Reducing Characteristics of Potassium Tri-*sec*-butylborohydride

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The approximate rates and stoichiometry of the reaction of excess potassium tri-*sec*-butylborohydride (K*s*-Bu_3BH) with selected organic compounds containing representative functional groups were determined under the standard conditions (0 °C, THF) in order to define the characteristics of the reagent for selective reductions. Primary alcohols evolve hydrogen in 1 h, but secondary and tertiary alcohols and amines are inert to this reagent. On the other hand, phenols and thiols evolve hydrogen rapidly. Aldehydes and ketones are reduced rapidly and quantitatively to the corresponding alcohols. Reduction of norcamphor gives 99.3% endo- and 0.7% exo-isomer of norboneols The reagent rapidly reduces cinnamaldehyde to the cinnamyl alcohol stage and shows no further uptake of hydride. *p*-Benzoquinone takes up one hydride rapidly with 0.32 equiv hydrogen evolution and anthraquinone is cleanly reduced to the 9,10-dihydroxyanthracene stage. Carboxylic acids liberate hydrogen rapidly and quantitatively, however further reduction does not occur. Anhydrides utilize 2 equiv of hydride and acyl chlorides are reduced to the corresponding alcohols rapidly. Lactones are reduced to the diol stage rapidly, whereas esters are reduced moderately (3-6 h). Terminal epoxides are rapidly reduced to the more substituted alcohols, but internal epoxides are reduced slowly. Primary and tertiary amides are inert to this reagent and nitriles are reduced very slowly. 1-Nitropropane evolves hydrogen rapidly without reduction and nitrobenzene is reduced to the azoxybenzene stage, whereas azobenzene and azoxybenzene are inert. Cyclohexanone oxime evolves hydrogen without reduction. Phenyl isocyanate utilizes 1 equiv of hydride to proceed to forma nilide stage. Pyridine and quinoline are reduced slowly, however pyridine N-oxide takes up 1.5 equiv of hydride in 1 hr. Disulfides are rapidly reduced to the thiol stage, whereas sulfide, sulfoxide, sulfonic acid and sulfone are practically inert to this reagent. Primary alkyl bromide and iodide are reduced rapidly, but primary alkyl chloride, cyclohexyl bromide and cyclohexyl tosylate are reduced slowly.

Introduction

Unlike sodium borohydride, a mild reducing agent, the trialkylsubstituted borohydride, lithium triethylborohydride, $LiEt_3BH$[1] is an exceptionally strong hydride donor, even stronger than lithium aluminum hydride[2]. Recently we have studied the reducing characteristics of potassium triethylborohydride, KEt_3BH[3] and potassium triphenylborohydride, KPh_3BH[4], and found KEt_3BH is a much milder reducing agent than $LiEt_3BH$ and capable of reducing esters in the presence of cyclohexene oxide or capronitrile. On the other hand, KPh_3BH is a very weak reducing agent and many functional groups are inert or react slowly with KPh_3BH. However KPh_3BH is proved to be excellent for the 1,4-reduction of α,β-unsaturated carbonyl compounds[5] and in the presence of Ph_3B, reduces epoxides rapidly and changes the regioselectivity in the case of trisubstituted epoxides.

Sometime ago K*s*-Bu_3BH was shown to be highly stereospecific in the reduction of 2-methylcyclohexanone[6], and was also utilized for the 1,4-reduction of α,β-unsaturated carbonyl compounds[7]. However the reaction of K*s*-Bu_3BH with most functional groups, frequently encountered in organic compounds, has been remained to be studied. Therefore we have decided to study the reducing characteristics of K*s*-Bu_3BH systematically, in the hope to find out a more selective hydride redcing agent which is milder than KEt_3BH but stronger than KPh_3BH.

Results and Discussion

Standard Solution of K*s*-Bu_3BH in THF. The K*s*-Bu_3BH solution (1M) in THF was obtained from Aldrich, and concentrated to 1.8-2.0 M solution under nitrogen. The concentration was determined by hydrolyzing a known aliquot of the solution with THF-water-glycerine (1:1:1) at room temperature and measuring the hydrogen evolved. Under a nitrogen atmosphere, the solution of potassium tri-*sec*-butylborohydride in THF appears to be stable with no change observed in months at room temperature.

