# The Fast and Selective Reduction of Organic Halides by Lithium Hydrotri-*s*-butylborate

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**Synopsis.** Lithium hydrotri-*s*-butylborate is shown to be a powerful reducing agent in its reducing abilities toward organic halides and discriminates structurally different organic halides due to the bulkiness of the reagent. Essentially complete utilization of the hydride of the reagent for the reduction of organic halides is also of synthetic significance.

The reductive dehalogenation of organic halides, one of the most fundamental reactions in organic chemistry, is often accomplished by various hydrido complex reducing agents.[1] Among many hydrido complex reducing agents for this purpose, lithium hydrotriethylborate has enjoyed its role as a source of an exceptionally powerful nucleophilic hydride in displacement reaction with organic halides after its discovery in 1973 by Brown.[2]

Although lithium hydrotri-*s*-butylborate, belonging to hydrotrialkylborates along with lithium hydrotriethylborate, has been widely used in the stereoselective reduction of cyclic and bicyclic ketones,[3] the reactivity of lithium hydrotri-*s*-butylborate toward organic halides has not been investigated. Furthermore, it was our purpose to explore the possibility of utilizing the bulkiness of the reagent for selective reduction of a variety of structurally different organic halides.

## Results and Discussion

Reductions were usually carried out in tetrahydrofuran at 25 °C under nitrogen using equimolar amounts of the reagent and the substrate and reaction mixtures were maintained at 0.25 M (1 M=1 mol dm$^{-3}$) in the substrate and 0.25 M in the reagent unless specified. The rate of reduction was followed by GLC at appropriate intervals of time and the yield was determined by GLC using an internal standard.

First, the reactivity of lithium hydrotri-*s*-butylborate toward 1-chlorooctane was examined in order to compare with that of lithium hydrotriethylborate. Employment of 2 molar equiv of each reagent allowed complete reduction of 1-chlorooctane into octane in 4 h, indicating that the reactivity achieved with lithium hydrotri-*s*-butylborate is comparable to lithium hydrotriethylborate.[2]

It has been known that the reaction of alkyl halides with equimolar amounts of lithium hydrotriethylborate proceeds rapidly up to 50%, with further reaction being sluggish probably due to the formation of lithium hydrotriethylborate-triethylborane complex during the reduction.[4] Thus, 2 molar equiv of lithium hydrotriethylborate are required for every molar equiv of alkyl halide for the complete reduction. This phenomenon has been observed with other hydride reducing agents such as sodium borohydride[5] and lithium hydrotrimethoxyaluminate.[6] Since it is expected that the bulkiness of lithium hydrotri-*s*-butylborate would prevent the formation of lithium hydrotri-*s*-butylborate-tri-*s*-butylborane complex, the reagent was reacted with equimolar amounts of 1-chlorooctane. Indeed, the reaction proceeded smoothly, yielding octane in 78, 85, and 94% yield in 2, 4, and 8 h, respectively.

Encouraged by these results, we examined various alkyl halides with equimolar amounts of lithium hydrotri-*s*-butylborate in tetrahydrofuran at 25 °C in order to establish its effectiveness in reduction of organic halides. Simple primary alkyl halides such as 1-iododecane and 1-bromododecane were almost instantly reduced to dodecane, whereas 1-bromooctane was generally inert toward the reagent at −78 °C and only 5% of 1-bromooctane was reduced to octane in 4 h. Thus, the reagent may be valuable for selective reduction of other readily reducible functional groups such as ketones and esters at −78 °C without simultaneous reduction on alkyl halides including relatively reactive primary alkyl bromides. Simple primary benzylic and allylic halides were rapidly and quantitatively reduced to the corresponding hydrocarbons, whereas secondary benzylic halides required longer reaction times as shown in Table 1. The simple secondary alkyl bromide like 2-bromooctane was reduced at a reasonable rate at 25 °C, whereas 2-chlorooctane was generally inert to the reagent. More sterically hindered cycloalkyl bromides such as cyclohexyl bromide and *exo*-2-bromonorbornane were extremely resistant to reduction. The analysis revealed 11% reduction of cyclohexyl bromide and the inertness of *exo*-2-bromonorbornane at 25 °C in 24 h. Unlike lithium hydrotriethylborate,[2] the low reactivity toward sterically hindered cycloalkyl bromides is attributed to the bulkiness of the reagent. The reduction of tertiary alkyl bromides did not occur and resulted predominantly in elimination in the case of 3-bromo-3-ethylheptane. Furthermore, the reagent was inert toward aryl halide like 1-bromonaphthalene at 25 °C in 24 h.

