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Reaction of Lithium *n*-Butylborohydride with Selected Organic Compounds Containing Representative Functional Groups

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Lithium *n*-butylborohydride was prepared from borane-dimethylsulfide (BMS) and *n*-butyllithium, and the approximate rates and stoichiometries of its reactions with selected organic compounds containing representative functional groups were studied in THF at room temperature. Phenol and benzenethiol liberated hydrogen quickly and quantitatively, and the reactions of primary alcohols, 2,6-di-*ter*-butylphenol and 1-hexanethiol liberated hydrogen quantitatively within 3 hrs, whereas the reactions of secondary and tertiary alcohols were very slow. Aldehydes and ketones were reduced rapidly and quantitatively to the corresponding alcohols. Cinnamaldehyde utilized 1 equiv. of hydride rapidly, suggesting the reduction to cinnamyl alcohol. Carboxylic acids evolved 1 equiv. of hydrogen rapidly and further reduction was not observed. Anhydrides utilized 2 equiv. of hydride rapidly but further hydride uptake was very slow, showing a half reduction. Acid chlorides were reduced to the alcohol stage very rapidly. All the esters examined were reduced to the corresponding alcohol rapidly. Lactones were also reduced rapidly. Epoxides took up 1 equiv. of hydride at a moderate rate to be reduced to the corresponding alcohols. Nitriles and primary amides were inert to this hydride system, whereas tertiary amide underwent slow reduction. Nitroethane and nitrobenzene were reduced slowly, however azobenzene and azoxybenzene were quite inert. Cyclohexanone oxime evolved 1 equiv. of hydrogen rapidly, but no further reduction was observed. Phenyl isocyanate and pyridine *N*-oxide were proceeded slowly, showing 1.74 and 1.53 hydride uptake, respectively in 24 hours. Diphenyl disulfide was reduced rapidly, whereas di-*n*-butyl disulfide, sulfone and sulfonic acids were inert or sluggish. *n*-Hexyl iodide and benzyl bromide reacted rapidly, but *n*-octyl bromide, *n*-octyl chloride, and benzyl chloride reacted very slowly.

Introduction

Since the first utilization of diborane¹ on the reduction of carbonyl compounds in 1930's and the discovery of sodium borohydride² and lithium aluminum hydride³ in 1940's, numerous hydride reagents have been prepared and studied for their reducing characteristics in the reactions with representative organic functional groups.⁴⁻¹⁰ In recent years a number of alkali metal trialkylborohydrides have emerged as highly attractive reducing agents in organic synthesis.¹¹⁻¹⁴ And the preparation methods of various trialkylborohydrides have already been reported.¹⁵ And also the reactions of lithium, sodium, and potassium hydrides with representative mono- and dialkylboranes (9-BBN, dicyclohexylborane, diisiamylborane, diisopinocampheylborane, thexylborane, monoisopinocampheylborane) in THF were examined in detail with respect to rate, stoichiometry, and products.¹⁶ Among these trialkylborohydrides, lithium triethylborohydride (super hydride) is known to be an exceptionally powerful and selective reducing agents in organic synthesis and its

reactions with selected organic compounds containing representative functional groups have been explored thoroughly.¹⁷ In contrast with lithium triethylborohydride, it was found that lithium borohydride has relatively mild reducing characteristics.¹⁸ Thus it seemed reasonable to assume that a monoalkylborohydride would show in-between reducing abilities. Since monoalkylborohydride system has not yet been studied systematically, we planned to investigate the reducing characteristics of lithium *n*-butylborohydride, lithium *t*-butylborohydride as well as lithium phenylborohydride. In the first place we undertook a study of approximate rate and stoichiometry of the reaction of $\text{Li}-\text{BuBH}_2$ with representative functional groups. The results are presented in this paper.

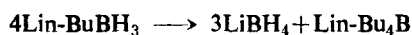
Results and Discussion

Preparation of Lithium *n*-Butylborohydride

Lithium *n*-butylborohydride ($\text{Li}-\text{BuBH}_2$) was prepared by addition of BMS (Borane-dimethyl sulfide complex) to equimolar amounts of *n*-butyllithium in *n*-hexane at -15°C . White precipitate was formed.

After decanting the solvent by filtration through a sintered glass filter under a slightly positive pressure of nitrogen, the residual white precipitate was dissolved in THF. The concentration was determined by hydrolyzing a known aliquot of the solution with THF-water-methanol-glycerine (1 : 1 : 1 : 1) at room temperature. Yield of Lin-BuBH₃ based on the hydride concentration and total volume was 83–85 %. Lin-BuBH₃ thus prepared was quite stable under nitrogen at 0 °C and the hydride concentration remained constant at room temperature at least over the period of a week.

