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Selective Reductions. 33. Potassium Triisopropoxyborohydride as a Selective Reducing Agent in Organic Synthesis. Reaction with Selected Organic Compounds Containing Representative Functional Groups

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The approximate rate and stoichiometry of the reaction of excess pure potassium triisopropoxyborohydride, KIPBH, with 56 selected compounds containing representative functional groups under standardized conditions (tetrahydrofuran, 0 °C) was examined in order to define the characteristics of the reagent for selective reductions. Primary, secondary, and tertiary alcohols evolve hydrogen partially, even after a long period of time. Phenol also generates partial hydrogen, and the reactions of those amines and thiols studied with the reagent are very slow. Aldehydes and ketones are reduced rapidly and quantitatively to give the corresponding alcohols. Unlike sodium and potassium borohydrides, KIPBH is very stereoselective. 2-Methylcyclohexanone can be reduced to the correspondingly less stable isomer, *cis*-2-methylcyclohexanol, in a high ratio (91% cis isomer). Cinnamaldehyde is rapidly reduced to cinnamyl alcohol, and further reduction is very slow under these conditions. Anthraquinone is cleanly reduced to 9,10-dihydro-9,10-anthracenediol. Carboxylic acids liberate hydrogen only partially, and further reduction is very slow. Acid chlorides consume 1 equiv of hydride rapidly, but the corresponding aldehydes do not form. Esters are almost inert toward the reagent. γ-Butyrolactone and phthalide are reduced only slowly. Epoxides are inert toward the reagent. Primary aliphatic amides evolve hydrogen slowly and primary aromatic amides evolve 1 equiv of hydrogen, but no significant reduction occurs. Tertiary amides and nitriles are inert toward the reagent. Of the nitrogen compounds studied, nitrobenzene is partially reduced after 48 h, while azobenzene and azoxybenzene are inert. Partial reduction of cyclohexanone oxime is observed, while phenyl isocyanate, pyridine, and pyridine *N*-oxide are inert under these conditions. Di-*n*-butyl disulfide and diphenyl disulfide are reduced rapidly and quantitatively to the corresponding mercaptans with partial hydrogen evolution. Other sulfur compounds studied, such as *p*-tolyl methyl sulfide, diphenyl sulfone, methanesulfonic acid, and *p*-toluenesulfonic acid, are inert toward the reagent. Only partial reduction of cyclohexyl tosylate is observed. Potassium triisopropoxyborohydride is a valuable reagent in boron chemistry. Thus, it transfers 1 equiv of hydride to dialkylhaloboranes, and the resulting dialkylborane can be transformed to a mixed trialkylborane, providing a potential route to mixed trialkylcarbinols or unsymmetrical ketones. The reagent rapidly transfers hydride to even severely hindered trialkylboranes, providing a simple synthetic route to these useful reagents. Finally, it readily converts 2-bromo-*trans*-vinylboronic esters to the *cis*-vinylboronic esters, providing a convenient synthetic route to these derivatives.

Unlike sodium triisopropoxyborhydride,[2] potassium triisopropoxyborohydride, KIPBH, can be easily prepared from triisopropoxyborane and potassium hydride[3] (eq 1 and 2).

$$\mathrm{NaH} + (i\text{-PrO})_3\mathrm{B} \xrightarrow[\Delta,\ 7\ \text{days}]{\text{THF}} \mathrm{Na}(i\text{-PrO})_3\mathrm{BH} \qquad (1)$$

$$\mathrm{KH} + (i\text{-PrO})_3\mathrm{B} \xrightarrow[\Delta,\ 12\text{–}18\ \text{h}]{\text{THF}} \mathrm{K}(i\text{-PrO})_3\mathrm{BH} \qquad (2)$$

