Lithium n-Butylborohydride as a Selective Reducing Agent for the Reduction of Enones, Cyclic Ketones, and Selected Carbonyl Compounds

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Lithium n-butylborohydride, the "ate" complex generated from n-butyllithium and borane–dimethyl sulfide complex in an equimolar ratio either in toluene–n-hexane or in tetrahydrofuran–n-hexane was reacted with enones, cyclic and bicyclic ketones, and selected carbonyl compounds in order to explore the reducing properties and to determine the synthetic utility of this reagent. Lithium n-butylborohydride in toluene–n-hexane is very effective for selective 1,2-reduction of acyclic enones and conjugated cyclohexenones and is solvent sensitive. The reduction of conjugated cyclopentenones is more prone to 1,4-reduction than that of conjugated cyclohexenones. The reagent in tetrahydrofuran–n-hexane reduces the unhindered cyclic ketones 3-methyl-, 4-methyl-, and 4-*tert*-butylcyclohexanone to the corresponding thermodynamically more stable isomers (equatorial OH) with stereoselecivities of 92%, 94%, and 98%, respectively. The stereoselectivities obtained with this reagent for such reductions are better than those reported with simple hydride reagents. Esters and lactones are rapidly and quantitatively reduced to the corresponding alcohols at 0 °C in toluene–n-hexane, whereas they are inert to this reagent at −78 °C, which permits the selective reduction of the ketones in the presence of the esters at the latter temperature. Acid chlorides are rapidly and quantitatively reduced to the corresponding alcohols. Acid anhydrides are reduced to an equimolar mixture of the acid and alcohol even at −78 °C. Carboxylic acids and primary and secondary amides are not reduced by the reagent at room temperature and are recovered unchanged. Tertiary amides are resistant to reduction and are only slowly converted to the corresponding amines and alcohols.

Recent developments in the area of alkali metal borohydrides have revealed that their reducing properties, e.g., functional group and regio- and stereoselectivity, are strongly influenced by the steric bulk and the number of alkyl substituents on the boron atom.[1] For instance, whereas sodium borohydride is a relatively mild and less stereoselective reducing agent, lithium tri-*sec*-butylborohydride (L-Selectride, Aldrich) is known to be an exceptionally powerful and highly stereoselective reducing agent.

Although the reducing properties of simple borohydrides and trialkylborohydrides have been intensively studied,[1] there are relatively few reports in the literature on the use of monoalkylborohydride reducing agents. Sodium ethylborohydride was briefly described by Köster, but its reducing ability is unexplored.[2] Lithium n-butylborohydride was recently utilized for the stereoselective reduction of enones successfully during the total synthesis of erythronolide B[3] and (−)-*N*-methylmaysenine.[4] More recently, the preparation of monoalkylborohydrides and dialkylborohydrides, produced by treatment of alkali metal hydrides with monoalkylboranes or dialkylboranes, has been reported by Brown.[5]

The lack of systematic investigations of the reducing properties of monoalkylborohydrides prompted a detailed study of the reduction of enones, cyclic and bicyclic ketones, and selected carbonyl compounds with lithium n-butylborohydride in toluene–n-hexane and/or tetrahydrofuran–n-hexane. This article describes the results of these investigaitons.

Results and Discussion

Preparation of Lithium n-Butylborohydride Either in Toluene–n-Hexane or in Tetrahydrofuran–n-Hexane.

A suspension of lithium n-butylborohydride in toluene–n-hexane was prepared from equimolar amounts of n-butyllithium and borane–dimethyl sulfide complex[6] as described.[3] A solution of lithium n-butylborohydride in tetrahydrofuran–n-hexane was prepared by the addition of equimolar amounts of n-butyllithium in n-hexane and borane–dimethyl sulfide complex in tetrahydrofuran at 0 °C under nitrogen. The reagent showed no sign of decomposition when kept at 0 °C under nitrogen for 1 month.

For the reductions, the ratio of toluene (or tetrahydrofuran) to n-hexane was adjusted to approximately 15:1.

