# Boron trihalide mediated haloallylation of aryl aldehydes: reaction and mechanistic insight†‡

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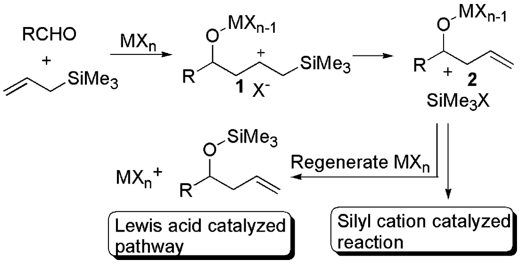
The reaction of aryl aldehydes with allylsilanes in the presence of boron trihalides produces haloallylated products. Mechanistic details are presented.

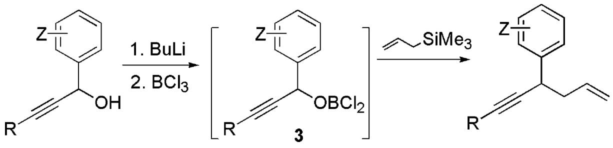
## A. Introduction

The Lewis acid mediated allylation of carbonyl compounds leading to homoallylic alcohols constitutes one of the most important synthetic reactions.[1] Numerous allylic organometallic reagents and Lewis acids have been investigated. In recent years, asymmetric allylation reactions have also been studied extensively due to their importance in medicinal and natural product chemistry. Lewis acid mediated allylations have been shown to be stepwise processes (Scheme 1). The addition of allylsilane to an activated aldehyde forms intermediate **1**. The silyl electrofuge cleavage then produces the metal homoallyloxide **2** and $Me_3SiX$. If the metal exchange between **2** and $Me_3SiX$ occurs smoothly, Lewis acid $MX_n$ is regenerated and the reaction is catalytic in nature. However, if the metal exchange does not occur, $Me_3SiX$ could also induce further allylations (silyl cation catalyzed pathway). To achieve high enantioselectivity in chiral Lewis acid catalyzed allylations, minimizing the contribution from the silyl cation catalyzed pathway is required.



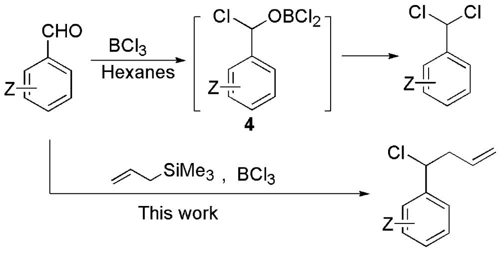
**Scheme 1**

In the last decade, our group has developed a number of novel reactions using the chemistry of boron halide derivatives. These include, for example, the dialkenylation of aryl aldehydes by divinylboron halides.[2] A reaction that appears to occur *via* an unprecedented process: C–O bond cleavage in the alkoxyboron monohalide intermediate. This discovery led us to develop reactions in which the hydroxyl groups were substituted with stereodefined alkenyl[3] and alkynyl[4] moieties using boron dihalides. Very recently we found that C–O bond cleavage also occurs smoothly in propargyloxyboron dihalides **3** (Scheme 2).[5]



**Scheme 2**

In an earlier study, we reported a new method for dihalogenating aryl aldehydes (Scheme 3).[6] A NMR study revealed that the reaction proceeds through an alkoxyboron dihalide intermediate **4**. The similarity between intermediates **3** and **4** led us to investigate the feasibility of capturing intermediate **4** with allyltrimethylsilane. According to the postulated mechanism shown in Scheme 3, we felt that the reaction of aryl aldehydes with allylsilane in the presence of a stoichiometric quantity of a boron halide would lead to haloallylated product **5** rather than the homoallylic alcohol. In fact, during a kinetic study of the reaction between a carbocation and allylsilane, Mayr and Gorath noted the chloroallylation of aryl aldehydes in the presence of 2–4 equivalents of $BCl_3$.[7] A sentence "in $BCl_3$ promoted reaction of aldehydes with allyltrimethylsilanes further halogeneration by excess $BCl_3$ took place, and consecutive products were isolated instead of the corresponding alcohols" was used to describe the reaction mechanism. Herein we report the results of a detailed study of this reaction, including a mechanistic discussion.



**Scheme 3**

## B. Results and discussions

Due to its air and moisture sensitivity, 1.1 equivalents of $BCl_3$ were utilized for the reaction of benzaldehyde with allyltrimethylsilane.