The reagent, KIPBH, can now be prepared in pure form,[3b] and no sign of disproportionation is observed while the reagent is kept over a small quantity of potassium hydride. This potassium hydride is insoluble in THF and readily settles to the bottom of the flask. Consequently, the clear solution can be readily removed and used for reductions and other reactions, so that the excess potassium hydride does not interfere with reduction. In this respect, potassium triisopropoxyborohydride is different from other alkali metal trialkoxyborohydrides, such as sodium trimethoxy- and triethoxyborohydrides, compounds that undergo a fast redistribution into sodium borohydride and sodium tetraalkoxyborate[2] (eq 3 and 4).

$$2\mathrm{Na(CH_3O)_3BH} \rightarrow \mathrm{Na(CH_3O)_2BH_2} + \mathrm{Na(CH_3O)_4B} \qquad (3)$$

$$2\mathrm{Na(CH_3O)_2BH_2} \rightarrow \mathrm{NaBH_4} + \mathrm{Na(CH_3O)_4B} \qquad (4)$$

Potassium triisopropoxyborohydride is a mild reducing agent (vide infra). This is unexpected because hydride transfer should be more difficult from a stronger Lewis acid, such as BH_3, than from a weaker Lewis acid, such as $(RO)_3B$, weakened by back bonding.[3a,4] It seems that back bonding does not play an important role in the transition state so that the inductive effect of the isopropoxy groups predominates. Because a full investigation of the reagent was not available, we undertook to study the approximate stoichiometry and rate of the reaction under standardized conditions (THF, 0 °C) of excess pure KIPBH with our standard 56 compounds containing representative functional groups.

In another study, the behavior of this pure KIPBH toward dialkylhaloboranes was examined. Potassium triisopropoxyborohydride has been shown to be an excellent reagent for the hydridation process.[5] For example, hy-

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[1] (a) Postdoctoral research associate on Grant ARO DAAG-29-79-C-0027 supported by the U.S. Army Research Office (Durham). (b) Graduate student on Grant ARO DAAG-29-76-G-0218 supported by the U.S. Army Research Office (Durham).

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Table I. Reaction of Potassium Triisopropoxyborohydride with Representative Active Hydrogen Compounds in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
1-hexanol	0.5	0.01	0.01	0.00
	1.0	0.02	0.02	0.00
	3.0	0.04	0.04	0.00
	6.0	0.05	0.05	0.00
	12.0	0.06	0.06	0.00
benzyl alcohol	3.0	0.01	0.01	0.00
	24.0	0.03	0.03	0.00
3-hexanol	1.0	0.02	0.02	0.00
	3.0	0.04	0.04	0.00
	6.0	0.08	0.08	0.00
	12.0	0.10	0.10	0.00
3-ethyl-3-pentanol	24.0	0.01	0.01	0.00
phenol	0.25	0.03	0.03	0.00
	0.5	0.06	0.06	0.00
	1.0	0.10	0.10	0.00
	3.0	0.26	0.26	0.00
	6.0	0.36	0.36	0.00
	24.0	0.48	0.48	0.00
n-hexylamine	0.25	0.00	0.00	0.00
	1.0	0.03	0.03	0.00
	3.0	0.08	0.08	0.00
	72.0	0.15	0.15	0.00
1-hexanethiol	0.5[d]	0.01	0.01	0.00
	1.0	0.06	0.06	0.00
	3.0	0.16	0.16	0.00
	6.0	0.21	0.21	0.00
	24.0	0.29	0.29	0.00
benzenethiol	0.25[d]	0.30	0.30	0.00
	0.5	0.32	0.32	0.00
	1.0	0.35	0.35	0.00
	3.0	0.41	0.41	0.00
	6.0	0.47	0.47	0.00
	24.0	0.52	0.52	0.00
	48.0	0.63	0.63	0.00

[a] 5.0 mmol of compound to 20 mmol of KIPBH (20 mmol of hydride) in 20.0 mL of solution; 0.25 M in compound and 1.0 M in hydride. [b] mmol/mmol of compound. [c] Hydrogen evolved from blank minus the hydrogen evolved on hydrolysis of the reaction mixture after the indicated reaction period. [d] White gel-like precipitate formed immediately.