Reduction of Enones. Selective 1,2-reduction of enones with hydride reducing agents is often difficult to achieve in organic synthesis due to competing 1,2- vs. 1,4-attack by hydride.[7] Among the many reducing agents which have been devised for this purpose, diisobutylaluminum hydride (DIBAH),[8] 9-borabicyclononane (9-BBN),[9] L- or K-Selectride,[10,11] and sodium borohydride–lanthanide salts[12] are generally the most effective and convenient,[13] although limitations have been noted.[11,14]

(1) For recent reviews see: (a) Walker, E. R. H. *Chem. Soc. Rev.* **1976**, *5*, 23. (b) Brown, H. C.; Krishnamurthy, S. *Tetrahedron* **1979**, *35*, 567.

(2) Binger, P.; Benedikt, G.; Rotermund, G. W.; Köster, R. *Justus Liebigs Ann. Chem.* **1968**, *717*, 21.

(3) Corey, E. J.; Kim, S.; Yoo, S.; Nicolaou, K. C.; Melvin, L. S.; Brunelle, D. J.; Falck, J. R.; Trybulski, E. J.; Sheldrake, P. W. *J. Am. Chem. Soc.* **1978**, *100*, 4620.

(4) Corey, E. J.; Weigel, L. O.; Chamberlin, A. R.; Lipshutz, B. *J. Am. Che. Soc.* **1980**, *102*, 1439.

(5) Brown, H. C.; Singaram, B.; Mathew, C. P. *J. Org. Chem.* **1981**, *46*, 2712.

(6) For the reaction of organometallic compounds with diborane see: (a) Pickles, G. M.; Thorpe, F. G. *J. Organomet. Chem.* **1974**, *76*, C23. (b) Breuer, S. W.; Thorpe, F. G. *Tetrahedron Lett.* **1974**, 3719. (c) Breuer, S. W.; Pickles, G. M.; Podesta, J. C.; Thorpe, F. G. *J. Chem. Soc., Chem. Commun.* **1975**, 36.

(7) (a) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972. (b) Ho, T.-L. "Hard and Soft Acids and Bases Principles in Organic Chemistry"; Academic Press: New York, 1977.

(8) Wilson, K. E.; Seidner, R. T.; Masamune, S. *J. Chem. Soc., Chem. Commun.* **1970**, 213.

(9) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1975**, *40*, 1864.

(10) Corey, E. J.; Becker, K. B.; Varma, R. K. *J. Am. Chem. Soc.* **1972**, *94*, 8616.

(11) (a) Ganem, B. *J. Org. Chem.* **1975**, *40*, 146. (b) Ganem, B.; Fortunato, J. M. *Ibid.* **1976**, *41*, 2194.

(12) (a) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226. (b) Gemal, A. L.; Luche, J.-L. *Ibid.* **1981**, *103*, 5454.

(13) For selective 1,2-reduction with other hydride reagents see: (a) Brown, H. C.; Hess, H. M. *J. Org. Chem.* **1969**, *34*, 2206. (b) Johnson, M. R.; Rickborn, B. *Ibid.* **1970**, *35*, 1041. (c) Hutchins, R. O.; Kandasamy, D. *Ibid.* **1975**, *40*, 2530. (d) Yoon, N. M.; Lee, H. J.; Kang, J.; Chung, J. S. *Taehan Hwahakhoe Chi* **1975**, *19*, 468. (e) Ashby, E. C.; Lin, J. J.; Goel, A. B. *J. Org. Chem.* **1978**, *43*, 183. (f) Fleet, G. W. J.; Harding, P. J. C. *Tetrahedron Lett.* **1981**, *22*, 675.

(14) (a) Winterfeldt, E. *Synthesis* **1975**, 617. (b) Brown, H. C.; Krishnamurthy, S.; Yoon, N. M. *J. Org. Chem.* **1976**, *41*, 1778. (c) Krishnamurthy, S.; Brown, H. C. *Ibid.* **1977**, *42*, 1197.

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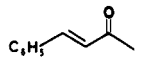
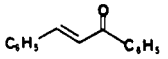
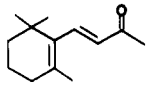
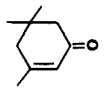
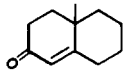
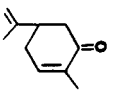
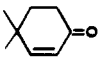
Table I. Reduction of Enones with Li-*n*-BuBH$_3$ in Toluene-*n*-Hexane at −78 °C

enone	no.	reaction time, h	product ratio, 1,2:1,4	isolated yield, %
	1	2	100:0	98
	2	2	100:0	99
	3	2	100:0	98
	4	4	100:0	98
	5	3	100:0	99
	6	2	100:0	96
	7	2	100:0	98
	8	2	92:8	84
	9	3	65:35	75[a]
	10	3	80:20	96[a]

[a] The yield was determined by GLC.