Procedure for Rate and Stoichiometry Studies. The general procedure adopted was to add 5 mmol of the organic compound under investigation to 20 mmol of K*s*-Bu_3BH in sufficient THF to give 20 m*l* of solution. The mixture was maintained at 0 °C (ice bath). This made the reaction mixture 1M in K*s*-Bu_3BH and 0.25M in the compound. Any hydrogen evolved was noted. Aliquots were then removed at appropriate intervals of time and analyzed for residual hydride by injecting them into a hydrolyzing mixture of THF-water- glycerine (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. In some cases, where the hydrogen evolution is continuous or a precipitate is formed, 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 and stoichiometry of the reaction.

Alcohols, Phenols, Amines and Thiols. Primary alcohols liberated hydrogen qantitatively in 1h, whereas secondary and tertiary alcohol are inert to this reagent. Phenol and a sterically hindered phenol, 2,6-di-*tert*-butylphenol both evolved hydrogen rapidly and quantitatively. The two thiols tested, hexanethiol and benzenethiol also evolved hydrogen instantly. *n*-Hexylamine proved to be inert to this reagent under the experimental conditions. These behaviors are very similar to those of KEt_3BH[3]. The results are summarized in Table 1.

Aldehydes and Ketones. The aldehydes and ketones examined rapidly utilized 1 equiv of hydride to proceed to the

Table 1. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Alcohols, Phenols, Amines, and Thiols in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
1-hexanol	5 min	0.77	0.77	0.00
	30 min	0.88	0.88	0.00
	1 hr	1.00	1.00	0.00
benzyl alcohol	5min	0.81	0.81	0.00
	30 min	0.91	0.91	0.00
	1 hr	0.97	0.97	0.00
	3 hr	1.01	1.01	0.00
3-hexanol	5 min	0.03	0.03	0.00
	3 hr	0.03	0.03	0.03
3-ethyl-3-pentanol	30 min	0.04	0.04	0.00
	3 hr	0.08	0.08	0.00
phenol	5 min	0.92	0.92	0.00
	30 min	0.98	0.98	0.00
	1 hr	0.98	0.98	0.00
2,6-di-*tert*-buthylphenol[c]	5 min	1.02	1.02	0.00
n-hexylamine	5 min	0.00	0.00	0.00
	6 hr	0.04	0.04	0.00
1-hexanethiol[c]	5 min	0.98	0.98	0.00
	3 hr	1.01	1.01	0.00
benzenethiol[c]	5 min	0.94	0.94	0.00
	6 hr	1.00	1.00	0.00

[a]Five mmol of compound was added to 20 mmol of K*s*-Bu_3BH in 20 m*l* of solution (0.25M in compound and 1.0M in K*s*-Bu_3BH). [b]In mmol/mmol of compound. [c]White precipitate within 5 min.

Table 2. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Aldehydes and Ketones in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
caproaldehyde	5 min	0.04	1.03	0.99
	1 hr	0.04	1.07	1.04
benzaldehyde	5 min	0.00	1.08	1.08
	1 hr	0.00	1.08	1.08
2-heptanone	5 min	0.00	0.76	0.76
	30 min	0.00	0.92	0.92
	1 hr	0.02	1.00	0.98
	3 hr	0.02	1.06	1.04
norcamphor	5 min	0.00	1.05	1.05
	3 hr	0.08	1.15	1.07
acetophenone	5 min	0.02	1.11	1.09
	1 hr	0.02	1.11	1.09
benzophenone	5 min	0.00	0.98	0.98
	1 hr	0.02	1.08	1.06
cinnamaldehyde	5 min	0.00	0.97	0.97
	30 min	0.00	1.01	1.01
	3 hr	0.01	1.04	1.03

[a,b]See the corresponding footnotes in Table 1.

Table 3. Stereoselective Reduction of Cyclic and Bicyclic Ketones with Potassium Tri-*sec*-buthyborohydride(K*s*-Bu_3BH) in Tetrahydrofuran[a,b]

ketone	temp (°C)	less stable isomer	ratio of less stable isomer(%)		
			K*s*-Bu_3BH	K-*s*-Am-9-BBN[c]	Lis-Bu_3BH[d]
2-methylcyclo-hexanone	0	*cis*	100(99)[e]	99.5	99.3
3-methylcyclo-hexanone	0	*trans*	96.7	96.5	85
4-*t*-butylcyclo-hexanone	0	*cis*	96.7	96.5	93
norcamphor	0	*endo*	99.3	95.5	99.6
d-camphor	0	*exo*	100[f]	99.9	99.6
	25		99[g]	—	—

