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Lithium Diisobutyl-*n*-butylaluminum Hydride. An Exceptionally Powerful and Selective Reducing Agent in Reduction of Organic Halides

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The reductive dehalogenation of organic halides is one of the fundamental reaction which is frequently used in organic synthesis. Complex hydride reducing agents are the most effective and convenient for this conversion.[1,2]

Although lithium diisobutylmethylaluminum hydride was originally utilized for the facile *trans*-hydroalumination of disubstituted alkynes by Zweifel,[3] relatively few reports on the reducing properties of lithium trialkylaluminum hydrides have appeared in the literature[4]. We wish to report on the interesting reducing characteristics of lithium diisobutyl-*n*-butylaluminum hydride, the ate complex generated from equimolar amounts of diisobutylaluminum hydride and *n*-butyllithium, toward organic halides.

Reductions were usually carried out in tetrahydrofuran-*n*-hexane (4:1) at room temperature under nitrogen using equimolar amounts of the reagent and the substrate,[5] and reaction mixtures were maintained at 0.20*M* in the substrate and 0.21*M* in the reagent. The rate of reduction was followed by GLC at appropriate intervals of time and the yield was determined by isolation or GLC using a suitable internal standard.

Figure 1 shows the results obtained in the reaction of structurally different alkyl bromides with a stoichiometric amount of the reagent. Simple primary alkyl bromide, 1-bromodo-

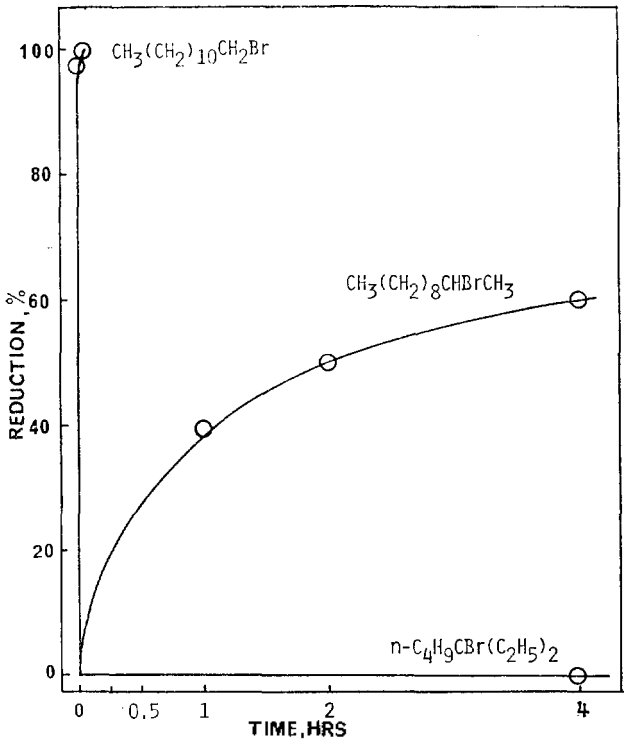

Figure 1. Rates of reduction of alkyl bromides with 1 molar equiv. of LiAl (i-Bu)$_2$(*n*-Bu)H at room temperature.

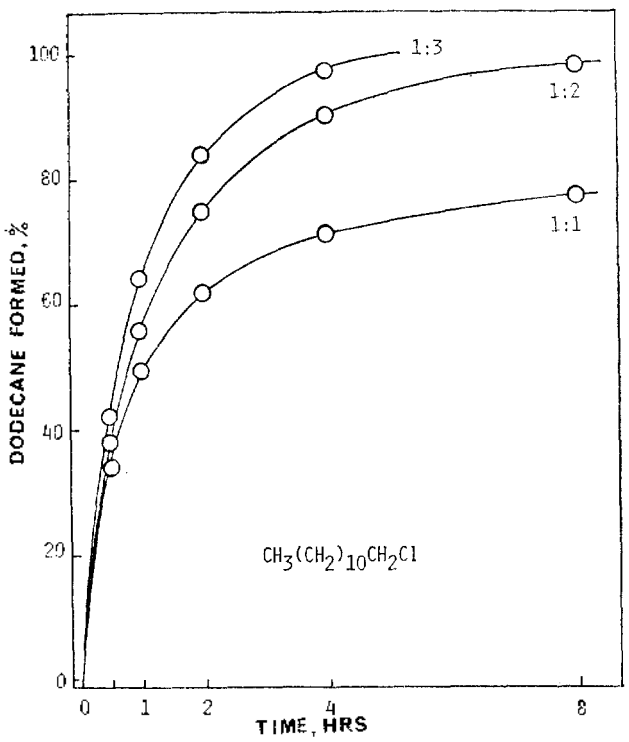

Figure 2: Rates of reduction of 1-chlorododecane with 1, 2, and 3 molar equiv of LiAl (i-Bu)$_2$(n-Bu)H at room temperature.

