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Reductive bromination of aromatic aldehydes using alkylboron dibromides

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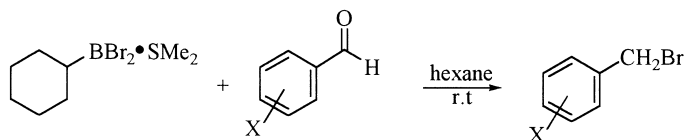
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Abstract

The reductive bromination of aromatic aldehydes with isopinocampheyl boron dibromide in hexane at room temperature produces the corresponding benzyl bromides in excellent yields. © 2000 Elsevier Science Ltd. All rights reserved.

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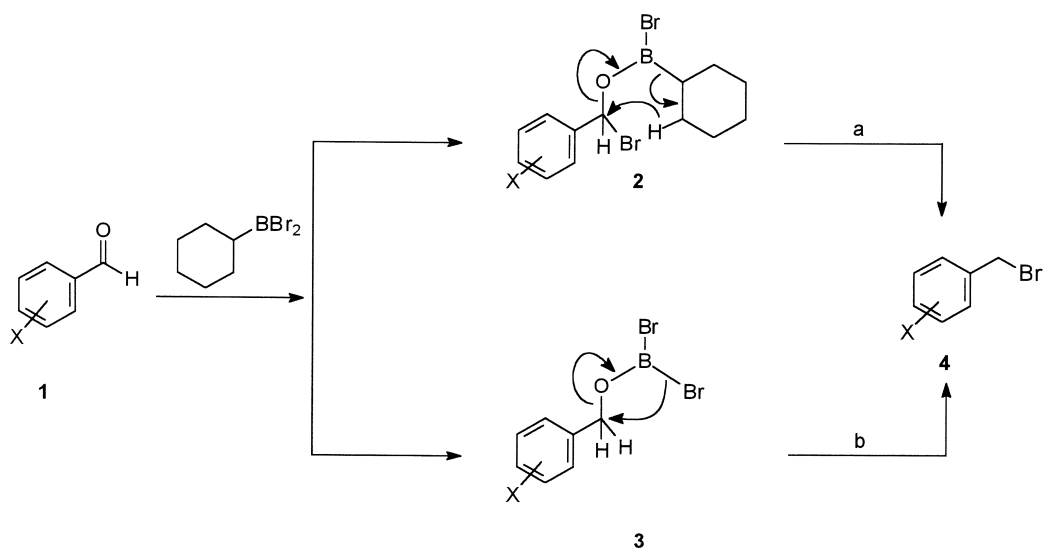
We recently reported that aromatic aldehydes react with dialkylboron chloride derivatives to yield 1-phenyl-1-alkanols.¹ Since dialkylboron bromide derivatives are readily available, we examined the reaction of dicyclohexylboron bromide with aryl aldehydes and found that no reaction occurred at room temperature although reduction of the aldehyde occurred upon heating.^{2,3} We then investigated the reaction of cyclohexylboron dibromide with aryl aldehydes and found that the desired alkylation reaction also did not occur. Instead, the corresponding benzyl bromides slowly formed.⁴



Formation of benzyl bromides was unexpected. Indeed, the direct conversion of aromatic aldehydes to benzyl bromide derivatives had been achieved in only two prior instances; these involved the use of a mixture of trimethylaminoborohydride and bromine⁵ or the use of a mixture of lithium bromide, chlorotrimethylsilane, and tetramethyldisiloxane.⁶

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Cyclohexene is also formed in the new reaction indicating that a reduction is occurring involving the hydrogen beta to the boron in the cyclohexane. This is a well known reaction in organoborane chemistry.^{2,3,7-15} Although a detailed mechanistic study has not yet been completed, benzyl bromide **4** could form via the bromoalkoxyborane **2** (pathway **a**) or via the dibromoalkoxyborane **3** (pathway **b**) as outlined in Scheme 1. A preliminary carbon-13 NMR experiment would appear to favor pathway **a** for reactions involving cyclohexylboron dibromide. Thus, when *p*-bromobenzaldehyde and cyclohexylboron dibromide are mixed, a new C-13 resonance appears at 86 ppm over a period of hours. Hydrolysis at this point leads to the regeneration of the starting material along with small quantities of benzylbromide. If the reaction mixture is not hydrolyzed, benzylbromide **4** gradually forms. In a separate experiment, *p*-bromobenzaldehyde was allowed to react with dibromoborane–dimethylsulfide to generate **3** directly (as evidenced by the appearance of a C-13 resonance for the benzylic carbon at 65 ppm) and benzyl bromide **4** formed in a matter of hours.