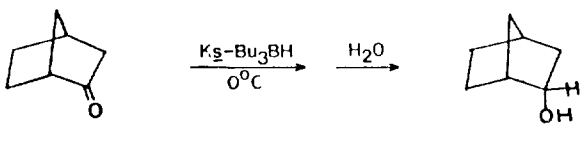
[a]Reaction mixture was 0.25M in ketone and the ratio of reagent/ketone was 1:1. [b]The yield of alcohols (GLC) were quantitative in 0.5 hr. [c]J. S. Cha, M. S. Yoon, K. W. Lee and G. C. Lee, *Bull. Korean Chem. Soc.*, **10**, 75 (1989). [d]H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, **94**, 7159 (1972). [e]C. A. Brown, *J. Am. Chem. Soc.*, **95**, 4100 (1973). [f]A 86% reduction to isoborneol in 12 hr at 0 °C. [g]A 100% reduction to isoborneol in 12 hr at 25 °C.

Table 4. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Quinones in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
p-benzo-quinone[c]	30 min	0.32	1.30	0.98
	1 hr	0.32	1.41	1.09
	3 hr	0.32	1.41	1.09
anthraquinone[d]	1 hr	0.00	0.75	0.75
	3 hr	0.00	1.44	1.44
	6 hr	0.00	1.56	1.56
	24 hr	0.00	2.04	2.04

[a,b]See the corresponding footnotes in Table 1. [c]Reverse addition (The reagent was added to the suspension of *p*-benzoquinone). Color changed to green immediately. [d]Reverse addition. Color changed to brown immediately.

cooresponding alcohol stage. Hydrolysis of the reaction products provides the corresponding alcohols in quantitative yield. Cinnamaldehyde utilized 1 equiv of hydride rapidly and showed no more uptake of hydride under the experimental conditions, indicating rapid reduction to the cinnamyl alcohol stage. The results are summarized in Table 2. The stereoselectivity (Table 3) of the reagent toward cyclic and bicyclic ketones was also studied. K*s*-Bu_3BH exhibited excellent stereoselectivity and is equal or surpasses the other reducing agents such as K*s*-Am-9BBN[8] and Lis-Bu_3BH[9].



99.3% endo

Quinones. *p*-Benzoquinone utilized 1.41 equiv of

Table 5. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
caproic acid[c]	5 mn	0.92	0.92	0.00
	1 hr	1.01	1.01	0.00
benzoic acid[d]	5 min	0.99	0.99	0.00
	1 hr	0.99	0.99	0.00
acetic	5 min	0.00	1.88	1.88
anhydride[e]	1 hr	0.02	1.96	1.94
	3 hr	0.02	1.96	1.94
succinic	5 min	0.24	2.08	1.84
anhydride[f]	30 min	0.24	2.16	1.92
	1 hr	0.24	2.23	1.99
	3 hr	0.24	2.31	2.07
phthalic	5 min	0.34	1.04	0.70
anhydride[g]	30 min	0.34	1.54	1.20
	1 hr	0.34	1.98	1.64
	3 hr	0.34	2.26	1.92
	6 hr	0.34	2.30	1.96
caproyl	5 min	0.04	1.66	1.62
chloride	30 min	0.08	1.82	1.74
	1 hr	0.08	2.13	2.05
	3 hr	0.08	2.13	2.05
benzoyl	5 min	0.00	2.07	2.07
chloride[c]	1 hr	0.00	2.07	2.07

[a,b] See the corresponding footnotes in Table 2. [c] The solution turns milky immediately. [d] White precipitate immediately. [e] Immediate color change to yellow. [f] Reverse addition. [g] Reverse addition. White precipitate within 5 min.

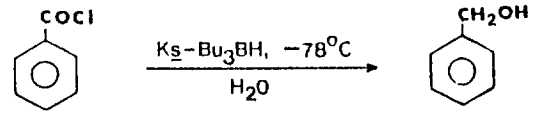
hydride, of which 0.32 equiv of hydride was utilized for hydrogen evolution, accompanying color change to green. The hydride uptake observed does not correspond to the clean reduction either to hydroquinone or to 1,4-dihydroxycyclohexadiene as pointed out earlier[10]. Anthraquinone, on the other hand, moderately utilized 2 equiv of hydride in 24h without hydrogen evolution, indicating a clean reduction to 9,10-dihydro-9,10-dihydroxyanthracene[1]. The results are summarized in Table 4.