The THF solution of this reagent exhibited B-H absorption band at 2,170 cm⁻¹ in IR spectrum, which is characteristic of monoalkylborohydride.¹⁶ And in the reaction with excess MeI (10 mmols), 5.40 mmols of methane gas was evolved from 15.5 mmols of "hydride" (5.16 mmols of Lin-BuBH₃ or 3.62 mmols of LiBH₄), suggesting that following disproportionation did not occur.



Above experimental data and different reducing characteristics of the reagent from LiBH₄ indicate the borohydride is "Lin-BuBH₃".¹⁹

Procedure for Rate and Stoichiometry Study

The general procedure adopted was to add 5 mmol of the organic compound under investigation to 6.67 mmol of Lin-BuBH₃ (20 mmol in hydride) in appropriate amount of tetrahydrofuran to give 20 ml of solution. The mixture were maintained at room temperature. This made the reaction mixture 1.0 M in hydride and 0.25 M in compound. Any hydrogen evolved was noted. Aliquots (4 ml or 2 ml) were then removed at appropriate intervals of time and analyzed for residual hydride by injecting them into a hydrolyzing mixture of THF-water-methanol-glycerine (1 : 1 : 1 : 1). Simultaneously, a blank was run, in which THF was added, in place of the THF solution of the compound, all other conditions being the same. When hydrogen evolution was continuous, individual experiments were conducted to measure the hydrogen evolution and to determine the residual hydride at different time intervals. In this way, it was possible to estimate both the approximate rate at which reduction proceeds and the stoichiometry of the reaction (number of hydride utilized per mol of the compound).

Product Analysis by GLC

Having established the approximate rate and stoichiometry of the reaction, it was desirable to establish the nature of the products wherever it is interesting and offers possibility for selective reduction. Accordingly, separate reactions on a 5 mmol or 2.5 mmol scale were carried out by using either a stoichiometric amount of the reagent or an excess amount, depending upon the nature of the reaction. The products were identified by GLC comparison with authentic samples, and the yields were determined by GLC utilizing internal standards and standard synthetic mixture.

Alcohols, Phenols, Amines, and Thiols. Among the alcohols examined, only primary alcohols liberated hydrogen quantitatively. Secondary alcohol, 3-hexanol, liberated hydrogen very slowly and tertiary alcohol, 3-ethyl-3-pentanol, was

TABLE 1: Reaction of Lin-BuBH₃ with Representative Alcohols, Phenols, Amine and Thiols in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
1-Hexanol	0.5	0.25	0.25	0.00
	1.0	0.46	0.46	0.00
	3.0	1.01	1.01	0.00
Benzyl alcohol	0.5	0.33	0.33	0.00
	1.0	0.58	0.58	0.00
	3.0	1.02	1.02	0.00
3-Hexanol	1.0	0.08	0.08	0.00
	3.0	0.09	0.09	0.00
	6.0	0.11	0.11	0.00
	24.0	0.23	0.23	0.00
3-Ethyl-3-pentanol	1.0	0.00	0.00	0.00
	3.0	0.02	0.02	0.00
	6.0	0.03	0.03	0.00
	24.0	0.07	0.07	0.00
Phenol	0.25	1.06	1.06	0.00
	0.5	1.06	0.16	0.00
2,6-Di-tert-butylphenol	0.5	0.56	0.56	0.00
	1.0	0.83	0.83	0.00
	3.0	1.01	1.01	0.00
<i>n</i> -Hexylamine	1.0	0.01	0.01	0.00
	3.0	0.03	0.03	0.00
	6.0	0.03	0.03	0.00
	24.0	0.05	0.05	0.00
1-Hexanethiol	0.5	0.45	0.45	0.00
	1.0	0.68	0.68	0.00
	3.0	1.06	1.06	0.00
Benzenethiol	0.25	1.09	1.09	0.00
	0.5	1.09	1.09	0.00

^a Five mmols of compound added to 6.67 mmols of Lin-BuBH₃ in 20 ml of solution (0.25 M in compound and 1.0M in hydride).

^b In mmole/mole of compound.

almost inert to the reagent under the experimental conditions. The rate of hydrogen evolution for alcohols decreases in the order of primary >> secondary > tertiary. Phenol, 2, 6-di-tert-butylphenol and thiols evolved hydrogen quantitatively. *n*-Hexylamine proved to be inert to the reagent under the experimental conditions. The rates of hydrogen evolution in the reaction of 1-hexanol, benzyl alcohol, and 1-hexanethiol with LiBH₄¹⁸ were slower than those with Lin-BuBH₃, showing that the monoalkylborohydride is a stronger hydride donor to these alcohols and the thiol than LiBH₄. The results are summarized in Table 1.