TABLE 1: Reduction of Halides by LiAl (*i*-Bu)$_2$(*n*-Bu)H in THF-*n*-Hexane at r.t.[a]

Substrate	Time	Product	Yield(%)[b]
1-Iodododecane	2 min	Dodecane	98(96)
1-Bromododecane	10 min	Dodecane	98(95)
1-Chlorododecxane	8 h	Dodecane	78,22[c]
2-Bromoundecane	4 h	Undecane	60,38[c]
Benzyl bromide	2 min	Toluene	92
Benzyl chloride	20 min	Toluene	95
α-Methylbenzyl bromide	1 h	Ethylbenzene	99
Cinnamyl bromide	5 min	β-Methylstyrene	100(95)[d]
β-Bromostyrene	24 h	styrene	63,35[c]
4-Bromotoluene	24 h	Toluene	0(94)[e]
3-Bromo-3-ethylheptane	24 h	3-Ethylheptane	0(90)[e]
Cycolhexyl bromide	24 h	Cyclohexane	<10[f],90[e]

[a] The solutions were 0.2M in the substrate and 0.21M in the reagent. [b] The yields were determined by GLC using internal standards. The isolated yields are indicated in the parentheses. [c] The unreacted halides were detected by GLC. [d] Trace amounts of allylbenzene (< 1 %) were detected. [e] The halides were recovered by isolation. [f] The yield was not determined by GLC and calculated based on the unreacted halide.

decane, was completely reduced in 10 min, whereas secondary alkyl bromide, 2-bromoundecane, was reduced much more slowly than the corresponding primary alkyl bromide. Tertiary alkyl bromide, 3-bromo-3-ethylheptane, was generally inert toward the reagent for 24 h. Thus, this reagent may be valuable for the selective reduction of primary alkyl iodides and bromides without simultaneous attack on tertiary alkyl bromides. 1-Chlorododecane was reduced to a 78:22 mixture of dodecane and the starting material in 8 h, whereas employment of either 2 or 3 molar equiv. of the reagent permited complete reduction in 8 h or 4 h, respectively (Figure 2). Simple benzylic and allylic bromides were rapidly and quantitatively reduced to the corresponding hydrocarbons. Vinyl bromide was reduced at a reasonable rate: 63% conversion in 24 h. In the reduction of cyclohexyl bromide, a sterically hindered halide, the unreacted halide was recovered in 90 % yield after 24 h. The low reactivity of this reagent toward the sterically hindered halide is attributed to the bulkiness of the reagent by the steric requirement of the three butyl groups. Table 1 summarizes the results obtained in the reduction of organic halides. Of special synthetic significance is the stoichiometric requ irement of the reagent for the reduction of organic halides. Essentially complete utilization of the hydride of the reagent is in marked contrast to the results obtained from reaction of complex hydride reducing agents with organic halides.[2i] Furthermore, empolyment of a stoichiometric amount of the reagent permits selective reduction of primary alkyl bromide into the corresponding alkane (97 % conversion) in the presence of primary alkyl chloride (2% conversion).[6] Similarly it is possible to selectively reduce primary benzylic bromide (95 % conversion) without significant attack on secondary benzylic bromide (1 % conversion).[7]

The results presented here indicate that this reagent is a source of exceptionally powerful nucleophilic hydride and allows employment of a stoichiometric amount of hydride ion in reduction of organic halides. Therefore, lithium diisobutyl-*n*-butylaluminum hydride should find many useful applications in organic synthesis.

The general procedure for the reduction of organic halides is as follows. To a solution of an organic halide (2 mmol) and a suitable internal standard (2 mmol) in THF (4.8 m*l*) at room temperature under nitrogen was added lithium diisobutyl-*n*-butylaluminum hydride (0.4 *M*, 5.4 m*l*, 2.16 mmol) in THF-*n*-hexane. The reaction mixture (0.5 m*l*) was withdrawn by a syringe at appropriate intervals of time, quenched with 10% HCl, extracted with ether, and analyzed by GLC. For isolation of reduction product, reduction was carried out in the similar manner without adding an internal standard.

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(6) The reagent (1 mmol) was reacted with a mixture of 1-bromooctane (1 mmol) and 1-chlorododecane (1 mmol) at room temperature for 10 min. The result was obtained by GLC analysis.

(7) Reduction was carried out in the same manner with benzyl bromide and α-methylbenzyl bromide.