Carboxylic Acids and Acyl Derivatives. Carboxylic acids evolved 1 equiv of hydrogen instantly to form their potassium salts. The reaction mixture became milky immediately and a precipitate was observed in 5 min in the case of benzoic acid. No further hydride uptake was observed with both caproic acid and benzoic acid. This result suggests that K*s*-Bu_3BH can be utilized for the selective reduction of other easily reducible functional groups in the presence of carboxylic acid. Acid chlorides were rapidly reduced to the corresponding alcohols, whereas cyclic anhydride was moderately reduced to the corresponding lactone. Such behavior of carboxylic acids and acyl derivatives has also been noted in the reaction with KEt_3BH[3] and $LiEt_3BH$[1]. In order to test for aldehyde formation, one equiv of K*s*-Bu_3BH was added to benzoyl chloride at -78 °C. However only benzyl alcohol was obtained in a yield of 47%. The results are summarized in Table 5.

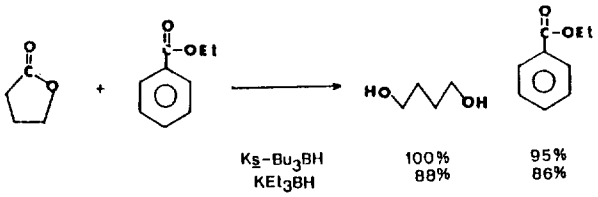
Table 6. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Esters and Lactones in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
ethyl	5 min	0.00	0.44	0.44
coproate	30 min	0.00	1.00	1.00
	1 hr	0.00	1.26	1.26
	3 hr	0.00	1.77	1.77
	6 hr	0.00	1.97	1.97
	24 hr	0.00	1.97	1.97
ethyl	30 min	0.00	1.18	1.18
benzoate	1 hr	0.00	1.61	1.61
	3 hr	0.00	2.05	2.05
phenyl	1 hr	0.00	1.99	1.99
acetate	3 hr	0.04	2.04	2.00
α-butyro-	5 min	0.00	1.99	1.99
lactone	1 hr	0.00	2.03	2.03
phthalide[c]	5 min	0.00	1.91	1.91
	1 hr	0.00	1.99	1.99
	3 hr	0.00	2.01	2.01
isopropenyl	5 min	0.04	2.08	2.08
acetate	1 hr	0.04	2.33	2.29
	3 hr	0.04	2.40	2.36
	6 hr	0.04	2.74	2.70
	24 hr	0.04	2.89	2.85

[a,b] See the corresponding footnotes in Table . [c] Immediate color change to yellow.



Esters and Lactones. Lactones took up 2 equiv of hydride rapidly, undergoing reduction to the corresponding diol stage, whereas esters were reduced moderately (3-6 h). It is interesting to note that the same esters were reduced much more slowly with K*s*-Am-9BBN (2-6 days)[8]. It was thought that the selective reduction of lactone in the presence of esters might be possible. We tested this possibility. As shown below, γ-butyrolactone was reduced to 1,4-butanediol quantitatively, leaving ethyl benzoate intact[11].



The chemoselectivity was also tested with KEt_3BH, which was inferior to K*s*-Bu_3BH. Isopropenyl acetate utilized 2 equiv of hydride rapidly, however further reduction proceeded very slowly. Presumably, the acetate group is rapidly reduced to the ethanol stage (two hydride) and the isopropenyl group of the bulky boron enolate was slowly reduced to the isopropyl alcohol stage (one hydride). The results are summarized in Table 6.

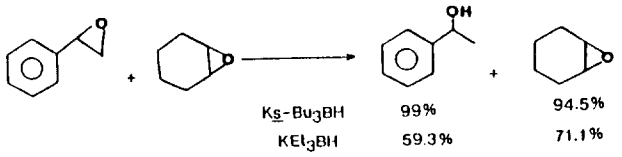
Epoxides. 1,2-Butylene oxide and styrene oxide utilized

Table 7. Reaction of Potassium Tri-*sec*-buthylborohydride with Representative Epoxides in Tetrahydrofuran at 0 °C