Aldehydes and Ketones. The aldehydes and ketones examined rapidly took up 1 equiv. of hydride to be reduced to the alcohol stage, similar to LiBH₄¹⁸ and LiEt₃BH.¹⁷ A representative α , β -unsaturated carbonyl compound, cinnamaldehyde, utilized 1 equiv. of hydride rapidly without conspicuous uptake of the second hydride. This corresponds to a rapid reduction to the cinnamyl alcohol stage. In fact, GLC analysis showed 95 % of cinnamyl alcohol was yielded from the reaction of the aldehyde with Lin-BuBH₃.

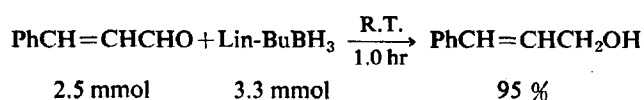


TABLE 2A: Reaction of Lin-BuBH₃ with Representative Aldehydes and Ketones in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Caproaldehyde	0.5	0.10	1.17	1.07
	1.0	0.10	1.17	1.07
Benzaldehyde	0.5	0.05	1.07	1.02
	1.0	0.05	1.07	1.02
2-Octanone	0.5	0.13	1.17	1.04
	1.0	0.13	1.17	1.04
Acetophenone	0.5	0.06	1.06	1.00
	1.0	0.06	1.06	1.00
Benzophenone	0.5	0.09	1.07	0.98
	1.0	0.09	1.07	0.98
Norcamphor	0.5	0.14	1.16	1.02
	1.0	0.14	1.16	1.02
Camphor	0.5	0.06	1.14	1.08
	1.0	0.06	1.09	1.03
Cinnamaldehyde	0.5	0.00	0.13	1.03
	1.0	0.00	1.03	1.03
	3.0	0.00	1.03	1.03
	6.0	0.00	1.03	1.03
	24.0	0.00	1.03	1.03

^{a,b} See the corresponding footnotes in Table 1. ^c Immediately became turbid.

TABLE 2B: Stereochemistry of Reduction of Representative Cyclic and Bicyclic Ketones with Lin-BuBH₃ in THF at 0°C

Compound	H-/cpd	Time h	Alcohol Product	
			Less stable isomer	Percentage ^a
2-Methylcyclohexanone	3.0	1.0	<i>cis</i>	33(31)
4- <i>tert</i> -Butylcyclohexanone	3.0	1.0	<i>cis</i>	9.0(7.0)
Norcamphor	3.0	1.0	<i>endo</i>	92(88)
Camphor	3.0	1.0	<i>exo</i>	80(77)

^a Numbers in the parenthesis are % of the isomers obtained with LiBH₄ (ref. W. S. Park, M. S. thesis, Sogang University, Seoul, Korea, 1979).

TABLE 3: Reaction of Lin-BuBH₃ with Representative Quinones in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
<i>p</i> -Benzoquinone ^{c,d}	1.0	0.54	2.00	1.46
	3.0	0.54	1.98	1.44
Anthraquinone ^{e,f}	1.0	0.34	2.09	1.75
	3.0	0.34	2.13	1.79

^{a,b} See the corresponding footnotes in Table 1. ^c Each measurement was done separately and hydrolyzing the reaction mixture in a reaction flask. ^d Immediately blue precipitate was formed, then its color was changed to pale green. ^e Reverse addition (solution of reagent added to suspension of anthraquinone). ^f Red precipitate via initial green precipitate

Similar observations was reported with LiBH₄,¹⁸ 9-BBN,²⁰ lithium tri-*tert*-butoxyaluminumhydride⁶, and with LiEt₃BH.¹⁷ The results are summarized in Table 2A. The stereochemistry of cyclic and bicyclic ketones such as 2-methylcyclohexanone, 4-*tert*-butylcyclohexanone, norcamphor, and camphor was examined. The experimental data with Lin-BuBH₃ were

TABLE 4: Reaction of Lin-BuBH₃ with Representative Acids and Acyl Derivatives in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Caproic acid ^c	1.0	1.08	1.09	0.01
	3.0	1.08	1.13	0.05
	6.0	1.08	1.13	0.05
	24.0	1.08	1.11	0.03
Benzoic acid ^d	1.0	1.04	1.04	0.00
	3.0	1.04	1.07	0.03
	6.0	1.04	1.07	0.03
	24.0	1.04	1.11	0.07
Acetic anhydride ^e	1.0	0.08	1.99	1.91
	3.0	0.08	2.10	2.02
	6.0	0.08	2.20	2.12
	24.0	0.08	2.29	2.21
Succinic anhydride ^e	1.0	0.29	2.10	1.81
	3.0	0.29	2.20	1.91
	6.0	0.29	2.30	2.01
	24.0	0.29	2.39	2.10
Phthalic anhydride ^f	1.0	0.32	2.20	1.88
	3.0	0.32	2.40	2.08
	6.0	0.32	2.40	2.08
	24.0	0.32	2.39	2.07
Caproyl chloride	0.5	0.02	2.07	2.05
	1.0	0.02	2.07	2.05
Benzoyl chloride	0.5	0.00	2.02	2.02
	1.0	0.00	2.02	2.02

^{a,b} See the corresponding footnotes in Table 1. ^c Immediate white precipitate. ^d White precipitate after 40 min. ^e Immediately became turbid. ^f Color changes to pale yellow.