dride transfer from KIPBH to dialkylhaloborane is instantaneous. The resulting dialkylborane can then be further transferred to an alkene to form a mixed trialkylborane. The byproduct, triisopropoxyborane, is inert and does not interfere with the hydroboration process. However, previous work was done with impure reagent and the yields were not quantitative. We sought to examine the possibility that the yields would be improved with the purer reagent.[3b]

Results and Discussion

The procedure used involved preparation of a reaction mixture of potassium triisopropoxyborohydride (1.0 *M*, 1.0 *M* in hydride) and the compound (0.25 *M*) under study in tetrahydrofuran at 0 °C. The solution was maintained at 0 °C. Hydrogen evolution following addition of the compound to the reagent was measured. A blank reaction was run under identical conditions but without addition of the compound. From time to time, aliquots were taken from the reaction mixture and analyzed for the remaining hydride by hydrolysis.[6] From the difference in yields of hydrogen in the two cases, the hydride used by the compound for reduction was calculated. In this way, it was possible to calculate the number of moles of hydride used by the compound for hydrogen formation and the number of moles of hydride utilized for reduction.

Alcohols, Phenols, Amines, and Thiols (Active Hydrogen Compounds). Of the active hydrogen compounds studied, none evolved an equivalent of hydrogen rapidly and quantitatively. Primary, secondary, and tertiary alcohols evolved only a partial equivalent of hydrogen under these conditions. Phenol and benzenethiol were more reactive than alcohols and 1-hexanethiols, while *n*-hexylamine reacted sluggishly similar to alcohols. These results are summarized in Table I.

Aldehydes and Ketones. All of the saturated and unsaturated aldehydes[7] and ketones examined used 1 equiv of hydride rapidly. Hence, in these cases, the reduction went cleanly to the corresponding alcohol stage. Cinnamaldehyde used 1 equiv of hydride to yield the corresponding cinnamyl alcohol, followed by a slow reduction of the double bond.[7] These results are summarized in Table II. The stereoselectivity of the reagent toward cyclic ketones was also studied. Generally, potassium triisopropoxyborohydride exhibited very good stereoselectivity, compared with other mild hydride reducing agents, such as sodium borohydride and lithium tri-*tert*-butoxyaluminum hydride. These results are summarized in Table III.

Quinones. Both *p*-benzoquinone and anthraquinone reacted readily with potassium triisopropoxyborohydride. Typical reduction of a quinone to hydroquinone uses 2

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(6) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.

(7) GC analysis showed 97% yield of cinnamyl alcohol and 3% of the saturated alcohol after 1 h. However, the yield of cinnamyl alcohol decreased to 86% with an increase in the yield of saturated alcohol to 14% after 48 h.

Table II. Reaction of Potassium Triisopropoxyborohydride with Representative Aldehydes and Ketones in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
caproaldehyde	5 min	0.00	0.96	0.96
	0.25	0.00	1.00	1.00
	0.5	0.00	1.00	1.00
benzaldehyde	5 min	0.00	0.95	0.95
	0.25	0.00	1.02	1.02
	0.5	0.00	1.02	1.02
2-heptanone	5 min	0.00	0.94	0.94
	0.25	0.00	1.00	1.00
	0.5	0.00	1.00	1.00
norcamphor	5 min	0.00	0.70	0.70
	0.25	0.00	0.91	0.91
	0.5	0.00	1.01	1.01
	1.0	0.00	1.01	1.01
acetophenone	5 min	0.00	0.97	0.97
	0.25	0.00	1.01	1.01
	0.5	0.00	1.01	1.01
benzophenone	1.0	0.00	0.20	0.20
	3.0	0.00	0.45	0.45
	6.0	0.00	0.99	0.99
cinnamaldehyde	5 min[d]	0.00	0.96	0.96
	0.25	0.00	0.98	0.98
	0.5	0.00	0.99	0.99
	1.0[e]	0.00	1.04	1.04
	3.0	0.00	1.07	1.07
	24.0[f]	0.00	1.11	1.11

