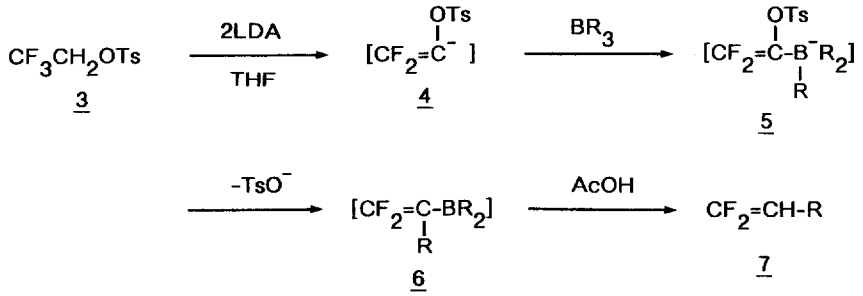
might be applicable to the above mentioned substitution reaction by using organoboranes as alkylating agents, because the attack at difluoromethylene carbon could be prevented by the intramolecular displacement of tosyloxy group *via* ate-complex formation and subsequent 1,2-migration as shown in Scheme 2.[8] Our interest in developing new and facile methods for the synthesis of fluoroolefins led us to explore this approach using 3 and trialkylboranes.

Treatment of 4 with tris(4-phenylbutyl)borane, generated *in situ* by hydroboration, induced the 1,2-migration of the alkyl group from boron onto the vinylic carbon, providing the *gem*-difluoroalkenylborane 6. The protonolysis of 6 was effected by adding acetic acid at room temperature to afford the desired compound, 1,1-difluoro-6-phenylhexene (8) in 63% yield. Although the vinylic carbon-boron bond in 6 was susceptible to protonolysis even by methanol, heating in acetic acid was required to complete the protonolysis. Thus, 8 was obtained in 90% yield without any detectable by-products such as derived from the nucleophilic attack at the difluoromethylene carbon.

The reactions of several other organoboranes were examined and results are summarized in Table 1.[9] The corresponding 1,1-difluoroolefins with various alkyl substituents were obtained in good yields. Furthermore, the reaction led to a 1,1-difluoro-1,3-diene in the case of using a trialkenylborane (Entry 8).

A typical reaction procedure is as follows: 1,1,1-trifluoroethyl *p*-toluenesulfonate (3) (90 mg, 0.35 mmol) in tetrahydrofuran (THF, 1 ml) was added dropwise to a solution of LDA (0.75 mmol) in THF (1 ml) at -78 °C under an argon atmosphere. After 30 min of stirring at that temperature was added tris(4-phenylbutyl)borane, generated from 4-phenylbutene (155 mg, 1.17 mmol) and borane-THF complex (0.40 mmol) in THF (2 ml). The reaction mixture was stirred for 1 h, and allowed to come up to room temperature, followed by stirring for an additional 10 h. Then, the solvent was evaporated *in vacuo*, and the residue was heated under reflux with acetic acid (3 ml) for 3 h. After usual workup, 1,1-difluoro-6-phenylhexene (8) (56 mg, 81%) was isolated by thin layer chromatography on silica gel (hexane).[10]

It is noted that i) the nucleophilic substitution of gem-difluorovinylic tosyloxy group is effected to afford 1,1-difluoroolefins; ii) trifluoroethyl *p*-toluenesulfonate acts as the reagent for the *gem*-difluorovinyl cation synthon. Our current efforts are directed to the further application of *gem*-difluoroalkenylboranes 6, which can be a versatile synthetic intermediate for fluorine containing compounds by taking advantage of organoborane chemistry.[11]



Scheme 2

Table 1. Synthesis of 1,1-Difluoroolefins[a]

Entry	R	BR_3/3	Yield of 7/%[b]
1	$-(CH_2)_4Ph$	1.1	90 (81)[c]
2[d,e]	$-(CH_2)_7CH_3$	1.1	84
3	$-CH_2\overset{CH_3}{\overset{\vert}{C}}HPh$	1.1	75
4		1.5	90
5[d]	$-CH_2$ 	1.1	74
6[d]	*cyclo*-C_8H_{15}	1.1	83
7[e]		1.5	75
8[d]	$-\overset{(CH_2)_2CH_3}{\overset{\vert}{C}}=CH(CH_2)_2CH_3$	1.1	41

[a]Unless otherwise noted, all reactions were carried out under conditions described in the text. [b]^{19}F NMR yield relative to internal $C_6H_5CF_3$ standard. All products were fully characterized by ^1H NMR, ^{19}F NMR, ^{13}C NMR and IR spectra. [c]Isolated yield is given in parentheses. [d]Reaction mixture was heated under reflux for 2 h before protonolysis. [e]Protonolysis was carried out in THF-AcOH (4:3) under reflux for 3 h.

References and Notes

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10. 8: IR (neat): ν 1750 cm^{-1}; ^1H NMR ($CDCl_3$/TMS): δ 1.15-2.14 (6H, m), 2.61 (2H, br t, J=8 Hz), 4.10 (1H, dtd, J=25 Hz, 8 Hz, 3 Hz), and 7.02-7.39 ppm (5H, m); ^{19}F NMR ($CDCl_3/C_6F_6$): δ 69.9 (1F, ddt, J=49 Hz, 25 Hz, 2 Hz) and 72.3 ppm(1F, br d, J=49 Hz); ^{13}C NMR ($CDCl_3$/TMS): δ 22.3 (d, J_{CF}=4 Hz), 29.3 (d, J_{CF}=2 Hz), 31.0, 35.9, 78.1 (t, J_{CF}=22 Hz), 126.0, 128.6, 128.7, 142.7, and 156.6 ppm (t, J_{CF}=286 Hz); Found: m/z 196.1058. Calcd for $C_{12}H_{14}F_2$ 196.1064.
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