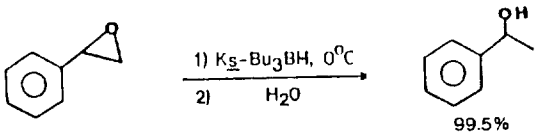
compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
1,2-butylene oxide	5 min	0.00	1.05	1.05
	1 hr	0.00	1.05	1.05
styrene oxide[c]	5 min	0.03	1.07	1.04
	1 hr	0.03	1.07	1.04
cyclohexene oxide	30 min	0.00(0.00)[e]	0.08(0.23)	0.08(0.23)
	1 hr	0.00(0.00)	0.15(0.51)	0.15(0.51)
	3 hr	0.00(0.00)	0.25(0.66)	0.25(0.66)
	6 hr	0.00(0.00)	0.37(0.87)	0.37(0.87)
	24 hr	0.00(0.00)	0.74(1.00)	0.74(1.00)
	48 hr	0.00	1.00	1.00
	3 hr[d]	0.00	0.74	0.74
	24 hr[d]	0.00	1.00	1.00
	3 hr[d,e]	0.00	0.86	0.86
	6 hr[d,e]	0.00	1.00	1.00
1-methyl-1,2-cyclohexene oxide	3 hr	0.00(0.00)[e]	0.22(0.21)	0.22(0.21)
	6 hr	0.00(0.00)	0.33(0.33)	0.33(0.33)
	24 hr	0.00(0.00)	0.45(0.46)	0.45(0.46)
	24 hr[d]	0.00	0.47	0.47

[a,b]See the corresponding footnotes in Table 1. [c]100% yield of phenylethanol, the product was 99.5% of 1-phenylethanol and trace of 2-phenylethanol. [d]In the presence of 100% of *sec*-Bu_3B. [e]At 25 °C.

1 equiv of hydride rapidly to proceed to the corresponding alcohol stage. However internal epoxides such as cyclohexene oxide and 1-methylcyclohexene oxide are reduced very slowly. Thus styrene oxide could be reduced selectively in the presence of cyclohexene oxide. KEt_3BH showed a poor selectivity. The presence of *sec*-Bu_3B increased the rate moderately in the case of cyclohexene oxide, however, not so dramatic as observed with KPh_3BH-Ph_3B.[4]



The ring opening of terminal epoxides proceeds with exceptional regioselectivity, yielding the Markovnikov alcohol exclusively. Thus, styrene oxide gave 1-phenylethanol quantitatively. $LiEt_3BH$[1] and KEt_3BH[3] both give 97% of 1-phenylethanol and 3% of 2-phenylethanol. The results are summarized in Table 7.



Amides and Nitriles. Primary amides reacted to evolve 1 equiv of hydrogen in 30 min; further hydrogen evolution did not occur even over extended periods of time. They were not reduced with Ks-Bu_3BH. Tertiary amides, such as N,N-dimethylhexamide and N,N-dimethylbenzamide also were not reduced with Ks-Bu_3BH under these experimental conditions. Capronitrile and benzonitrile were reduced sluggishly showing 20% and 71% reduction in 24h, respectively. However here also Ks-Bu_3BH showed faster reaction with nitriles than Ks-Am-9-BBN[8]. Both nitriles are reduced readily in 1-3 h with KEt_3BH[3]. The results are summarized in Table 8.

Table 8. Reaction of Potassium Tri-*sec*-butylborohyride with Representative Amides and Nitriles in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
caproamide	30 min	0.90	0.90	0.00
	3 hr	0.99	1.02	0.03
benzamide[c]	30 min	0.98	1.01	0.03
	3 hr	0.98	1.01	0.03
N,N-dimethyl-caproamide	1 hr	0.09	0.12	0.03
	6 hr	0.09	0.14	0.05
N,N-dimethyl-benzamide	1 hr	0.03	0.08	0.05
	6 hr	0.03	0.11	0.08
	24 hr	0.03	0.21	0.18
capronitrile	1 hr	0.00(0.00)[e]	0.08(0.12)	0.08(0.12)
	3 hr	0.00(0.00)	0.23(0.28)	0.23(0.28)
	6 hr	0.00(0.00)	0.37(0.52)	0.37(0.52)
	24 hr	0.00(0.00)	0.40(0.61)	0.40(0.61)
benzonitrile[d]	1 hr	0.00(0.00)[e]	0.26(0.73)	0.26(0.73)
	3 hr	0.00(0.00)	0.52(0.94)	0.52(0.94)
	6 hr	0.00(0.00)	0.78(1.60)	0.78(1.60)
	24 hr	0.00(0.00)	1.42(1.81)	1.42(1.81)

[a,b]See the corresponding footnotes in Table 1. [c]Solution becomes turbid within 5 min. [d]Color changes to pale yellow within 5 min [e]At 25 °C.

