

# Nucleophilic fluoroalkylation of (bromomethyl)pinacolborane using silicon reagents

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## ABSTRACT

A method for the synthesis of pinacol boronic esters bearing a fluorinated group at the  $\alpha$ -carbon atom ( $R_fCH_2Bpin$ ) from corresponding bromomethyl borane ( $BrCH_2Bpin$ ) and fluorinated silanes ( $R_fSiMe_3$ ) is described. The fluoroalkylation reaction involves formation of borate anions followed by intramolecular nucleophilic substitution of bromine.

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## 1. Introduction

Fluorinated organoboron compounds have emerged as valuable reagents with broad scope of applications [1–3]. While various structural types of fluoroboron compounds have been synthesized, boranes **1** bearing a methyl group substituted with a fluorinated fragment have been poorly studied (Scheme 1). Indeed, only compounds with pentafluorophenyl [4] or difluorovinyl [5] groups were described, which were prepared by nucleophilic substitution of halogen in halomethylboranes using fluorinated lithium or magnesium reagents [6]. At the same time, boranes **1** containing trifluoromethyl or fluorinated alkyl substituent at the  $\alpha$ -carbon have not been reported. Herein we describe the application of fluorinated silanes as equivalents of fluorinated carbanions for the preparation of boranes **1**.

Reactions of fluorinated silanes with  $sp^2$ -centered electrophiles, such as  $C=O$ ,  $C=N$ , and electron-deficient  $C=C$  bonds [7], as well as substitution of halogen at  $sp^2$ -carbon [8], have been studied intensively, whereas reactions with  $sp^3$ -centered electrophiles are notably less general. The displacement of halogen at the  $sp^3$ -carbon by fluorinated group can be performed by using fluorinated copper species  $R_fCu$  generated either from silane [9] or by other means [10]. Alternatively, direct  $S_N2$  type substitution can be realized when silane is activated by Lewis base without transition metal [11], though this process provides reasonable yields mainly with alkyl iodides or benzyl and alkyl bromides.

The major difference of halomethylboranes from conventional alkyl electrophiles is the ability of boron atom to interact with nucleophile to generate tetracoordinate borate salt [12]. Such a behavior was observed in reaction of alkylborates  $B(OR)_3$  and esters of boronic acids  $RB(OR)_2$  with  $TMSCF_3$  [13]. Therefore, it can be expected that the overall substitution of halogen in halomethylboranes can proceed in two steps: by formation of tetracoordinate borate salt followed by intramolecular  $S_N2$  substitution (Scheme 1).

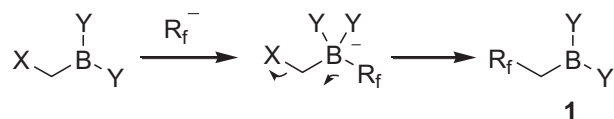
## 2. Results and discussion

Bromomethyl pinacolborane **2** was reacted with  $CF_3$ - and  $C_2F_5$ -substituted silanes (**3a** and **3b**, respectively) in the presence of potassium fluoride in DMF at room temperature (Scheme 2). Trifluoromethylated borate salt **4a** was formed cleanly and its structure was supported by  $^{19}F$  and  $^{11}B$  NMR spectroscopy. The yield of salt **4a** was ca. 85% determined by  $^{19}F$  NMR spectroscopy with internal standard. To effect intramolecular substitution, the resulting solution of salt **4a** was briefly heated at 70 °C to effect complete conversion. However, the desired product **5a** was isolated in only 45% yield. Analysis of reaction mixture by  $^{19}F$  NMR spectroscopy showed the formation of by-products which we could not identify. The reaction of borane **2** with  $TMSC_2F_5$  (**3b**) proceeded similarly generating borate salt **4b**, and its subsequent transformation was carried out at 50 °C affording product **5b** in 80% yield after vacuum distillation.

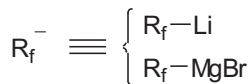
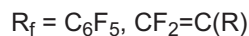
Functionalized silanes **3c–f** were reacted with borane **2** under standard conditions (Table 1). In this case the formation of products **5** did not require heating, and proceeded at a rate

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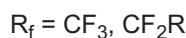
E-mail addresses: [adil25@mail.ru](mailto:adil25@mail.ru), [dilman@ioc.ac.ru](mailto:dilman@ioc.ac.ru) (A.D. Dilman).