Although 1,2-selectivity has been reported in the reduction of enones with lithium *n*-butylborohydride,[3,4] the result is obscured by the fact that a number of other similar reducing agents including sodium borohydride and L-Selectride gave the corresponding allylic alcohol in 100% 1,2-selectivity.[15] In view of these facts, we undertook the reaction of lithium *n*-butylborohydride with both acyclic and cyclic enones.

Reductions were carried out in toluene–*n*-hexane at −78 °C by using equimolar amounts of enones and lithium *n*-butylborohydride. Under the present reaciton conditions, saturated ketones via 1,4-reduction were reduced to saturated alcohols. Reduction of acyclic enones such as **1–3** afforded exclusively the corresponding allylic alcohols, resulting only from 1,2-reduction. It is noteworthy that **2** was reduced by this reagent in 100% 1,2-selectivity in contrast with predominant 1,4-reduction by DIBAH (1,2/1,4 ratio of 35:65).[16]

β-Substituted cyclohexenones such as **4** and **5** underwent exclusive 1,2-reduction as was obtained with K-Selectride.[11] However, when β-unsubstituted cyclohexenones such as **6** and **7** were reacted with lithium *n*-butylborohydride, exclusive 1,2-reduction occurred. These results are in sharp contrast with earlier findings that the reduction of β-unsubstituted cyclohexenones with K-Selectride gives the exclusive 1,4-reduction products.[11] In the case of **8**, a mixture of 1,2- and 1,4-reduction products was obtained in ratio of 92:8. Presumably γ,γ-dimethyl substituents in **7** suppress 1,4-reduction by steric hindrance. Conjugated cyclopentenones were considerably more prone to 1,4-reduction by lithium *n*-butylborohydride than conjugated cyclohexenones. Thus, **9** gave a mixture of 1,2- and 1,4-reduction products in a ratio of 65:35, and **10** gave 1,2-reduction product as a major product (80% 1,2-selectivity).

The effect of reaction temperature was briefly investigated. The reduction of **5–7** at 0 or 25 °C afforded the corresponding allylic alcohols in 98% or better 1,2-selectivity. This result suggests that the ratio of 1,2 vs. 1,4 reduction is relatively temperature independent.

Table I summarizes the reduction results for a variety of structurally different enones chosen to determine the synthetic usefulness of this reagent in toluene–*n*-hexane.

(15) Corey, E. J.; Kim, S., unpublished results.
(16) Ashby, E. C.; Lin, J. J. *Tetrahedron Lett.* **1976**, 3865.

Table II. Reduction of Enones with Li-*n*-BuBH$_3$ in THF-*n*-Hexane at −78 °C

enone	reaction time, h	product ratio, 1,2:1,4	isolated yield, %
1	4	100:0	99
2	4	100:0	96
4	8	92:8	97
6	3	85:15	98
6[a]	1	10:90	90
7	3	98:2	98
8	3	67:33	90

[a] The reduction was carried out in THF–*n*-hexane–HMPA (5:1:5) at 25 °C.

The rates of 1,2- and 1,4-reduction appear to be solvent sensitive as seen in Table II. Thus, reductions in tetrahydrofuran–*n*-hexane at −78 °C gave, in many cases, substantially more 1,4-reduction. Such sensitivity has been noted previously.[17]

Reduction of Cyclic and Bicyclic Ketones. The stereoselective reduction of cyclic and bicyclic ketones by borohydride reducing agents has been studied intensively in recent years.[18] It has been demonstrated that the stereoselectivity depends critically on the steric bulk of alkyl substituents on the boron atom.[19] Sodium borohydride, the unhindered simple borohydride, in 2-propanol produces 70%, 75%, and 86% of the more stable isomer from axial attack on 2-methyl-, 3-methyl-, and 4-*tert*-butylcyclohexanone, respectively.[20] However, the bulky trialkylborohydride lithium tri-*sec*-butylborohydride (L-Selectride) approaches the corresponding ketones from the equatorial side, producing the less stable axial isomers with greater than 90% stereoselectivity.[19a]