Table 9. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Nitro Compounds and Their Derivatives in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
nitropropane[c]	5 min	1.02	1.02	0.00
	1 hr	1.02	1.02	0.00
nitrobenzene[d]	30 min	0.04	1.34	1.30
	1 hr	0.04	1.42	1.38
	3 hr	0.04	1.57	1.53
	6 hr	0.04	1.60	1.56
azobenzene	5 min	0.00	0.00	0.00
	24 hr	0.00	0.00	0.00
azoxybenzene	5 min	0.00	0.00	0.00
	3 hr	0.04	0.04	0.00

[a,b]See the corresponding footnotes in Table 1. [c]The solution turns milky immediately. [d]Orange precipitate immediately.

Nitro Compounds and Their Derivatives. 1-Nitropropane rapidly evolved 1 equiv of hydrogen, forming a milky solution with no hydride being consumed for reduction. Presumably, the active α-hydrogen was involved in this reaction. Nitrobenzene utilized 1.5 equiv of hydride, indicating the reduction to the azoxybenzene stage. Azo- and azoxybenzene are inert to this reagent. The results are summariz-

Table 10. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Other Nitrogen Compounds in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
cyclohexa-	5 min	0.83	0.83	0.00
none oxime	30 min	0.97	0.97	0.00
	1 hr	1.05	1.10	0.05
	3 hr	1.05	1.10	0.05
phenyl	5 min	0.00	0.96	0.96
isocyanate	1 hr	0.00	1.00	1.00
pyridine[c]	30 min	0.00	0.48	0.48
	1 hr	0.00	0.53	0.53
	3 hr	0.00	0.62	0.62
	6 hr	0.00	0.75	0.75
quinoline	5 min	0.00	0.21	0.21
	30 min	0.00	0.29	0.29
	1 hr	0.00	0.54	0.54
	3 hr	0.00	0.63	0.63
	6 hr	0.00	0.93	0.93
	24 hr	0.00	0.99	0.99
pyridine[d]	1 hr	0.00	1.55	1.55
N-oxide	3 hr	0.00	1.63	1.63
	6 hr	0.00	1.71	1.71
	24 hr	0.00	1.72	1.72

[a,b]See the corresponding footnotes in Table 1. [c]Color changes to yellw within 5 min. [d]Reverse addition. Color changes to red.

Table 11. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Sulfur Compounds in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
di-*n*-butyl	5 min	0.97	1.99	1.02
disulfide	1 hr	0.97	1.99	1.02
diphenyl	5 min	0.93	1.91	0.98
disulfide[c]	1 hr	0.97	2.07	1.10
methyl	5 min	0.00	0.00	0.00
p-tolyl sulfide	6 hr	0.00	0.00	0.00
dimethyl	5 min	0.06	0.07	0.01
sulfoxide	3 hr	0.06	0.06	0.00
diphenyl	30 min	0.00	0.00	0.00
sulfone	3 hr	0.00	0.12	0.12
	6 hr	0.00	0.20	0.20
	24 hr	0.00	0.24	0.24
methane	30 min	0.94	1.01	0.07
sulfonic acid	6 hr	1.02	1.05	0.03
p-toluene-	5 min	2.12	2.12	0.00
sulfonic acid monohydrate	1 hr	2.12	2.12	0.00

[a,b]See the corresponding footnotes in Table 1. [c]White precipitate immediately.

ed in Table 9.

Other Nitrogen Compounds. Cyclohexanone oxime rapidly liberated 1 equiv of hydrogen, without undergoing reduction under the experimental conditions. Consequently, the formation of oximes would provide another means for protecting carbonyl group toward K*s*-Bu_3BH. Such a trend was also observed in the reaction with $LiEt_3BH$[1], KEt_3BH[3], and Li9-BBNH[12]. Phenyl isocyanate utilized 1 equiv of hydride rapidly, corresponding to the reduction to the formanilide stage. Pyridine and quinoline were reduced slowly and pyridine N-oxide consumed about 1.5 hydride rapidly in 1h and slowly thereafter, accompanying color change to dark red. The results are summarized in Table 10.