Literature:



This work:



Scheme 1.

comparable to that of the formation of the intermediate borate salts. These observations suggest that the rate of intramolecular  $\text{S}_{\text{N}}2$  substitution increases with increasing carbanion stability of migrating group. As a rule, products **5** were formed with the yields exceeding 50%, while their purification was accompanied by product losses.

The general problem for the preparation of 2,2,2-trifluoroethyl and related organometallic reagents is the facile  $\beta$ -elimination of metal fluoride from the fragment  $\text{RCF}_2\text{CH}_2\text{M}$ . Rewardingly, boranes **5** are thermally stable compounds showing no tendency for  $\beta$ -elimination under neutral conditions. However, borane **5c** is prone to decomposition in  $\text{CDCl}_3$  solution, as well as neat upon storage at  $5^\circ\text{C}$ , leading to unidentified mixture despite the fact that it can be distilled under vacuum.

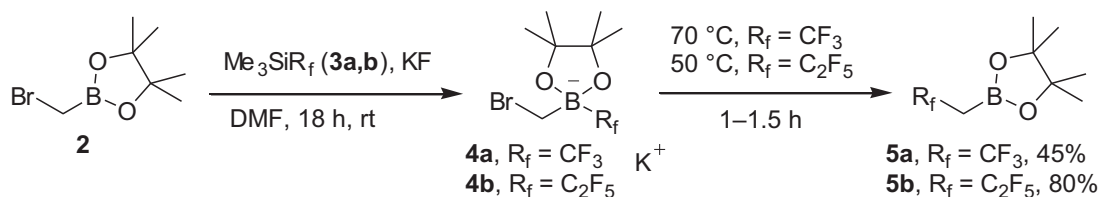
### 3. Conclusions

In summary, a method for the synthesis of fluorine-substituted pinacolboranes by nucleophilic fluoroalkylation has been described. Taking into account the rich chemistry of organoboron compounds, the obtained boranes may find applications in transition metal catalyzed cross-couplings, as well as in other reactions involving transfer of a partially fluorinated group from boron.

### 4. Experimental

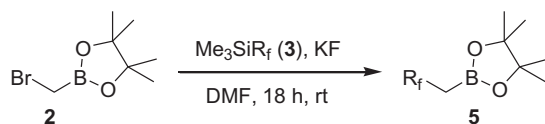
#### 4.1. General experimental procedures

All reactions were performed under an argon atmosphere. DMF was distilled under vacuum from  $\text{P}_2\text{O}_5$  and stored over MS 4 Å. NMR spectra were recorded on a Bruker AM-300 instrument. Microanalyses were performed on KarloErba 1106 instrument.  $\text{Me}_3\text{SiCF}_3$  and  $\text{Me}_3\text{SiC}_2\text{F}_5$  were purchased from P&M. Silanes **3c** [14], **3d,f** [15] were obtained according to the literature procedures.



Scheme 2.

**Table 1**  
Fluoroalkylation of bromomethyl pinacolborane **2**.



Silane	Product	Yield of <b>5</b> (%) <sup>a</sup>
		85
		55
		59
		28 (50) <sup>b</sup>

<sup>a</sup> The yield of purified product.

<sup>b</sup> The yield determined by NMR spectroscopy.

#### 4.2. 2-(Bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2**) [16]

To a stirred solution of triisopropylborate (32.5 mL, 141 mmol) and dibromomethane (10.8 mL, 154 mmol) in anhydrous THF (150 mL) at  $-94^\circ\text{C}$  (acetone/liquid nitrogen), *n*-BuLi (54 mL of 2.4 M solution in hexane, 128 mmol) was added dropwise over 2 min at such a rate that the internal temperature did not rise above  $-80^\circ\text{C}$ . The resulting mixture was stirred for 15 min at  $-78^\circ\text{C}$ , the cooling bath was removed, and the mixture was stirred for 2 h at room temperature. The reaction mixture was cooled to  $0^\circ\text{C}$  (ice/water bath) and a solution of concentrated sulfuric acid (3.8 mL, 70 mmol) in methanol (8.0 mL) was added dropwise over 2 min. The reaction was allowed to reach room temperature and was stirred for 1 h. Pinacol (12.1 g, 128 mmol) was added in one portion, and the mixture was stirred for 1 h at room temperature. The volatiles were removed under vacuum, and the residue was distilled ( $70^\circ\text{C}/12$  Torr) to give 25.5 g (90% yield) of borane **2** as a colorless liquid.

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