Scheme 1.

We reasoned that isopinocampheylboron dibromide would be more efficacious since the isopinocampheyl group is one of the most effective groups for reducing carbonyl compounds via beta-hydrogen transfer reactions. When a reaction of *p*-bromobenzaldehyde with isopinocampheylboron dibromide was monitored by carbon-13 NMR, **3** was formed immediately as evidenced by the appearance of a resonance at 65 ppm. A new resonance at 32 ppm then appeared over a period of hours indicative of the formation of **4**. Clearly, pathway **b** predominates when isopinocampheylboron dibromide is utilized.

The reaction of isopinocampheylboron dibromide with a variety of aryl aldehydes resulted in the formation of the corresponding benzyl bromides in excellent yields. As can be seen from the results tabulated in Table 1, essentially, all of the aldehydes investigated were successfully converted to the corresponding benzyl bromides. However, aromatic aldehydes containing strong electron withdrawing substituents were reduced at a slower rate and generated lower yields.

Table 1
Reductive bromination of aldehydes with isopinocampheylboron dibromide^a

Entry	Substrate	Product ^b	Time(hr)	Yield% ^c
1	C ₆ H ₅ CHO	C ₆ H ₅ CH ₂ Br	3	85
2	4-ClC ₆ H ₄ CHO	4-ClC ₆ H ₄ CH ₂ Br	3	80
3	4-BrC ₆ H ₄ CHO	4-BrC ₆ H ₄ CH ₂ Br	3	87
4	4-FC ₆ H ₄ CHO	4-FC ₆ H ₄ CH ₂ Br	5	85
5	2-FC ₆ H ₄ CHO	2-FC ₆ H ₄ CH ₂ Br	5	78
6	4-MeC ₆ H ₄ CHO	4-MeC ₆ H ₄ CH ₂ Br	1	80
7	2-MeC ₆ H ₄ CHO	2-MeC ₆ H ₄ CH ₂ Br	1	83
8	4-NO ₂ C ₆ H ₄ CHO	4-NO ₂ C ₆ H ₄ CH ₂ Br	10	65
9	4-(NC)C ₆ H ₄ CHO	4-(NC)C ₆ H ₄ CH ₂ Br	5	82
10	C ₁₀ H ₇ CHO	C ₁₀ H ₇ CH ₂ Br	3	75
11	1,4-(CHO) ₂ C ₆ H ₄	1,4-(CH ₂ Br) ₂ C ₆ H ₄	5	81
12	C ₆ H ₅ CH=CHCHO	C ₆ H ₅ CH ₂ =CHCH ₂ Br	3	70

^aAll reactions were carried out in hexane at room temperature. ^bAll reaction products exhibited physical and spectral characteristics in accord with literature values. ^c Isolated yields based on aldehyde.

The reductive bromination of 4-chlorobenzaldehyde is representative: 4-chlorobenzaldehyde (2.0 mmol, 0.28 g) was dissolved in hexane (10 mL) at room temperature in a dry flask maintained under a nitrogen atmosphere. Isopinocampheyl–boron dibromide dimethylsulfide complex, generated by refluxing HBBR₂(SMe₂) with α -pinene in CH₂Cl₂¹⁶ (2.0 mmol, 2.0 mL of a 1.0 M solution in CH₂Cl₂), was added to the aldehyde at room temperature. The reaction was allowed to stir at room temperature for 3 h, during which time a white precipitate formed. The mixture was then filtered and hydrolyzed with water, the organic layer separated, dried over anhydrous magnesium sulfate and the product isolated by column chromatography (hexane, silica gel) to yield 0.33g (80%) of the desired product.¹⁷

The new method provides a general, high yield synthesis of benzyl bromides from aromatic aldehydes. The method is also useful for converting α,β -unsaturated aldehydes to the corresponding bromides. However, it is not suitable for the preparation of arylalkyl bromides from carbonyl compounds containing enolizable hydrogens.

Acknowledgements

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