Sulfur Compounds. Disulfides were rapidly reudced to the thiol stage, utilizing 2 equiv of hydride, one for reduction and another for hydrogen evolution. Sulfides, sulfoxides and sulfones are practically inert to this reagent. It is interesting to note the K*s*-Bu_3BH evolves only 2 equiv of hydrogen with toluenesulfonic acid monohydrate, similar to KPh_3BH[4] and $LiEt_3BH$[1] but in contrast to KEt_3BH[3] and $LiBH_4$[13] which evolves 3 equiv of hydrogen. The results are summarized in Table 11.

Alkyl Halides. Primary alkyl bromide and iodide were reduced rapidly. In the reaction of *n*-octyl bromide with a stoichiometric amount of KEt_3BH, the reaction proceeds rapidly up to 50%, with further reduction being sluggish. This is similar to $LiEt_3BH$[1]. However, the reaction with a stoichiometric amount of K*s*-Bu_3BH proceeds to completion rapidly. This suggests that the bulky *s*-Bu_3B does not form addition compound with the bulky hydride K_s-Bu_3BH[14]. Primary alkyl chloride was reduced slowly in 24 h, however, cyclohexyl bromide and cyclohexyl tosylate were reduced only 40% and 20%, respectively in the same period of time. The results are summarized in Table 12.

Table 12. Reaction of Potassium Tri-*sec*-butylborohydride with Representative Halides and Tosylate in Tetrahydrofuran at 0 °C

compound[a]	time	hydrogen evolved[b]	total hydride used[b]	hydride used for reduction[b]
1-chloro-	5 min	0.00	0.12	0.12
octane	1 hr	0.00	0.58	0.58
	3 hr	0.04	0.88	0.84
	24 hr	0.04	1.09	1.05
1-bromo-	5 min	0.00	0.98	0.98
octane	1 hr	0.00	1.00	1.00
1-iodooctane	5 min	0.00	0.97	0.97
	1 hr	0.00	1.05	1.05
cyclohexyl	3 hr	0.04	0.12	0.08
bromide	6 hr	0.04	0.22	0.16
	24 hr	0.04	0.44	0.40
cyclohexyl	5 min	0.00	0.12	0.12
tosylate	30 min	0.04	0.12	0.08
	6 hr	0.04	0.13	0.09
	24 hr	0.04	0.25	0.21

[a,b]See the corresponding footnotes in Table 1. [c]White precipitate immediately.

Conclusion

The reaction of the representative organic compounds with K*s*-Bu_3BH in THF at 0 °C has been studied sys-

tematically. The data cleanly reveals that K*s*-Bu_3BH is an exceptionally stereoselective reducing agent on cyclic and bicyclic ketones, and a good regio- and chemoselective reducing agent for epoxides. And it is also evident that K*s*-Bu_3BH is a rather mild reducing agent, and possesses a special chemoselectivity on lactones. Therefore K*s*-Bu_3BH should find useful application is in organic synthesis.

Experimental

General. The reaction flasks and other glassware required for the experiments were oven dried at 140 °C for several hours, assembled hot and cooled under a stream of dry nitrogen. All reactions were carried out under a static pressure of nitrogen in flasks fitted with septum-covered sidearms, using standard techniques for handling air-sensitive materials[15]. Hypodermic syringes were used to transfer the solutions.

Materials. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl and stored under dry nitrogen. K*s*-Bu_3BH was obtained from Aldrich (1M in THF), and concentrated to 1.8-2.0 M under nitrogen. Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation or recrystallization when necessary.

Instruments. A Varian 3700 chromatograph equipped with a thermal conductivity detector was used. All of the yields of products were determined by utilizing suitable internal standards and authentic mixtures. Refractive index were measured on a Baush and Lomb Abbe-3L refractometer. Melting point was measured on an Electrochemical melting point apparatus. NMR spectrometer used was a Varian model E-M 360A (60 MHz).