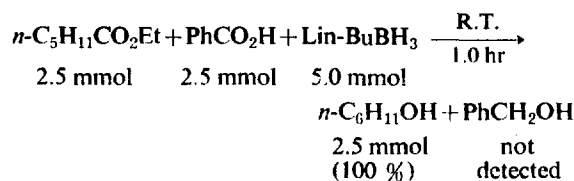
very similar to those with LiBH₄.²¹ The results are summarized and compared with the results with LiBH₄²¹ in Table 2B.

Quinones. The reduction of a quinone to hydroquinone should utilize 2 equiv. of hydride, one for reduction and one for hydrogen evolution. On the other hand, reduction to the 1,4-dihydroxycyclohexadiene stage should utilize 2 equiv. of hydride without hydrogen evolution. *p*-Benzoquinone rapidly consumed 2.0 equiv of hydride, of which 0.54 equiv. was used for hydrogen evolution. An immediate formation of precipitate was observed. This changed its color from an initial blue to pale green within 30 min. The value observed for the hydride uptake does not correspond to clean reduction to either stage. Anthraquinone rapidly consumed about 2.0 equiv. of hydride, of which 0.34 equiv. was utilized for hydrogen evolution. These results indicate that the major product would be 9,10-dihydro-9,10-dihydroxyanthracene. The results are summarized in Table 3.

Carboxylic Acids and Acyl Derivatives. Carboxylic acids instantly liberated 1 equiv. of hydrogen to form white precipitate. But no further hydride uptake was observed with both caproic acid and benzoic acid. Similar observations for carboxylic acids were reported with sodium borohydride,²² lithium tri-*tert*-butoxyaluminumhydride,⁶ and lithium triethylborohydride.¹⁷ Acid anhydrides utilized 2 equiv. of hydride rapidly. This corresponds to a half reduction. The results are summarized in Table 4.

Esters and Lactones. Ethyl caproate and ethyl benzoate

consumed 2 equiv. of hydride within 1.0 and 2.0 hrs, respectively. Hydrolysis of the reaction mixtures provided 1-hexanol and benzyl alcohol, respectively, in quantitative yields. Ethyl caproate was demonstrated to be selectively reduced in the presence of benzoic acid.

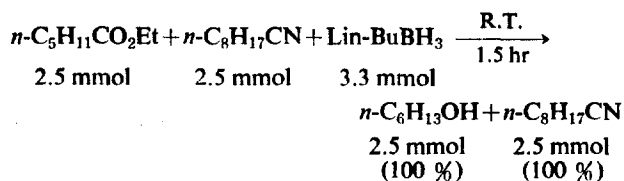


LiBH_4 has been utilized for the selective reduction of ester in the presence of carboxylic group. For example, the half ester of β -hydroxy- β -methylglutaric acid was reported to be reduced to give mevalonolactone by using LiBH_4 .²³ However, Lin-BuBH_3 seems to be more advantageous for such selective reductions, because the reduction with LiBH_4 is known to be very slow.¹⁸

Phenyl acetate rapidly utilized 2 equiv. of hydride and isopropenyl acetate consumed about 3 equiv. of hydride. Lactones examined were also reduced very rapidly. These results indicate that Lin-BuBH_3 is much more powerful than LiBH_4 ¹⁸ in the reduction of esters and lactones. The results are summarized in Table 5.

Epoxides. The rates of reduction of epoxides with Lin-BuBH_3 are much faster than those with LiBH_4 ,¹⁸ however much slower than those with LiEt_3BH .¹⁷ For example, complete reduction of 1,2-butylene oxide with LiBH_4 at room temperature required more than 24 hrs, whereas the epoxide was completely reduced by Lin-BuBH_3 within 2 hrs. LiEt_3BH ¹⁷ was reported to reduce the same epoxide within 5 min even at 0°C. The results of our study are summarized in Table 6.