(17) (a) Jackson, W. R.; Zurqiyah, A. *J. Chem. Soc.* **1965**, 5280. (b) Snyder, E. I. *J. Org. Chem.* **1967**, *32*, 3531. (c) Handel, H.; Pierre, J. L. *Tetrahedron* **1975**, *31*, 2799.
(18) For the stereochemistry and mechanism of cyclic ketone reductions by hydride reagents see: (a) Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449. (b) Boone, J. R.; Ashby, E. C. *Top. Stereochem.* **1979**, *11*, 53. (c) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.
(19) (a) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159. (b) Brown, C. A. *Ibid.* **1973**, *95*, 4100. (c) Hooz, J.; Akiyama, S.; Cedar, F. J.; Bennett, M. J.; Tuggle, R. M. *Ibid.* **1974**, *96*, 274. (d) Krishnamuthy, S.; Brown, H. C. *Ibid.* **1976**, *98*, 3383.
(20) Wigfield, D. C.; Feiner, S.; Gowland, F. W. *Tetrahedron Lett.* **1976**, 3377.

Table III. Reduction of Cyclic and Bicyclic Ketones with Li-*n*-$BuBH_3$ at −78 °C

ketone	solvent[a]	time, h	% less stable Li-*n*-$BuBH_3$	isomer, % $NaBH_4$[b]	isolated yield, %
2-methylcyclohexanone	A	3	31	30	93
	B	2	31		90
3-methylcyclohexanone	A	2	8	25	93
	B	2	10		88
4-methylcyclohexanone	A	2	6	16	94
	B	2	10		91
4-*tert*-butylcyclohexanone	A	2	2	14	98
	B	2	6		98
2-*tert*-butylcyclohexanone	A	4	65	50	96
	B	2	55		94
3,3,5-trimethylcyclohexanone	A	4	66	55	95
	B	2	41		92
norcamphor	A	2	94	89	95
	B	2	96		96
camphor	A	3	85	89	97
	B	2	88		97

[a] A and B refer to THF–*n*-hexane and toluene–*n*-hexane, respectively. [b] The data were obtained from the literature (see ref 20 and 22).

Of special concern to us was to determine whether lithium *n*-butylborohydride resembles simple borohydrides or relatively hindered trialkylborohydrides in stereoselective reductions of cyclic and bicyclic ketones.[21]

The stereochemical results of our study are summarized in Table III along with comparative data for sodium borohydride reductions of the corresponding ketones.[20,22] The reduction was carried out in toluene–*n*-hexane and tetrahydrofuran–*n*-hexane with equimolar amounts of the reagent and cyclic ketones at −78 °C. Under these conditions, the ketones were rapidly and quantitatively reduced to the corresponding alcohols in 2–4 h.

Lithium *n*-butylborohydride reduced the moderately hindered ketone 2-methylcyclohexanone to *trans*-2-methylcyclohexanol as a major product with a stereoselectivity comparable to that of sodium borohydride. The unhindered ketone 3-methylcyclohexanone afforded primarily the cis alcohol in 92% stereoselectivity with tetrahydrofuran–*n*-hexane as the reaction solvent. Under similar reaction conditions, L-Selectride affords the trans alcohol in 95% stereoselectivity.[19a] Even better discrimination was observed in the reduction of 4-alkylcyclohexanones, the least hindered of the alkylcyclohexanones. 4-Methylcyclohexanone and 4-*tert*-butylcyclohexanone were reduced to the corresponding trans alcohols in 94% and 98% stereoselectivity, respectively. The stereoselectivity obtained with this reagent is apparently unprecedented for other similar hydride reagents.[20,23]

The unhindered bicyclic ketone norcamphor was reduced to the endo alcohol in 94% or better stereoselectivity while the hindered bicyclic example, camphor, was reduced to the exo alcohol in 85% or better stereoselectivity. The stereoselectivity for the bicyclic ketones norcamphor and camphor is comparable to that of simple hydride reagents such as sodium borohydride[22a] and lithium aluminum hydride.[23]

Although changes in solvent do not seem to affect the stereochemical results of this reagent significantly, it appears that the hydride is slightly more prone toward equatorial attack in tetrahydrofuran–*n*-hexane than in toluene–*n*-hexane for the relatively hindered cyclohexanones such as 2-*tert*-butylcyclohexanone and 3,3,5-trimethylcyclohexanone. This trend is in agreement with previous investigaitons.[24] However, it is of interest to note that this trend is reversed for the relatively unhindered cyclohexanones such as 3-methylcyclohexanone and 4-alkylcyclohexanones and for bicyclic ketones.