Since essentially complete utilization of the hydride of the reagent toward relatively reactive organic halides and the low reactivity toward sterically hindered organic halides have been observed in the reduction of organic halides, it is expected that employment of a stoichiometric amount of the reagent may permit selective reduction of structurally different organic halides. For selective reductions, equimolar amounts of two different organic halides were allowed to compete for a limited quantity of the reagent (1 molar equiv) at 25 °C and the results were determined by GLC analysis. 1-Bromododecane was selectively reduced to dodecane (98%) in the presence of 1-chlorooctane (1% reduction) for 5 min, whereas 1-bromododecane was selectively reduced to dodecane (96%) in the presence of 2-bromooctane (4% reduction) under the same reaction

Table 1. Reduction of organic halides with Li[BH(*s*-Bu)$_3$] in THF at 25 °C[a]

| Substrate | Time | Product | Yield/%[b] |
|---|---|---|---|
| 1-Iodododecane | 2 min | Dodecane | 100 |
| 1-Bromododecane | 2 min | Dodecane | 99 |
| Benzyl bromide | 2 min | Toluene | 100 |
| Cinnamyl bromide | 2 min | β-Methylstyrene | 99 |
| Benzyl chloride | 10 min | Toluene | 98 |
| α-Methylbenzyl bromide | 30 min | Ethylbenzene | 99 |
| Benzhydryl bromide | 1 h | Diphenylmethane | 97 |
| 1-Chlorooctane | 8 h | Octane | 94 |
| 1-Chlorododecane | 8 h | Dodecane | 90 |
| 2-Bromooctane | 24 h | Octane | 56 |
| Cyclohexyl bromide | 24 h | Cyclohexane | 11 |
| 2-Chlorooctane | 24 h | Octane | 2 |
| 3-Bromo-3-ethylheptane | 24 h | 3-Ethylheptane | 0[c] |
| 1-Bromoadamantane | 24 h | Adamantane | 0 |
| *exo*-2-Bromonorbornane | 24 h | Norbornane | 0 (5)[d] |
| 1-Bromonaphthalene | 24 h | Napthalene | 0 |

a) The solutions were 0.25 M in the substrate and 0.25 M in the reagent. b) The yields were determined by GLC using internal standards. c) Elimination products (60%) were observed. d) The reduction was carried out at 65 °C for 24 h.

conditions. Similarly, benzyl bromide was selectively reduced to toluene (98%) without simultaneous attack on α-methylbenzyl bromide (2% reduction) at 25 °C for 5 min. However, the selectivity was somewhat decreased in the reduction of organic halides containing two bromo substituents in a molecule. 1,2-Dibromononane was reduced to a 84 : 10 mixture of 2-bromononane and nonane along with 5% of the unreacted original halide at 25 °C in 30 min.

## Experimental

Lithium hydrotri-*s*-butylborate in THF was purchased from Aldrich Chemical Co. The hydride concentration (0.90 M) was determined by removing a known aliquot with a hypodermic syringe, hydrolyzing with a THF–water–glycerol mixture (1 : 1 : 1) at room temperature and measuring the hydrogen evolved. Tetrahydrofuran was distilled from sodium benzophenone under nitrogen. All glasswares were dried in a drying oven and cooled under nitrogen. All reduction experiments were carried out under nitrogen, and hypodermic syringes were used to transfer the solutions.

GLC analysis was performed on a Varian 2800 gas chromatograph with an FID detector. All analyses were carried out on 7 ft×0.125 in[†] or 4 ft×0.125 in 5% SE-30 on Chromosorb W columns.

Since the reactions performed are all similar in many respects, typical reactions will be described as specific examples.

*Reduction of 1-Chlorooctane with Equimolar Amounts of Li[BH(s-Bu)$_3$] in THF.* A 25 ml oven-dried flask with a magnetic stirring bar and a rubber septum under a balloon-filled atmosphere of nitrogen was immersed in a water bath at 25 °C. Then a solution of lithium hydrotri-*s*-butylborate (2.2 ml of a 0.90 M solution, 2.0 mmol) in THF was injected into the reaction flask by a hypodermic syringe, followed by the addition of a solution of decane (2.0 mmol) in THF (2.8 ml) as an internal standard. Finally, a solution of 1-chlorododecane (2.0 mmol) in THF (3 ml) was added and the reaction mixture was stirred at 25 °C. After 30 min, the reaction mixture was withdrawn with a syringe, quenched with water, extracted with ether, and analyzed by GLC. Analysis revealed the presence of 49% of octane. Similarly, aliquots were removed after 1, 2, 4, and 8 h and analyzed by GLC. Analysis revealed the presence of octane in 61, 78, 85, and 94 %, respectively.

*Selective Reduction of 1-Bromododecane in the Presence of 2-Bromooctane with Li[BH(s-Bu)$_3$] in THF.* A 25 ml oven-dried flask with a magnetic stirring bar and a rubber septum under a balloon-filled atmosphere of nitrogen was immersed in a water bath at 25 °C. Then a solution of 1-bromododecane (2.0 mmol) in THF (2.8 ml) was injected, followed by the addition of a solution of 2-bromooctane (2.0 mmol) and decane (2.0 mmol) in THF (2.8 ml). A solution of lithium hydrotri-*s*-butylborate (2.2 ml of a 0.90 M solution, 2.0 mmol) in THF was slowly added to the reaction flask for 1 min and the reaction mixture was stirred for an additional 4 min at 25 °C. The reaction mixture was quenched with water, extracted with ether, and analyzed by GLC. Analysis revealed the presence of 96% dodecane and 4% octane along with 4% 1-bromododecane and 95% 2-bromooctane.

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### References

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[†] 1 ft=0.30479 m, in=$2.54\times10^{-2}$ m