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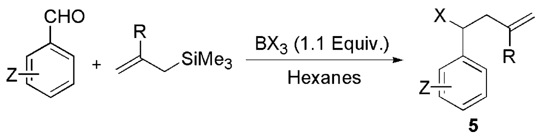
† We would like to dedicate this paper to Professor Ken Wade on the occasion of his 75th birthday.

‡ Electronic supplementary information (ESI) available: Experimental details and analytical data for all new compounds. See DOI: 10.1039/b715395c

**Table 1** Haloallylation of aryl aldehydes[a]

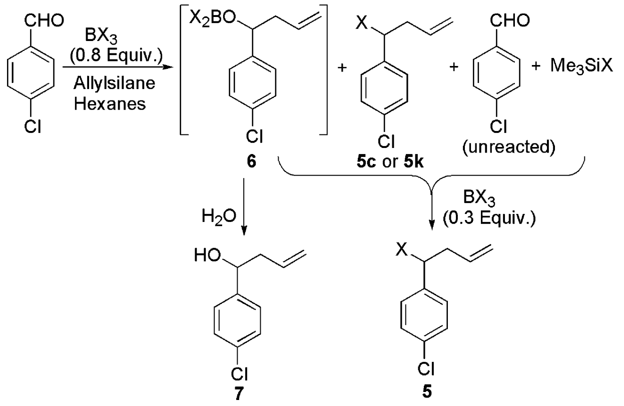


| Entry | Z | R | X | Time/min | Yield[b] (%) | |
|---|---|---|---|---|---|---|
| 1 | H | H | Cl | 30 | **5a** | 85 |
| 2 | 4-F | H | Cl | 30 | **5b** | 62 |
| 3 | 4-Cl | H | Cl | 20 | **5c** | 90 |
| 4 | 4-Br | H | Cl | 30 | **5d** | 87 |
| 5 | 2-Me | H | Cl | 20 | **5e** | 73 |
| 6 | 3,5-$Br_2$ | H | Cl | 120 | **5f** | 61 |
| 7 | 4-Cl | Me | Cl | 60 | **5g** | 92 |
| 8 | 2-Me | Me | Cl | 60 | **5h** | 69 |
| 9 | 2,3,4,5,6-$F_5$ | Me | Cl | 180 | **5i**[c] | 67 |
| 10 | 4-$CF_3$ | Me | Cl | 120 | **5j** | 89 |
| 11 | 4-Cl | H | Br | 10 | **5k** | 81 |
| 12 | 4-Cl | Me | Br | 10 | **5l** | 72 |
| 13 | 4-Br | Me | Br | 10 | **5m** | 78 |
| 14 | 3-Cl | Me | Br | 20 | **5n** | 63 |

[a] Boron halide was added at 0 °C and then the reaction mixture was warmed to room temperature until complete (see ref. 8 for details). [b] Isolated yield based on aldehyde. [c] Refluxing is required for completion

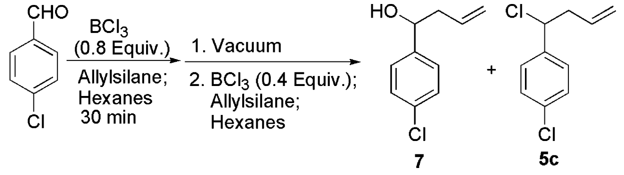
We found that the reaction proceeded readily in hexanes and gave the expected haloallylated product **5a** in 85% yield. A series of aryl aldehydes were subjected to the reaction (Table 1). Essentially all of the aryl aldehydes investigated were successfully converted to the haloallylated products with the exception of *p*-anisaldehyde (the cleavage of the methoxy ether by $BCl_3$ and $BBr_3$ is well known). Generally, reactions with $BBr_3$ are faster than those using $BCl_3$. Bromoallylated product **5k** formed exclusively when a mixture of $BBr_3$ and $BCl_3$ (1.1 equivalents each) was added to the reaction with *p*-chlorobenzaldehyde, demonstrating a high chemoselectivity.