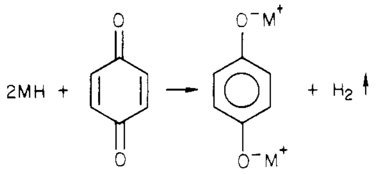
[a–c] See corresponding footnotes in Table I. [d] Color changed to brown. [e] 97% cinnamyl alcohol, 3% 3-phenyl-1-propanol. [f] 86% cinnamyl alcohol, 14% 3-phenyl-1-propanol.

Table III. Reaction of Potassium Triisopropoxyborohydride with Different Cyclic Ketones in Tetrahydrofuran[a]

compound	temp, °C	less stable isomer,[b] %
2-methylcyclohexanone	0	91
	−25	91.5
3-methylcyclohexanone	0	74
	−25	80
4-methylcyclohexanone	0	66.5
	−25	69
4-*tert*-butylcyclohexanone	0	53
	−25	54.5
3,3,5-trimethylcyclohexanone	0	95.5
	−25	96
norcamphor	0	95.5
	−25	97.5

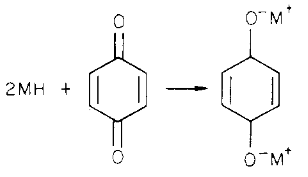
[a] A 2:1 ratio for KIPBH:ketone was used. [b] The yields of alcohols were quantitative.

equiv of hydride per mol of the quinone, one mole being used for reduction and the second mole to give hydrogen eq 5).



(5)

For the reduction of a quinone to the corresponding 1,4-dihydroxycyclohexadiene, 2 equiv of hydride should be used with no hydrogen formation (eq 6).



(6)

Under these conditions, *p*-benzoquinone consumed almost 1 equiv of hydride for reduction with very slow partial evolution of hydrogen. Apparently, reduction of *p*-benzoquinone takes place to the hydroquinone stage, with subsequent evolution of hydrogen being very slow. Anthraquinone was reduced to the 1,4-dihydroxy stage with essentially no hydrogen evolved. This reaction must follow the path shown in eq 6. These results are summarized in Table IV.

Carboxylic Acids and Acyl Derivatives. Carboxylic acids evolved hydrogen only slowly and incompletely when added to the reagent at 0 °C in THF. Moreover, only partial reduction of the acids, presumably to the corresponding alcohols, was observed. (GC analysis of the reaction mixture did not show any aldehyde formation.) Reduction of acid anhydrides was very slow, with the uptake of hydride being incomplete, even after 24 h. Acid chlorides took up one hydride rapidly, with a second equivalent of hydride being taken up only quite slowly. However, GC analysis of the mixture did not show any aldehyde formation but revealed the presence of the corresponding isopropyl ester. We might postulate that the "ate" complex initially formed attacks the unreacted acid chloride to form the corresponding ester. The results are summarized in Table V.

Esters and Lactones. Potassium triisopropoxyborohydride showed very little reactivity toward different esters under these conditions. Ethyl caproate and ethyl benzoate were unreactive toward KIPBH, and only a partial reduction of phenyl acetate was observed. γ-Butyrolactone and isopropenyl acetate were also unreactive toward the reagent. These results are summarized in Table VI.

Epoxides. Potassium triisopropoxyborohydride did not react with any of the epoxides studied under these reaction conditions. The results are summarized in Table VII.