Procedure for Rate and Stoichiometry Studies. The reduction of ethyl benzoate is representative. 11 m*l* of 1.83 M K*s*-Bu_3BH solution (20 mmol) in THF and 4 m*l* of THF were introduced into a dried 50 m*l* flask, fitted with a rubber syringe cap on an inlet port, a magnetic stirring bar, and reflux condenser connected to a gas buret. The flask was maintained at 0 °C and 5 m*l* of 1 M solution of ethyl benzoate (5 mmol) in THF was injected slowly. In this way, the reaction mixture was 1.0 M in hydride and 0.25 M in ethyl benzoate. Upon addition of the compound, no hydrogen evolution was observed. After 30 min, 4 m*l* of the reaction mixture was removed and hydrolyzed with THF-water-glycerin (1:1:1). The hydrogen evolved was 2.79 mmol, indicating 1.18 mmol of hydride had been used for reduction per mmol of ethyl benzoate, since 4.0 m*l* of the blank solution contained 3.97 mmol of hydride (3.97-2.79 = 1.18). 4.0 m*l* aliquots were also removed and hydrolyzed after 1.0, 3.0, and 6.0h. The amounts of hydride used for reduction were 1.61(1h), 2.05(3h), and 2.03 mmol(6h) per mmol of ethyl benzoate. Therefore the reduction of ethyl benzoate was over in 3.0 h.

Procedure for Product Analysis by GLC. Having established the appropriate rate and stoichiometry of a reaction, we desired to establish the nature of the products wherever it appeared of interest, offering a valuable possibility for selective reduction. Accordingly, separate reactions on a 2 mmol scale were carried out by using either a stoichiometric amount of the reagent or excess amount, depending upon the nature of a reaction. The products were identified by GLC comparison with authentic sample and the yields were determined by GLC utilizing internal standard.

Reduction of Representative Cyclic and Bicyclic Ketones. The following procedure for the reduction of norcamphor is representative. In a 50 m*l* 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 1.0 m*l* (1 mmol) of 1M norcamphor in THF and 2.4 m*l* of THF maintaining at 0 °C. Then 0.6 m*l* (1.1 mmol) of 1.83 M K*s*-Bu_3BH solution was introduced while the reaction mixture was vigorusly stirred. After 1 h, the excees hydride was destroyed with 0.5 m*l* of water and 0.5 m*l* of 1M dodecane in THF was added. Then the reaction mixture was warmed to room temperature and oxidized by the addition of 0.5 m*l* of 2N NaOH, followed by 0.5 m*l* of 30% H_2O_3 for 2-3 h. The aqueous layer was saturated with anhydrous K_2CO_3 and the dry THF layer was subjected to GLC analysis, indicating the presence of 99.3% *endo*-norborneol and 0.7% *exo*-norborneol.

Regio- and Chemoselective Reduction of Epoxide. The reduction of styrene oxide in the presence of cyclohexene oxide is representative. The experimental set-up was the same as the reduction of representative cyclic and bicyclic ketones. To a well-stirred mixture of 1 mmol of styrene oxide and 1 mmol of cyclohexene oxide containing 0.5 mmol of dodecane (internal standard) was added to 0.6 m*l* (1.1. mmol) of 1.83 M K*s*-Bu_3BH solution at 0 °C. After 30 min, the remaining hydride was destroyed with 0.5 m*l* of water and oxidized by the addition of 0.6 m*l* of 2 N NaOH, followed by 0.6 m*l* of H_2O_2 for 2-3 h. The aqueous layer was saturated with anhydrous K_2CO_3 and the dry THF layer was subjected to GLC analysis, which showed a 99% yield of 1-phenylethanol while cyclohexene oxide remained intact.

Chemoselective Reduction of Lactone. The reduction of γ-butyrolactone in the presence of ethyl caproate is representative. The experimental set-up was the same as the rate study. To a well-stirred mixture of 1 mmol of γ-butyrolactone and 1 mmol of ethyl caproate containing 0.5 mmol of dodeane (internal standard) was added 4.2 m*l* (2.1 mmol) of 1.83 M K*s*-Bu_3BH solution at 0 °C. After 5 min, the remaining hydride was destroyed with 0.5 m*l* of water and oxidized by the addition of 0.6 m*l* of 2N NaOH, followed by 0.6 m*l* of 30% H_2O_2 for 2-3 h. After drying with K_2CO_3, the THF layer was subjected to GLC to analyze ethyl caproate (96%). And then, to the dry solution, 2.5 m*l* of pyridine and 1.6 m*l* of hexamethyldisilazane and 1 m*l* of trimethylsilyl chloride were added with stirring[16]. After 1 h, the GLC analysis of the supernatant liquid showed a 99% yield of 1,4-butanediol.

Acknowledgement. We are grateful to the Ministry of Education, and to the Korea Science and Engineering Foundation for financial support of this work.

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