Reduction of Selected Carbonyl Compounds. In order to establish the synthetic utility of this reagent, we studied the reductions of a series of selected carbonyl derivatives. In general, equimolar amounts of lithium *n*-butylborohydride and the substrate were utilized to ensure complete reduction, whereas stoichiometric amounts of the reactants were used for partial reductions. Reductions were carried out in toluene–*n*-hexane at −78, 0, and/or 25 °C, depending upon the nature of the reaction (discussed later).

Esters and Lactones. In order to evaluate both toluene–*n*-hexane and tetrahydrofuran–*n*-hexane as the reaction solvent in the reduction of slected carbonyl compounds, we performed the reduction of methyl caprylate at 0 °C for 1 h using both solvents. The reduction occurred rapidly and quantitatively in toluene–*n*-hexane. However, the reduction was slower in tetrahydrofuran–*n*-hexane and led to a complex mixture which included the alcohol and the starting material as major products. GLC analysis revealed 45% of capryl alcohol, 55% of the original ester, and 4% of two unidentified products (based on the ester). Capryl aldehyde was not detected in the reaction products. Thus, toluene–*n*-hexane was the solvent of choice, and the remaining reductions were conducted in this media.

With lithium *n*-butylborohydride in toluene–*n*-hexane at 0 °C the esters were cleanly reduced to the corresponding alcohols as shown in Table IV. When methyl benzoate was allowed to react with this reagent at −78 °C for 4 h, the original ester was recovered in essentially quantitative yield. This result suggests that selective reduction of the ketone in the presence of the ester group may be feasible. Indeed, the reduction of an equimolar mixture of 4-*tert*-butylcyclohexanone and methyl benzoate with this reagent in toluene–*n*-hexane at −78 °C for 4 h afforded 4-*tert*-butylcyclohexanol (100%), the original ester (98%), and a trace amount of benzyl alcohol (2%, based on the ester), which was determined by GLC analysis.

(21) After the completion of this work, the stereochemical course of an imino-substituted 4-*tert*-butylcyclohexanone reduction by lithium *n*-butylborohydride was reported by Ganem. This reagent behaved much like sodium cyanoborohydride: Wrobel, J. E.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 3447.

(22) (a) Brown, H. C.; Muzzio, J. *J. Am. Chem. Soc.* **1966**, *88*, 2811. (b) Wigfield, D. C.; Phelps, D. J. *Ibid.* **1974**, *92*, 543.

(23) Ashby, E. C.; Boone, J. R. *J. Org. Chem.* **1976**, *41*, 2890.

(24) (a) Haubenstock, H.; Eliel, E. L. *J. Am. Chem. Soc.* **1962**, *84*, 2368. (b) Haubenstock, H.; Hong, S.-J. *Tetrahedron* **1978**, *34*, 2445.

Table IV. Reduction of Selected Carbonyl Compounds with Li-*n*-BuBH$_3$ in Toluene–*n*-Hexane

compd	time, h	temp, 0 °C	products	yield,[a] %
methyl benzoate	1	0	benzyl alcohol	96
	2	−78	methyl benzoate	(98)
			benzyl alcohol	(1)
methyl caprylate	1	0	capryl alcohol	94
	4	−78	methyl caprylate	(95)
			capryl alcohol	(2)
methyl stearate	1	0	stearyl alcohol	98
methyl 1-adamantanecarboxylate	1	0	1-adamantanemethanol	99
phthalide	1	0	1,2-benzenedimethanol	96
4-*tert*-butyl-6-hexanolactone	1	0	3-*tert*-butyl-1,6-hexanediol	93
benzoic acid	24	25	benzoic acid	96
caprylic acid	24	25	caprylic acid	94
caprylyl chloride	1	0	capryl alcohol	94
	2	−78	capryl alcohol	92
benzoyl chloride	1	0	benzyl alcohol	95
benzoic anhydride	1	0	benzyl alcohol	94
			benzyl acid	98
phthalic anhydride	1	0	phthalide	96
	2	−78	phthalide	92
caprylamide	24	25	caprylamide	90
N-*n*-butylcaprylamide	24	25	*N*-*n*-butylcaprylamide	98
N,*N*-di-*n*-butylcaprylamide	24	25	*N*,*N*-di-*n*-butylcaprylamide	99
N,*N*-diethylbenzamide	24	25	*N*,*N*-diethylbenzamide	(77)
			N,*N*-diethylbenzylamine	(13)
			benzyl alcohol	(10)

[a] The yields were determined by isolation. The numbers in parentheses indicate the GLC yield.