Several control experiments were performed to probe the reaction mechanism. First, the reaction of allyltrimethylsilane with *p*-chlorobenzaldehyde using a substoichiometric amount of boron trihalide (0.8 equivalent) was carried out to determine whether the reaction was catalytic (Scheme 4). *p*-Chlorobenzaldehyde was not completely consumed after 24 hours clearly indicating that the reaction is not catalytic. Remarkably, the $Me_3SiX$ (X = Cl, Br) generated in the reaction did not initiate a silyl cation catalyzed allylation. The discovery that $Me_3SiX$ (X = Cl, Br) was not a catalyst in non-polar solvent hexanes could be significant for allylation reaction involving chiral Lewis catalysts. Hydrolysis of the reaction mixture at this stage revealed products **7** and **5**. Homoallylic alcohol **7** was isolated as the major product (70% yield) along with chloroallylated product **5c** (8% yield) when $BCl_3$ was employed. In contrast, bromoallylated product **5k** was the main product if boron tribromide was used; the yields of **7** and **5k** were 26% and 41%, repectively. In a separate experiment, an additional 0.3 equivalent of boron trihalide was added to the substoichiometric (0.8 equivalent) mediated reactions. Both intermediate **6** and the unreacted *p*-chlorobenzaldehyde disappeared (no homoallylic alcohol **7** detected). Clearly the conversion of intermediate **6** to haloallylated product **5** occured.[9]



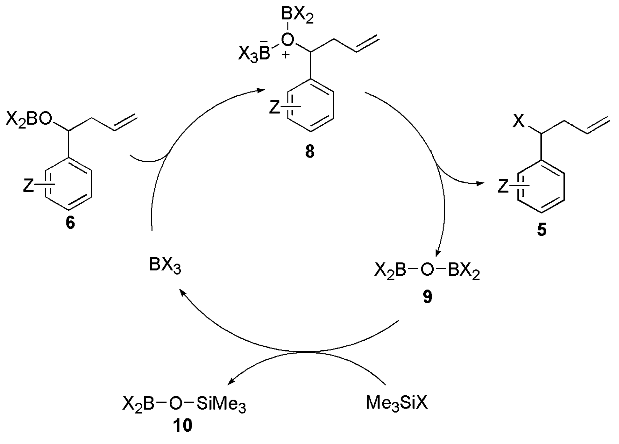
**Scheme 4**

The complete conversion of intermediate **6** and unreacted *p*-chlorobenzaldehyde to haloallylated product **5** using only an additional 0.3 equivalent of boron trihalide (Scheme 4) was somewhat surprising. The isolation of homoallylic alcohol **7** in 53% yield from a modified reaction (Scheme 5) helps explain the earlier observation. Removal of the $Me_3SiCl$ prior to addition of the extra $BCl_3$ inhibits the conversion of intermediate **6** to product **5c**.



**Scheme 5**

Based on these experiments, a tentative mechanism is proposed to explain the boron trihalide catalyzed transformation of **6** to **5** (Scheme 6). Boron trihalide coordinates with the oxygen in intermediate **6** to form **8**. Rearrangement of **8** generates the desired product **5** along with $X_2B–O–BX_2$ (**9**). Exchange between **9** and $Me_3SiX$ regenerates boron trihalide and mixed anhydride **10**.



**Scheme 6**

## C. Conclusions

In summary, a facile haloallylation of aryl aldehydes using boron trihalide is reported. A mechanistic study revealed the reaction involves two-steps: i) conversion of aldehydes to homoallyloxide borates in the presence of a stoichiometric amount of boron trihalides; ii) a boron trihalide catalyzed conversion of homoallyloxide borates into halogenerated products in the presence of $Me_3SiX$ ($X = Br, Cl$).

## Acknowledgements

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8 Typical reaction procedure: Finely ground 4-chlorobenzaldehyde (210 mg, 1.5 mmol), allyltrimethylsilane (2.56 mg, 2.25 mmol) and dry hexane (16 mL) were placed in a dry argon-flushed, 50 mL round-bottomed flask equipped with a magnetic stirring bar. The solution was cooled to 0 °C, and boron trichloride (1.65 mmol, 1.65 mL of a 1.0 M $CH_2Cl_2$ solution) was added *via* syringe. After completion of the addition, the ice-bath was removed and the resulting solution allowed warm to room temperature. The reaction mixture was hydrolyzed with water and extracted with hexanes. The organic layer was separated, dried over anhydrous $MgSO_4$ and the product isolated by flash column chromatography.

9 Although it is difficult to rule out the possibility of directly producing **5** from the aldehyde through a cation generated from intermediate **4** *via* a C–O bond cleavage, the high electronegativity of chlorine makes this route unlikely.