Amides and Nitriles. Caproamide and benzamide were inert to Lin-BuBH_3 . Aliphatic and aromatic nitriles were also proved to be inert to this borohydride. Tertiary amides, *N,N*-dimethylacetamide and *N,N*-dimethylbenzamide, were reduced slowly. This suggests the possibility of the selective reduction of esters, lactones, and epoxides in the presence of these inert functional groups. In fact, ethyl caproate was selectively reduced to 1-hexanol in quantitative yield in the presence of *n*-octyl cyanide.



Selective reduction of ester in the presence of cyano group can be also achieved by utilizing LiBH_4 in THF. A cyano ester, methyl 9-cyano-2-methoxynon-2-enoate, was reduced to the corresponding cyano alcohol in 91% yield at 25°C in 52 hrs.²⁴ As the selective reducing agent, equimolar mixture of NaBH_4 and LiBr was used. The actual reducing species is presumably LiBH_4 .²⁴ Compared with LiBH_4 , Lin-BuBH_3 seems to be more attractive reagent for such selective reduction, because the reaction time can be reduced to less than 2

TABLE 5: Reaction of Lin-BuBH_3 with Representative Esters and Lactones in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Ethyl caproate	0.5	0.05	1.77	1.72
	1.0	0.05	2.12	2.07
	3.0	0.05	2.12	2.07
Ethyl benzoate	0.5	0.04	1.11	1.06
	1.0	0.04	1.81	1.77
	2.0	0.04	2.02	1.98
	3.0	0.04	2.02	1.98
Phenyl acetate	1.0	0.00	2.05	2.05
	3.0	0.00	2.05	2.05
γ -Butyrolactone ^c	0.5	0.05	1.91	1.86
	1.0	0.05	2.02	1.97
	3.0	0.05	2.02	1.97
Phthalide ^d	1.0	0.04	2.08	2.04
	3.0	0.04	2.08	2.04
Isopropenyl acetate	1.0	0.04	2.54	2.50
	3.0	0.04	2.88	2.84
	6.0	0.04	2.88	2.84

^{a,b} See the corresponding footnotes in Table 1. ^c Immediate white precipitate. ^d Immediate color change to yellow.

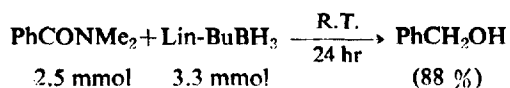
TABLE 6: Reaction of Lin-BuBH_3 with Representative Epoxides in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
1,2-Butylene oxide	1.0	0.03	0.76	0.73
	2.0	0.03	1.08	1.05
	3.0	0.03	1.08	1.05
Styrene oxide	1.0	0.05	0.38	0.33
	3.0	0.05	0.88	0.83
	6.0	0.05	1.09	1.05
Cyclohexene oxide	1.0	0.06	0.17	0.11
	3.0	0.06	0.35	0.29
	6.0	0.06	0.40	0.34
	24.0	0.06	1.01	0.95
1-Methy-1,2-cyclohexene oxide	1.0	0.11	0.23	0.12
	3.0	0.11	0.33	0.22
	6.0	0.11	0.39	0.28
	24.0	0.11	0.43	0.32

^{a,b} See the corresponding footnotes in Table 1.

hrs from more than 2 days.

It is interesting to note that *N,N*-dimethylbenzamide was reduced by Lin-BuBH_3 to benzyl alcohol in 88% yield by GLC analysis.



However, $\text{Li}_9\text{-BBNH}$ ²⁵ reduced the tertiary amide to benzyl-dimethylamine, whereas benzyl alcohol was formed from the reaction of the amide with LiEt_3BH .¹⁷ The results are summarized in Table 7.

Nitro Compounds and Their Derivatives. Nitroethane evolved 1 equiv. of hydrogen, forming white precipitate. However the reduction was very sluggish, showing only 0.39 hydride

TABLE 7: Reaction of Lin-BuBH₃ with Representative Amides and Nitriles in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Caproamide	1.0	0.06	0.14	0.08
	3.0	0.06	0.14	0.08
	6.0	0.06	0.14	0.08
	24.0	0.06	0.10	0.04
Benzamide	1.0	0.08	0.14	0.06
	3.0	0.08	0.15	0.07
	6.0	0.08	0.15	0.07
	24.0	0.08	0.10	0.02
N,N-Dimethyl acetamide	1.0	0.04	0.13	0.09
	3.0	0.04	0.13	0.09
	6.0	0.04	0.16	0.12
	9.0	0.04	0.43	0.39
N,N-Dimethyl benzamide	1.0	0.08	0.33	0.25
	3.0	0.08	0.68	0.60
	6.0	0.08	1.26	1.18
	9.0	0.08	1.18	1.73
Capronitrile	1.0	0.03	0.09	0.06
	3.0	0.03	0.11	0.08
	6.0	0.03	0.09	0.06
	24.0	0.03	0.09	0.06
Benzonitrile	1.0	0.00	0.00	0.00
	3.0	0.00	0.00	0.00
	6.0	0.00	0.00	0.00
	24.0	0.00	0.00	0.00