Amides and Nitriles. Caproamide showed only partial hydrogen evolution without any sign of reduction. The reaction of benzamide with KIPBH evolved 1 equiv of hydrogen within 48 h, but the reduction process was very

Table IV. Reaction of Potassium Triisopropoxyborohydride with Representative Quinones in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
p-benzoquinone[d]	0.25[e]	0.01	0.90	0.89
	0.5	0.02	0.97	0.95
	1.0	0.04	1.01	0.97
	3.0	0.07	1.08	1.01
	6.0	0.09	1.11	1.02
anthraquinone[f]	0.5[g]	0.00	1.17	1.17
	1.0	0.00	1.38	1.38
	3.0	0.00	1.78	1.78
	6.0	0.01	1.89	1.88
	24.0	0.02	2.04	2.02

[a–c] See corresponding footnotes in Table I. [d] Each measurement was done separately, and the reaction mixture was hydrolyzed in a flask. [e] Color changed to dark green immediately, and a precipitate was formed and then color changed to violet. [f] Inverse addition; solution of reagent added to a suspension of anthraquinone. [g] Color changed into dark green immediately.

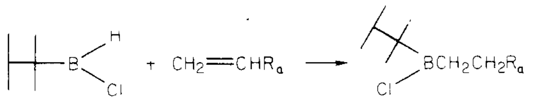
sluggish. Disubstituted amides, such as *N*,*N*-dimethylbutyramide and *N*,*N*-dimethylbenzamide, were unreactive. Similarly, capronitrile and benzonitrile also did not react with KIPBH under these conditions. The results are summarized in Table VIII.

Nitro Compounds and Their Derivatives. Nitrobenzene was reduced slowly with KIPBH. However, all other nitro compounds and their derivatives studied—1-nitropropane, azobenzene, and azoxybenzene—showed no reactivity toward KIPBH. These results are summarized in Table IX.

Other Nitrogen Compounds. KIPBH reacted with cyclohexanone oxime to evolve hydrogen, but no further reduction of the compound was observed. Of the other nitrogen compounds studied, phenyl isocyanate, pyridine, and pyridine *N*-oxide were unreactive toward KIPBH under these conditions. These results are summarized in Table X.

Sulfur Derivatives. Disulfides were the only sulfur compounds that reacted readily with potassium triisopropoxyborohydride. The reduction was relatively slow for alkyl disulfides but very fast for aryl disulfides. The reduction of disulfides proceeded with some hydrogen evolution. The corresponding mercaptans were isolated and identified. This is an interesting development because the sulfur–sulfur bond plays an important role in biochemistry. Further study of this reaction is under investigation. These results are summarized in Table XI.

Applications to Boron Chemistry. Although KIPBH in THF was shown to be a very mild reducing agent toward different organic functional groups (vide supra), its capability to transfer hydride to haloboranes is an exception. This reaction has been fully studied in order to prepare mixed organoboranes (eq 7–9).



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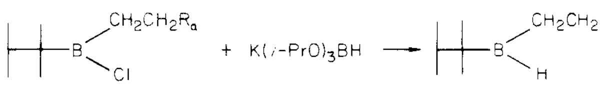

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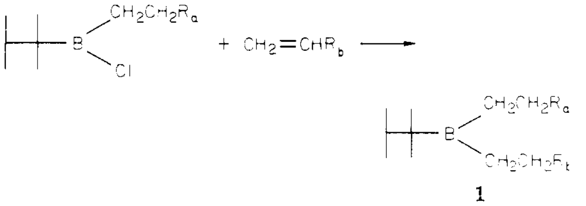

(9)

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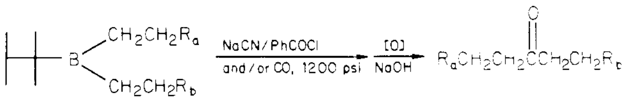
The mixed trialkylborane 1 can be further reacted with sodium cyanide/benzoyl chloride or carbon monoxide to prepare the corresponding unsymmetrical ketones (eq 10).



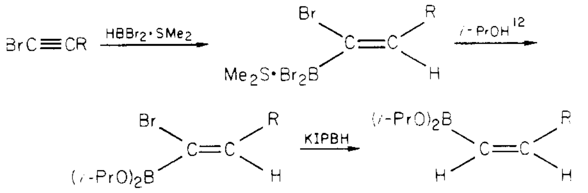
(10)

The use of KIPBH will overcome the problem that is associated with utilizing saline hydrides like potassium hydride[8] in which, through the hydride transfer process, a coat of potassium halide covers the metal hydride and consequently makes it less reactive. The results for these hydride transfer reactions are summarized in Table XII.

