Tetrabutylammonium Fluoride Promoted Regiospecific Reactions of Trimethylsilyl-*o*-Carborane with Aldehydes

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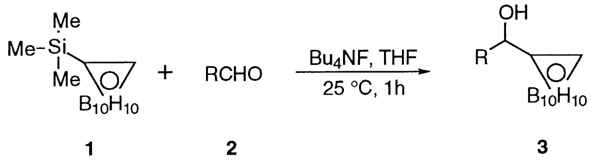
Trimethylsilyl-*o*-carborane serves as *o*-carborane carbanion upon fluoride ion promoted reaction with carbonyl compounds. Thus, in the presence of tetrabutylammonium fluoride, trimethylsilyl-*o*-carborane undergoes facile, unprecedented, carbodesilylation with aromatic and aliphatic aldehydes.

Boron neutron capture therapy (BNCT) is a highly promising therapy for certain tumors, such as gliomas and melanomas.[1] *o*-Carborane, one of the most stable boron cluster, and its derivatives are appropriate candidates for use as ^{10}B carriers in BNCT.[1] Substituted *o*-carboranes are usually prepared by the reaction of *o*-carboranyllithiums with electrophiles.[2] Unfortunately, reaction of simple *o*-carboranyllithium with alkyl halides usually leads to a mixture of products due to an equilibrium that exists between mono- and dilithiocarborane and the parent carborane.[3] This problem has recently been circumvented by temporarily protecting one of the *o*-carborane vertex with *tert*-butyldimethylsilyl (TBDMS) group, lithiation and reaction of the other *o*-carborane vertex with electrophiles, and subsequent protodesilylation of TBDMS group with tetrabutylammonium fluoride.[4] Carbon-carbon bond forming reaction by nucleophile promoted carbodesilylation is an important synthetic transformation due to the chemo- and regio-selectivity of the reaction.[5] Thus, certain organosilanes can be considered as stable yet reactive carbanions which allow many unique fluoride ion catalyzed carbon-carbon forming reactions under very mild conditions.[6] The fluoride ion presumably attacks silicon atom and leads to the formation of pentacoordinated silicon containing anions which are implicated as reactive intermediates in these kind of reactions.[7] However, in spite of large number of papers in this field, this synthetic methodology has not been applied to silyl substituted carboranes.

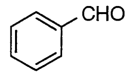
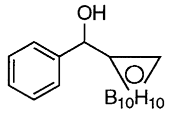
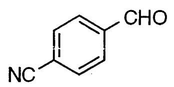
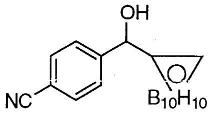
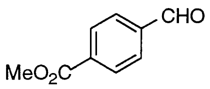
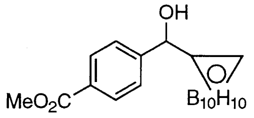
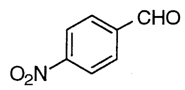
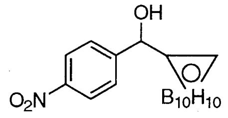
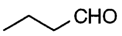
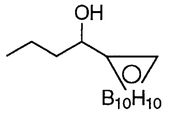
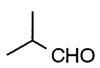
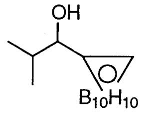
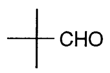
We have found that Bu_4NF facilitates the reaction of trimethylsilyl-*o*-carborane **1**[8] with aldehydes **2** readily. Reaction was complete within an hour at ambient conditions, giving the corresponding alcohols **3** (eq 1). The results are summarized in Table 1. Both aliphatic and aromatic aldehydes can be utilized for this reaction (entries 1-4 vs. entries 5-6).[9] This reaction is sensitive to stereorequirements and reaction of pivalaldehyde gave exclusive protodesilylated product, *o*-carborane (entry 7). This reaction is also highly chemoselective. Thus, functional groups, such as nitriles (entry 2), esters (entry 3), and nitro group (entry 4), are tolerated and the reaction takes place exclusively at the aldehyde group.

We have discovered that trimethylsilyl-*o*-carborane **1** can undergo fluoride promoted reaction with reactive electrophiles, such as aldehydes. Alcohol derivatives of o-carborane cannot be prepared directly from the hydroboration of acetylenic alcohols with decaborane.[4] This novel reaction has great potential for the syntheses of ^{10}B carriers bearing biologically active molecules where essentially neutral reaction conditions are highly desirable.



1 **2** **3** (1)

Table 1. Reaction of trimethylsilyl-*o*-carborane **1** with aldehydes promoted by TBAF[a,b]

Entry	Aldehyde **2**	Product[c] **3**	Yield / %[d]
1			98
2			82
3			95
4			75
5			75
6			95
7			99[e]

[a]Reactions run at 25 °C for 1 h. [b]TBAF=tetrabutylammonium fluoride. [c]Product purity determined by 250 MHz ^1H- and ^{13}C-NMR and FT-IR. [d]Isolated yields. [e]Quantitative formation of *o*-carborane.

References and Notes

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8 The preparation of trimethylsilyl-o-carborane **1** is as follows; To a solution of o-carborane (0.72 g, 5 mmol) in a dry THF (50 ml) at -78 °C was added a 1.6 mol dm^{-3} solution of n-BuLi in hexane (3.13 ml, 5 mmol) dropwise with stirring. The mixture was allowed to stir for 30 min at -78 °C and trimethylsilyl chloride was added dropwise. The solution was stirred for 1 h and then warmed to ambient temperature. The reaction was quenched with water, extracted with ether, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was purified by short column chromatography on silica gel with hexane as eluent, which afforded **1** as a white solid in 86% yield (0.93 g, 4.3 mmol). In this case, di-trimethylsilyl substituted carborane was not obtained. The use of diluted solution of lithium carborane is essential to obtain the mono-silyl substituted carborane derivative.

9 The following procedure for the reaction of 2-(trimethylsilyl)-*o*-carborane with *p*-cyanobenzaldehyde in the presence of tetrabutylammonium fluoride (Bu_4NF) is representative. To a solution of 2-(trimethylsilyl)-*o*-carborane (0.22 g, 1 mmol) and *p*-cyanobenzaldehyde (0.13 g, 1 mmol) in THF (5 ml), a solution of Bu_4NF in THF (1 mol dm^{-3}, 1 ml) was added at 25 °C and stirred for 1h. The reaction mixture was diluted with ether (20 ml), washed with water (2x5 ml) and dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was purified by column chromatography [silica gel, hexane-ethyl acetate (2:1) as eluent] to afford essentially pure 1-(*o*-carboranyl)-4'-cyanobenzyl alcohol (0.23 g, 82%).