Similarly, lactones were quantitatively reduced to the diols. Lactones such as phthalide and 4-*tert*-butyl-6-hexanolide were reduced in toluene–*n*-hexane at 0 °C to 1,2-benzenedimethanol and 3-*tert*-butyl-1,6-hexanediol in the yields of 96% and 93%, respectively.

Carboxylic Acids, Acid Chlorides, and Acid Anhydrides. Lithium *n*-butylborohydride failed to reduce both caprylic acid and benzoic acid for 24 h at 25 °C. The original acids were quantitatively recovered after the usual workup. Acid chlorides were rapidly and quantitatively reduced to the corresponding alcohols. When caprylyl chloride was reacted with this reagent at −78 °C for 2 h, capryl alcohol was isolated in 92% yield.

Partial reduction of an acid chloride to the aldehyde stage[25] was not observed when caprylyl chloride was reacted with stoichiometric amounts of this reagent (0.37 molar equiv) at −78 °C for 4 h. After the usual workup, 40% of capryl alcohol and 45% of caprylic acid (resulting from hydrolysis of the acid chloride) were obtained.

Acid anhydrides were rapidly and quantitatively reduced to an equimolar mixture of acid and alcohol at 0 and −78 °C. The reduction of phthalic anhydride with this reagent at −78 °C for 4 h followed by acid hydrolysis resulted in the direct conversion of phthalic anhydride into phthalide.[26] The reduction results for carboxylic acids and acyl derivatives are summarized in Table IV.

Amides. When caprylamide was allowed to react with lithium *n*-butylborohydride at room temperature for 24 h, reduction did not occur, and the original amide was recovered in essentially quantitative yield. Also, *N*-*n*-butylcaprylamide and *N*,*N*-di-*n*-butylcaprylamide were inert to this reagent at room temperature for 24 h. However, in the case of *N*,*N*-diethylbenzamide, the reduction occurred slowly, giving 77% of the original amide, 13% of *N*,*N*-diethylbenzylamine, and 10% of benzyl alcohol in 24 h at room temperature.

In view of the fact that this reagent is shown to be a relatively powerful reducing agent from the present study, the exceptionally low reactivity of this reagent toward amides including tertiary amides is quite surprising. Such behavior with amides has been obtained for mild reducing agents such as sodium borohydride[27] and lithium tri-*tert*-butoxyaluminum hydride.[28] Thus, this reagent is very useful for the selective reduction of many other reducible functional groups in the presence of the amide group.

Conclusion

The present study confirms the versatility of lithium *n*-butylborohydride and provides a general understanding of the reducing properties of this reagent. Although 1,2-selectivity is rather low for conjugated cyclopentenones, selective 1,2-reduction of acyclic enones and conjugated cyclohexenones with this reagent in toluene–*n*-hexane can be achieved. This reagent resembles simple borohydrides in the reduction of cyclic and bicyclic ketones and can convert unhindered cyclic ketones to the corresponding thermodynamically more stable alcohols in excellent stereoselectivity. In its reducing properties toward selected carbonyl compounds, the reagent is shown to be a relatively powerful reducing agent, far more powerful than simple borohydrides and comparable to trialkylborohydrides in some cases.

In conclusion, lithium *n*-butylborohydride has unique and unusual reducing properties not present in other hydride reducing agents and should, therefore, find many useful applicaitons in organic synthesis.

Experimental Section

Proton nuclear magnetic resonance spectra were obtained on a Varian A-60 spectrometer. Infrared spectra were measured on a Perkin-Elmer 267 spectrometer. Gas chromatographic (GLC)

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analyses of product mixtures and purified samples were performed on a Varian 2800 gas chromatograph. All analyses were carried out on 7 ft × 0.125 in. or 12 ft × 0.125 in. 10% Carbowax 20M on 60/80-mesh Chromosorb W, 4 ft × 0.125 in. 2% Carbowax 20M on 60/80-mesh Chromosorb W, and 10 ft × 0.125 in. 10% THEED on 60/80-mesh Chromosorb W columns. Analytical thin-layer chromatography was performed on precoated silica gel glass plates (0.25 mm, 60F-254, E. Merck), and silica gel (activity III, ICN) was used for column chromatography.