Attention is called to two other important applications of KIPBH in boron chemistry. The reagent rapidly transfers hydride to trialkylboranes, even very highly hindered derivatives,[9] providing a valuable synthetic route to the highly hindered, remarkably stereoselective trialkylborohydrides[10] (eq 11). It also provides a valuable

$$K(i\text{-PrO})_3BH + Sia^3B \rightarrow KSia_3BH + (i\text{-PrO})_3B \qquad (11)$$

procedure for the synthesis of *cis*-vinylboronic esters[11] (eq 12).



(12)

Conclusion

The reducing properties of potassium triisopropoxyborohydride, KIPBH, are now characterized. The reagent is a very mild reducing agent. With the exception of aldehydes, ketones, and disulfides, most functional groups studied were inert toward KIPBH. However, KIPBH showed an exceptional reactivity toward the boron-halogen bond. For example, dialkylboranes can easily be prepared from the corresponding dialkylhaloborane. The byproduct

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[8] Maddocks, P. J.; Pelter, A.; Rowe, K.; Smith, K.; Subrahmanyam, C. *J. Chem. Soc., Perkin Trans. 1* **1981**, 653.

[9] Brown, C. A.; Hubbard, J. L. *J. Am. Chem. Soc.* **1979**, *101*, 3966.

[10] Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3383.

[11] Research in progress with T. Imai.

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Table V. Reaction of Potassium Triiospropoxyborohydride with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
caproic acid[d]	0.25	0.10	0.15	0.05
	1.0	0.17	0.25	0.08
	12.0	0.45	0.59	0.14
	24.0	0.45	0.61	0.16
benzoic acid[d]	0.25	0.05	0.09	0.04
	12.0	0.15	0.26	0.11
	24.0	0.17	0.56	0.39
acetic anhydride[d]	1.0	0.00	0.40	0.40
	3.0	0.00	0.61	0.61
	6.0	0.00	0.71	0.71
	24.0	0.00	0.95	0.95
succinic anhydride	1.0	0.00	0.25	0.25
	3.0	0.00	0.43	0.43
	6.0	0.00	0.51	0.51
	24.0	0.00	0.65	0.65
phthalic anhydride	1.0	0.00	0.05	0.05
	6.0	0.00	0.09	0.09
	12.0	0.00	0.20	0.20
	24.0	0.00	0.46	0.46
caproyl chloride	0.25	0.00	1.16	1.16
	0.5	0.00	1.35	1.35
	1.0	0.00	1.38	1.38
	3.0	0.00	1.46	1.46
	12.0	0.00	1.54	1.54
benzoyl chloride	0.25	0.00	1.10	1.10
	1.0	0.00	1.36	1.36
	3.0	0.00	1.45	1.45
	12.0	0.00	1.56	1.56

[a-c] See corresponding footnotes in Table I. [d] A white gel formed immediately.

Table VI. Reaction of Potassium Triisopropoxyborohydride with Representative Esters and Lactones in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
ethyl caproate	24.0	0.00	0.00	0.00
ethyl benzoate	0.5	0.00	0.00	0.00
	1.0	0.00	0.01	0.01
	3.0	0.00	0.02	0.02
	6.0	0.00	0.04	0.04
phenyl acetate	0.5	0.00	0.10	0.10
	1.0	0.01	0.12	0.11
	3.0	0.01	0.14	0.13
	6.0	0.01	0.24	0.23
	24.0	0.01	0.54	0.53
	48.0	0.01	0.62	0.61
γ-butyrolactone	1.0	0.00	0.05	0.05
	6.0	0.00	0.09	0.09
	24.0	0.00	0.23	0.23
	48.0	0.00	0.32	0.32
phthalide	12.0	0.00	0.00	0.00
isopropenyl acetate	1.0	0.01	0.07	0.06
	6.0	0.01	0.09	0.08
	24.0	0.01	0.16	0.15
	48.0	0.01	0.25	0.24

[a-c] See corresponding footnotes in Table I.