^{a,b} See the corresponding footnotes in Table 1.**TABLE 8: Reaction of Lin-BuBH₃ with Representative Nitro Compounds and Their Derivatives in THF at Room Temperature**

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Nitroethane ^c	1.0	0.33	0.33	0.00
	3.0	0.53	0.53	0.00
	6.0	0.82	1.04	0.22
	24.0	1.14	1.53	0.39
Nitrobenzene ^d	1.0	0.10	0.24	0.14
	3.0	0.22	0.55	0.33
	6.0	0.35	0.80	0.45
	24.0	0.94	1.92	0.98
Azobenzene	1.0	0.00	0.00	0.00
	3.0	0.00	0.07	0.07
	6.0	0.00	0.07	0.07
	24.0	0.00	0.05	0.05
Azoxybenzene	1.0	0.04	0.07	0.03
	3.0	0.04	0.07	0.03
	6.0	0.04	0.07	0.03
	24.0	0.04	0.09	0.05

^{a,b} See the corresponding footnotes in Table 1. ^c Immediately became turbid and white precipitate with time. ^d Color change to orange.

uptake in 24 hrs. And nitrobenzene utilized slowly 2 equiv. of hydride, one for hydrogen evolution and one for reduction. Azobenzene and azoxybenzene were inert to this reagent under the experimental conditions. The results are summarized in Table 8.

TABLE 9: Reaction of Lin-BuBH₃ with Representative Other Nitrogen Compounds in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Cyclohexanone oxime ^c	1.0	1.12	1.20	0.08
	3.0	1.12	1.20	0.08
	6.0	1.12	1.21	0.09
	24.0	1.12	1.19	0.07
Phenyl isocyanate	1.0	0.06	1.46	1.40
	3.0	0.06	1.61	1.55
	6.0	0.06	1.66	1.60
	24.0	0.06	1.80	1.74
Pyridine	1.0	0.08	0.10	0.02
	3.0	0.08	0.10	0.02
	6.0	0.08	0.08	0.00
	24.0	0.08	0.11	0.03
Pyridine N-oxide	1.0	0.14	1.13	0.99
	3.0	0.14	1.55	1.41
	6.0	0.14	1.65	1.51
	24.0	0.14	1.67	1.53

^{a,b} See the corresponding footnotes in Table 1. ^c Immediately became turbid.**TABLE 10: Reaction of Lin-BuBH₃ with Representative Sulfur Compounds in THF at Room Temperature**

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
Di- <i>n</i> -butyl disulfide	1.0	0.02	0.10	0.08
	3.0	0.03	0.12	0.09
	6.0	0.05	0.23	0.18
	24.0	0.52	1.11	0.59
Diphenyl disulfide	0.25	1.10	2.15	1.05
	0.5	1.10	2.15	1.05
Methyl phenyl sulfide	1.0	0.03	0.06	0.03
	3.0	0.03	0.04	0.01
	6.0	0.03	0.04	0.01
	24.0	0.03	0.10	0.07
Dimethyl sulfoxide	1.0	0.05	0.10	0.05
	3.0	0.05	0.07	0.02
	6.0	0.05	0.07	0.02
	24.0	0.05	0.11	0.06
Diphenyl sulfone	1.0	0.00	0.00	0.00
	3.0	0.00	0.00	0.00
	6.0	0.00	0.01	0.01
	24.0	0.00	0.00	0.00
Methanesulfonic acid	1.0	1.10	1.10	0.00
	3.0	1.10	1.10	0.00
	6.0	1.10	1.10	0.00
<i>p</i> -Toluenesulfonic acid monohydrate	1.0	3.09	3.19	0.10
	3.0	3.09	3.19	0.10
	6.0	3.09	3.19	0.10
Cyclohexyl tosylate	1.0	0.01	0.03	0.02
	3.0	0.01	0.09	0.08
	6.0	0.01	0.11	0.10
	24.0	0.01	0.19	0.18

^{a,b} See the corresponding footnotes in Table 1.