Toluene was distilled over sodium under nitrogen, and tetrahydrofuran was distilled from sodium–benzophenone under nitrogen. Most of the organic compounds utilized in this study were commercial products of the highest purity. Some compounds including 5[29] and 7[30] were prepared by known procedures. The products obtained were readily available materials in many cases. If not, identification was effected through alternate preparation by known procedures. All glassware was dried in a drying oven and cooled under a dry nitrogen atmosphere. All reduction experiments were carried out under a dry nitrogen atmosphere, and hypodermic syringes were used to transfer the solutions.

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

Preparation of Li-n-BuBH$_3$ in THF–n-Hexane. In a 100-mL flask with a magnetic stirring bar and a rubber septum under a dry nitrogen atmosphere was placed borane–dimethyl sulfide complex (1.0 mL, 10.0 mmol). THF (32.5 mL) was added, and the flask was immersed in an ice bath. *n*-Butyllithium in *n*-hexane (1.5 M, 6.6 mL, 9.9 mmol) was slowly added to the flask with vigorous stirring, and the resulting solution was stirred for an additional 30 min to give a solution of lithium *n*-butylborohydride (0.25 M) in THF–*n*-hexane. The hydride concentraiton was determined by hydrolyzing a known aliquot of the solution with a mixture of THF and 1 N H_2SO_4 and room temperature and measuring the hydrogen evolved. A suspension of lithium *n*-butylborohydride in toluene–*n*-hexane was prepared in the same way by substituting toluene for THF.

Reduction of Isophorone with Li-n-BuBH$_3$ in Toluene–n-Hexane. Isophorone (140 mg, 1.0 mmol) was placed in a 25-mL flask with a magnetic stirring bar and a rubber septum under a dry nitrogen atmosphere. After toluene (6 mL) was added, a suspension of lithium *n*-butylborohydride (4 mL of a 0.25 M solution, 1.0 mmol) in toluene–*n*-hexane was added dropwise over 5 min with vigorous stirring in a dry ice–acetone bath. After 4 h of being stirred at −78 C, the reaction mixture was hydrolyzed with water (0.5 mL) and then allowed to warm to room temperature. The reaction mixture was oxidized with 10% NaOH (3 mL) and 30% H_2O_2 (2 mL) by vigorous stirring overight at room temperature. The aqueous layer was separated and extracted twice with *n*-hexane. The combined organic layers were washed with water, $NaHSO_3$ solution, and saturated NaCl solution, dried over anhydrous $MgSO_4$, and then evaporated to dryness under reduced pressure. The residue was purified by filtration through a pad of silica gel with methylene chloride to give the allylic alcohol (139 mg, 98%). The product was analyzed by GLC on 7 ft × 0.125 in. 10% Carbowax 20M column at 130 °C and further identified by NMR, IR, and TLC.

Reduction of 4-tert-Butylcyclohexanone with Li-n-BuBH$_3$ in THF–n-Hexane. In a 25-mL flask with a magnetic stirring bar and a rubber septum under a dry nitrogen atmosphere 4-*tert*-butylcyclohexanone (72 mg, 0.47 mmol) was placed, and THF (2.7 mL) was added. To the resulting solution in a dry ice–acetone bath under a dry nitrogen atmosphere was added dropwise a solution of lithium *n*-butylborohydride (1.8 mL of a 0.25 M solution, 0.45 mmol) in THF–*n*-hexane. After 2 h of being stirred at −78 °C, the reaction mixture was hydrolyed with water (0.5 mL), allowed to warm to room temperature, and oxidized with 10% NaOH (3 mL) and 30% H_2O_2 (2 mL) by stirring overnight at room temperature. After diethyl ether (10 mL) was introduced, the aqueous layer was separated and extracted three times with diethyl ether. The combined organic layers were washed with $NaHSO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, and evaporated to dryness under reduced pressure to give the corresponding alcohol (72 mg, 98%). The product was subjected to GLC analysis (7 ft × 0.125 in. 10% Carbowax 20M column at 125 °C), which showed 98% of the trans alcohol and 2% of the cis alcohol.

