



Reactions of organoboranes with carbanions bearing three potential leaving groups: unusual processes, products and mechanisms



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ABSTRACT

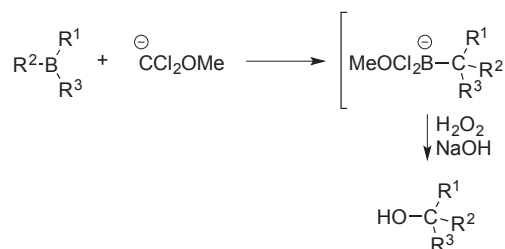
Known reagents that transfer three alkyl groups of a trialkylborane intramolecularly to a single carbon atom lack features to influence stereochemistry. We have investigated four reagents of type LiCCl_2X , where X might be amenable to variation. All behaved differently. With $\text{X}=\text{OR}$ ($\text{R}=\text{cyclohexyl}$, menthyl), the reagent decomposed, leading to only low yields of triple migration products. With $\text{X}=\text{S}(\text{O})\text{Ph}$, a single migration occurred, followed by isomerisation to boron enolate-like species that hydrolysed to α -chloroalkyl phenyl sulfoxides or reacted with aldehydes to aldol-like products. With $\text{X}=\text{SO}_2\text{Ph}$, the major product was the corresponding α,α -dichloroalkyl phenyl sulfone, apparently formed through a redox reaction. With $\text{X}=\text{S}(\text{O})(\text{NMe})\text{Ph}$, products of three intramolecular alkyl migrations were obtained with unhindered trialkylboranes. Attempts have been made to gain understanding of the sulfoxide process by investigating proportions of aldol-like products, using X-ray crystallography and ab initio calculations.

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1. Introduction

Rearrangement reactions of organoboron species provide many well-established synthetic methods, several of which have no counterparts outside of organoboron chemistry. For example, several types of reaction, including carbonylation,¹ cyanidation² and the DCME (dichloromethyl methyl ether) reaction (Scheme 1),³ allow transfer of all three alkyl groups from a trialkylborane to a single carbon atom to generate tertiary-alkylboron compounds, which can be oxidised to tertiary alcohols. Under different conditions the carbonylation reaction can be controlled to allow synthesis of products from just one or two alkyl group migrations,⁴ and cyanidation can also be controlled to give products of two alkyl migrations,⁵ but the DCME reaction proceeds so readily to give three migrations that it cannot be stopped at an intermediate stage except by using alternative substrates possessing fewer alkyl groups.

In principle, variants of the DCME reaction could have enormous synthetic potential, for example if one or more of the three leaving groups on carbon could be changed to render it less readily



Scheme 1. Formation of tertiary alcohols by reaction of a trialkylborane with the anion of DCME.

displaced (so that the reaction could be intercepted before all three groups had migrated) or incorporate a chiral moiety (leading to the possibility of asymmetric induction). However, only a few attempts at variation have been reported. Anions derived from haloforms behave in much the same manner as the anion from DCME, although the yields are somewhat poorer.⁶ The reactions of trialkylboranes with the anion derived from tris(phenylthio)methane result in two spontaneous alkyl group migrations, allowing synthesis of ketones following oxidation, but the third migration can be induced by addition of mercuric chloride to the mixture.⁷

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In the present study we have undertaken reactions of organoboranes with anions derived from an alternative alkoxydichloromethane, a dichloromethyl sulfoxide, a dichloromethyl sulfone and a dichloromethyl sulfoximine. The behaviour of each anion type turned out to be quite different from the others, revealing some new reaction types and indicating some novel reaction mechanisms.

2. Results and discussion

2.1. Reaction with dichloro(menthyl)oxy)methane (1)

The simplest analogues of DCME, which might nevertheless offer interesting new possibilities in reactions with trialkylboranes, would involve replacing the methoxy group of DCME by an alternative alkoxy group. We decided to investigate the reactions of dichloro(menthyl)oxy)methane (1), the anion of which (2) might complex to an unsymmetrical trialkylborane (i.e., one bearing three different alkyl groups) to give two different diastereoisomeric complexes (3 and 4), the stabilities of which would not be identical and the rearrangements of which might differ in terms of which diastereotopic chlorine would be displaced first and/or which alkyl groups were located appropriately to displace particular leaving groups (Fig. 1).⁸ In principle, this could lead to the production of a significant excess of one enantiomer of the final tertiary alcohol over the other. Therefore, we decided to look at the reaction of the anion with such an unsymmetrical trialkylborane, and in order that the three alkyl groups should have significantly different characteristics and the tertiary alcohol product could be readily monitored by HPLC, we selected cyclopentyl(2-(4-methoxyphenyl)ethyl)thexylborane (5) as the substrate.