Other Nitrogen Compounds. Cyclohexanone oxime rapidly liberated 1 equiv. of hydrogen without consumption of the next hydride. The reaction of the oxime with LiBH₄ consumed 1.03 hydride for reduction 24 hrs, suggesting the reduc-

TABLE 11: Reaction of Lin-BuBH₃ with Representative Alkyl Halides in THF at Room Temperature

Compound ^a	Time h	Hydrogen evolved ^b	Hydride used ^b	Hydride used for redn ^b
<i>n</i> -Hexyl iodide	1.0	0.06	1.05	0.99
	3.0	0.06	1.05	0.99
<i>n</i> -Octyl bromide	1.0	0.04	0.20	0.16
	3.0	0.04	0.30	0.26
	6.0	0.04	0.35	0.31
	24.0	0.04	0.58	0.54
<i>n</i> -Octyl chloride	1.0	0.08	0.12	0.04
	3.0	0.08	0.14	0.08
	6.0	0.08	0.21	0.13
	24.0	0.08	0.32	0.24
Benzyl bromide	1.0	0.04	1.04	1.00
	3.0	0.04	1.04	1.00
Benzyl chloride	1.0	0.07	0.10	0.03
	3.0	0.07	0.21	0.14
	6.0	0.07	0.22	0.15
	24.0	0.07	0.24	0.17

^{a, b} See the corresponding footnotes in Table 1.

tion to the hydroxylamine stage.^{13a} Consequently, the formation of oximes would provide a means for protecting carbonyl groups toward Lin-BuBH₃. Phenyl isocyanate utilized 1 equiv. of hydride rapidly, but further reduction was very slow. Pyridine was inert to the reagent, but pyridine N-oxide consumed 1.5 equiv. of hydride within 24 hrs. The results are summarized in Table 9.

Sulfur Compounds. Diphenyl disulfide utilized 2 equiv. of hydride within 15 min, one for hydrogen evolution and one for reduction. Thus, diphenyl disulfide undergoes reduction to benzenethiol rapidly and quantitatively. The corresponding reaction with LiBH₄ required 24 hrs.^{18a} However, di-*n*-butyl disulfide was reduced very slowly. Cyclohexyl tosylate was also reduced sluggishly. Sulfoxide, sulfone, and sulfide examined were all inert to the reagent. Sulfonic acids rapidly evolved theoretical amount of hydrogen, but were not reduced. The results are summarized in Table 10.

Alkyl Halides. Among the alkyl halides examined, *n*-hexyl iodide and benzyl bromide were reduced rapidly. However, *n*-octyl bromide, *n*-octyl chloride, and benzyl chloride reacted with the reagent very slowly. The results are summarized in Table 11.

Conclusions

Reducing characteristic of "Lin-BuBH₃" in its reaction with representative functional groups were systematically explored in THF at room temperature. The experimental results indicate that this reagent is more powerful than LiBH₄, but weaker than LiEt₃BH in the reduction of esters, epoxides, tertiary amides, phenyl isocyanate, pyridine N-oxide, and alkyl halides. And it has been demonstrated in this study that "Lin-BuBH₃" is a useful selective reducing agent for reducing ester in the presence of carboxylic or cyano group.

Thus "Lin-BuBH₃" occupies a unique position among the wide spectrum of various borohydride reductions.

Experimental

Materials. Tetrahydrofuran was distilled over lithium aluminum hydride under nitrogen and stored over 4A molecular sieves. Most of the compounds utilized in this study were commercial products of the highest available purity. They were used without further purification. Some compounds were synthesized by using standard procedures. In all of the cases, physical constants agreed satisfactorily with constants in the literature. All glassware was dried thoroughly in a drying oven and cooled under a dry stream of nitrogen. All reduction experiments were carried out under a dry nitrogen atmosphere. Hypodermic syringes were used to transfer the solutions and liquid materials.

Standard Solution of Lin-BuBH₃. A 500 ml hot, dry flask, equipped with a inlet tube and reflux condenser connected to a mercury bubbler, was placed in an ice-salt bath (-15 °C) and cooled under a stream of dry nitrogen. In this flask, 125 ml of *n*-hexane and 125 ml (200 mmol) of 1.6 M *n*-butyllithium in *n*-hexane were introduced and cooled down by stirring for 15 min. Then 20 ml (200 mmol in BH₃, 600 mmol in hydride) of 10M BMS was added dropwise with vigorous stirring, and the stirring was continued for further 0.5 h (addition time; 40 min). White precipitate was formed on the addition of BMS. After allowing to stand at -15 °C for 0.5 hr to settle down the white precipitate, the solvent was decanted by filtration through a Gas Dispersion, Fritted Cylinder (Cat. No. 39533-12C, Corning) under a slight positive pressure of nitrogen. Then the white precipitate was dissolved in 150 ml of dry THF at -15 °C. The resulting clear solution was standardized by removing an aliquot, hydrolyzing it with a THF-water-methanol-glycerine (1 : 1 : 1 : 1) mixture, and measuring the hydrogen evolved. With a series of preparations, the concentrations were determined to be in the range of 2.26-2.44 M in hydride and the total volumes were 220-210 ml. Therefore the approximate yields of Lin-BuBH₃ based on the hydride concentration and total volume were 83-85 %. This hydride solution did not consume the hydride in the attempted reaction with 1-hexene, showing that the hydride solution was not contaminated with BMS. The THF solution of Lin-BuBH₃ showed a strong, broad absorption in the IR around 2,170 cm⁻¹ (ν_{B-H}). And Lin-BuBH₃ thus prepared was quite stable under nitrogen at 0 °C and the hydride concentration remained practically unchanged at least over the period of a week at room temperature. And 15.5 mmoles of "hydride" (5.16 mmoles of "Lin-BuBH₃" or 3.62 mmoles of LiBH₄) was allowed to react with 10 mmoles of MeI and collected 5.40 mmoles of methane gas. The amount methane evolved corresponds to 105% or 149% yields, based on the assumption that "the borohydride" is Lin-BuBH₃ or LiBH₄, respectively. This result suggests that the hydride reagent did not disproportionate into Lin-Bu₂B and LiBH₄.