Reduction of Methyl Caprylate with Li-n-BuBH$_3$ in Toluene–n-Hexane. In a 25-mL flask was placed methyl caprylate (126 mg, 0.80 mmol), and toluene (5 mL) was added. An ice bath was placed under the flask, and a suspension of lithium *n*-butylborohydride (3.2 mL of a 0.25 M solution, 0.80 mmol) in toluene–*n*-hexane was added with vigorous stirring. After 1 h of being stirred at 0 °C, the reaction mixture was hydrolyzed with water (0.5 mL) and oxidized with 10% NaOH (3 mL) and 30% H_2O_2 (2 mL) by vigorous stirring overnight at room temperature. After diethyl ether (20 mL) was added, the aqueous layer was separated and extracted three times with diethyl ether. The combined organic layers were washed with water, $NaHSO_3$ solution, and saturated NaCl solution, dried over anhydrous $MgSO_4$, and evaporated to dryness under reduced pressure to give capryl alcohol (98 mg, 94%). The purity of the product was analyzed by GLC on a 7 ft × 0.125 in. 10% Carbowax 20M column at 120 °C, and the product was further identified by NMR and IR.

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Registry No. 1, 122-57-6; 2, 94-41-7; 3, 14901-07-6; 4, 78-59-1; 5, 826-56-2; 6, 99-49-0; 7, 1073-13-8; 8, 930-68-7; 9, 930-30-3; 10, 2758-18-1; 2-methylcyclohexanone, 583-60-8; 3-methylcyclohexanone, 591-24-2; 4-methylcyclohexanone, 589-92-4; 4-*tert*-butylcyclohexanone, 98-53-3; 2-*tert*-butylcyclohexanone, 1728-46-7; 3,3,5-trimethylcyclohexanone, 873-94-9; norcamphor, 497-38-1; camphor, 76-22-2; methyl benzoate, 93-58-3; methyl caprylate, 111-11-5; methyl stearate, 112-61-8; methyl 1-adamantanecarboxylate, 711-01-3; phthalide, 87-41-2; 4-*tert*-butyl-6-hexanolactone, 34680-83-6; caprylyl chloride, 111-64-8; benzoyl chloride, 98-88-4; benzoic anhydride, 93-97-0; phthalic anhydride, 85-44-9; benzoic acid, 65-85-0; caprylic acid, 124-07-2; caprylamide, 629-01-6; *N*-butylcaprylamide, 24928-30-1; *N,N*-dibutylcaprylamide, 57303-23-8; *N,N*-diethylbenzamide, 1696-17-9; lithium butylborohydride, 82111-98-6; 4-phenyl-3-buten-2-ol, 17488-65-2; 1,3-diphenyl-2-propen-1-ol, 4663-33-6; 4-(2,6,6-trimethyl-1-cyclohexene)-3-buten-2-ol, 27008-60-2; 3,5,5-trimethyl-2-cyclohexen-1-o, 470-99-5; 4a-methyl-2,3,4,4a,5,6,7,8-octahydro-2-naphthol, 26675-10-5; 2-methyl-5-(1-propen-2-yl)-2-cyclohexen-1-ol, 99-48-9; 4,4-dimethyl-2-cyclohexen-1-ol, 5020-09-7; 2-cyclohexen-1-ol, 822-67-3; 2-cyclopenten-1-ol, 3212-60-0; 3-methyl-2-cyclopenten-1-ol, 3718-59-0; *trans*-2-methylcyclohexanol, 7443-52-9; *cis*-3-methylcyclohexanol, 5454-79-5; *trans*-4-methylcyclohexanol, 7731-29-5; *trans*-4-*tert*-butylcyclohexanol, 21862-63-5; *endo*-bicyclo[2.2.1]heptan-2-ol, 497-36-9; *exo*-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol, 124-76-5; benzyl alcohol, 100-51-6; capryl alcohol, 123-96-6; stearyl alcohol, 112-92-5; 1-adamantanemethanol, 770-71-8; 1,2-benzenedimethanol, 612-14-6; 3-*tert*-butyl-1,6-hexanediol, 82111-97-5; butyllithium, 109-72-8; borane–dimethylsulfide complex, 13292-87-0.

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