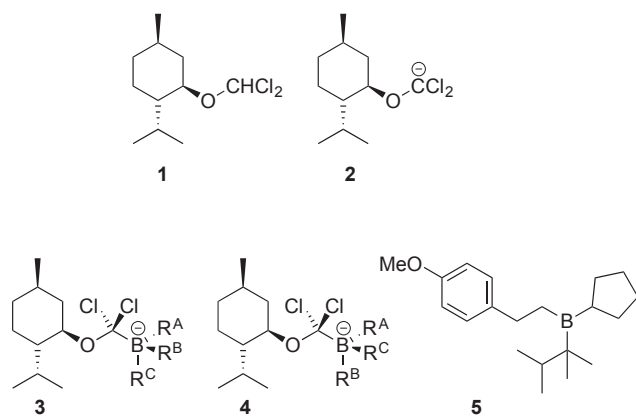


Fig. 1. Structures 1–5.

The first task was to prepare 1. A literature procedure⁹ was used to prepare the formate ester of (–)-menthol, the purity of which was confirmed by comparison of its reported ¹H NMR data⁹ and its reported optical rotation¹⁰ with those of the isolated product. Several different methods^{11–13} were tried in order to convert the menthyl formate into 1. In all cases there were problems with formation of menthyl chloride as a significant by-product, but a reasonably pure sample of 1 could be obtained by use of a mixture of PCl_5 and POCl_3 to introduce the chlorines, then removal of the POCl_3 under reduced pressure and extraction of the product into hexane, leaving the PCl_5 as a residue.

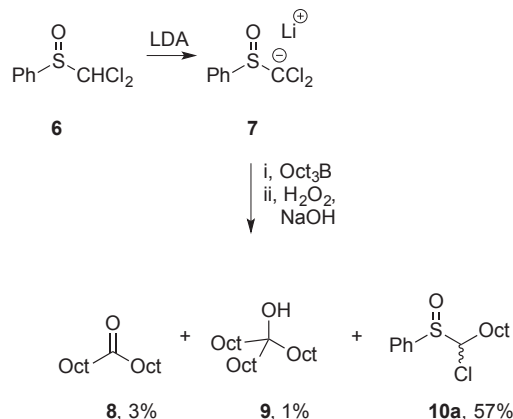
Unfortunately, when this product was subjected to a standard DCME-like reaction with 5, no tertiary alcohol was formed. Even with the less hindered tri-*n*-octylborane and tricyclopentylborane

only very low yields of tertiary alcohols were obtained (5% and 4%, respectively) and similarly generated cyclohexoxydichloromethane also did not provide encouraging results. Although we did not rule out the possibility of finding an appropriate alkoxydichloromethane that might react in the desired manner, in view of the disappointing results with 1 we decided to look instead at alternative types of reagents.

2.2. Reaction with (dichloromethylsulfinyl)benzene (6)

Compound 6 offers interesting possibilities as a reagent because of its chirality, resulting from the presence of a stereogenic sulfur atom. It was prepared by chlorination of methyl phenyl sulfoxide according to a literature procedure¹⁴ and was obtained as a colourless oil in 73% yield after column chromatography. We presumed that the two chloride groups would be more readily displaced than the sulfoxide group but hoped that the third group might be susceptible to displacement under appropriate conditions.¹⁵

A solution of trioctylborane was prepared by hydroboration of 1-octene with borane dimethyl sulfide complex in THF. This was then added at -78°C to a solution of anion 7, prepared by deprotonation of 6 (1 equiv) using lithium diisopropylamide (LDA, 1.1 equiv). The solution was stirred at -78°C for 1 h then the cooling bath was removed and the mixture stirred for a further 1 h before oxidation of the organoboron product with alkaline hydrogen peroxide. Work-up and separation of the products by column chromatography gave the products expected from two alkyl group migrations (dioctyl ketone, 8, Scheme 2) and three alkyl group migrations (trioctylmethanol, 9), but in low isolated yields, 3% and 1%, respectively; GC yields were 6% and 3%, respectively. The major product (57% yield) was a diastereoisomeric mixture of 1-chlorononyl phenyl sulfoxides (10a), evidently formed via a single alkyl group migration followed by hydrolysis of the organoboron intermediate rather than oxidation. The rest of the material was octanol, resulting from the oxidation of residual octylborane moieties. All of the products contained small quantities of the 2-octyl isomers because of the formation of about 6% of 2-octyl groups during the hydroboration step.



Scheme 2. Initial reaction of the anion derived from 6 with trioctylborane.

To our knowledge there are no known reactions of substituted sulfoxides with organoboron compounds similar to that resulting in the formation of compound 10a. Reactions of dimethylsulfoxonium ylides with trialkylboranes are known, but in those reactions dimethyl sulfoxide serves as a leaving group.¹⁶ Reactions of α -

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