Procedure for Study of the Rate and Stoichiometry. The reduction of ethyl benzoate is representative. The Lin-BuBH₃ solution (8.8 ml of 2.26 M solution, 20 mmol), and 6.2 ml of THF were introduced into a dried 100 ml flask fitted with a

rubber syringe cap on an inlet port, a magnetic stirring bar, and a reflux condenser connected to a gas buret. The flask was maintained at room temperature, and 5 ml of a 1 M solution of ethyl benzoate in THF was injected rapidly. Hydrogen evolution was monitored. In this way, a solution was obtained which was 0.33 M in Lin-BuBH₃ and 0.25 M in ethyl benzoate. Upon addition of the compound, 5.0 ml of hydrogen was evolved, corresponding to 0.04 mmol/mmol of compound. No more hydrogen evolution was observed throughout the reaction. After 0.5 h, a 4.0 ml aliquot of the reaction mixture was removed and injected into a hydrolyzing mixture of THF-water-methanol-glycerine (1 : 1 : 1 : 1). The hydrogen evolved was 2.86 mmol, indicating that 1.01 mmol of hydride had used per mmol of the ester, when compared to 3.96 mmol for blank experiment (in which 5 ml of THF had been substituted for 5 ml of ethyl benzoate solution). Therefore, 1.06 mmol of hydride was used for reduction per mmol of the ester, or $1.10 - 0.04 = 1.06$. Aliquots were also removed and hydrolyzed after 1.0, 2.0, and 3.0 h of reaction time. The amounts of hydrogen evolved in these experiments were 2.15, 1.94, 1.94 mmol, indicating 1.77, 1.98, and 1.98 to be the numbers of milimoles of hydride used for reduction per milimole of compound in 1.0, 2.0, and 3.0 h, respectively. Therefore the reaction was completed within 2.0 h.

Procedure for Product Analysis by GLC. The reduction of ethyl caproate is representative. In a 50 ml flask, fitted with a rubber syringe cap on an inlet port, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler, were placed 4.2 ml (3.4 mmol) of a 0.81 M solution of Lin-BuBH₃ and 5.4 ml of THF. Then 0.41 ml (2.5 mmol) of ethyl caproate was introduced while the reaction mixture was vigorously stirred at room temperature. After 1.0 h, the excess hydride was destroyed with 0.8 ml of water. Then the reaction mixture was cooled to 0 °C in an ice bath, and oxidized by the addition of 0.8 ml of 6N aqueous NaOH, followed by 1.0 ml of 30 % H₂O₂ and heating at 40–50 °C for 1.0 h. After addition of 1-octanol (2.5 mmol; 0.39 ml) as an internal standard, the aqueous layer was saturated with 5 g of anhydrous potassium carbonate and the dry THF layer was subjected to GLC analysis on a 10 % Carbowax 20M column, 8 ft × 0.125 in., indicating the presence of 100% 1-hexanol. And other compounds discussed were also examined in this manner by using appropriate internal standard.

Procedure for Competition Reaction. The reaction of ethyl caproate in the presence of benzoic acid is representative. 6.2 ml of 0.81 M Lin-BuBH₃ solution (5.1 mmol in hydride), and 11.0 ml of THF were introduced into a dried, 50 ml flask fitted with a rubber syringe cap on an inlet port, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler. The flask was maintained at room temperature with stirring, and 2.5 ml of THF solution containing 2.5 mmol of ethyl caproate and 2.5 mmol of benzoic acid was injected slowly. After 1.0 h, the remaining hydride was destroyed with water. Then the reaction mixture was oxidized with NaOH-H₂O₂, followed by addition of 2.5 mmol (0.39 ml) of 1-octanol as an internal standard. GLC analysis of the reac-

tion mixture revealed that the presence of 2.5 mmol of 1-hexanol and the absence of benzyl alcohol.

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