Table VII. Reaction of Potassium Triisopropoxyborohydride with Representative Epoxides in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
1,2-butylene oxide	120.0[d]	0.00	0.01	0.01
styrene oxide	48.0[e]	0.01	0.04	0.03
cyclohexene oxide	48.0	0.00	0.00	0.00
1-methyl-1,2-cyclohexene oxide	72.0	0.00	0.00	0.00

[a-c] See corresponding footnotes in Table I. [d] Only a trace of 2-butanol was identified by GC analysis. [e] No sign of reduction was observed by GC analysis.

triisopropoxyborane is unreactive under these reaction conditions and does not interfere with a second hydroboration utilizing the dialkylborane produced. In comparison with potassium triisopropoxyborohydride, sodium and potassium borohydrides suffer from a disadvantage of having four equivalent hydrides per molecule. Consequently, through the reduction process, different intermediates with different reactivities form. Sodium and

Table VIII. Reaction of Potassium Triisopropoxyborohydride with Representative Amides and Nitriles in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
caproamide	6.0	0.06	0.06	0.00
	24.0	0.20	0.20	0.00
	48.0	0.30	0.30	0.00
	72.0	0.36	0.36	0.00
benzamide[d]	0.5	0.02	0.02	0.00
	3.0	0.19	0.21	0.02
	6.0	0.36	0.40	0.04
	24.0	0.80	0.89	0.09
	48.0	1.03	1.14	0.11
	72.0	1.07	1.20	0.13
	96.0	1.07	1.22	0.15
N,N-dimethylbutyramide	48.0	0.00	0.00	0.00
N,N-dimethylbenzamide	1.0	0.00	0.01	0.01
	48.0	0.00	0.02	0.02
capronitrile	48.0	0.00	0.01	0.01
benzonitrile	6.0	0.01	0.08	0.07
	48.0[e]	0.01	0.21	0.20

[a-c] See corresponding footnotes in Table I. [d] A faint yellow precipitate formed. [e] Color changed to yellow.

Table IX. Reaction of Potassium Triisopropoxyborohydride with Representative Nitro Compounds and Their Derivatives in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
1-nitropropane[d]	24.0	0.00	0.00	0.00
nitrobenzene[e]	1.0	0.00	0.04	0.04
	3.0	0.00	0.12	0.12
	24.0	0.00	0.30	0.30
	48.0	0.00	0.43	0.43
azoxybenzene	48.0	0.00	0.00	0.00
azobenzene[f]	3.0	0.00	0.01	0.01
	24.0[g]	0.00	0.05	0.05
	48.0	0.00	0.08	0.08

[a-c] See corresponding footnotes in Table I. [d] A white precipitate formed immediately. [e] The color changed to dark brown immediately. [f] The color changed to dark green immediately. [g] The color changed to brown.

potassium borohydrides have a very low solubility in common organic solvents such as THF and Et_2O. The use of potassium triisopropoxyborohydride will overcome these problems associated with other alkali metal borohydrides. The KIPBH reagent carried only one equivalent hydride per molecule and it shows an excellent solubility in common solvents such as THF, Et_2O, and monoglyme. These and other potential uses of the KIPBH reagent make it a unique soluble hydride source available to the research chemist.

Experimental Section

Materials. The compounds examined were the same as those used in the previous studies.[13] Tetrahydrofuran was dried over a 4-Å molecular sieve and distilled from benzophenone sodium ketyl prior to use. Potassium hydride was purchased from Alfa and was freed from the mineral oil according to the published procedure.[14] Triisopropoxyborane was either purchased from Aldrich Chemical Co. or prepared from 2-propanol and methyl sulfide–borane complex.[15] Triisopropoxyborane was distilled from a small piece of potassium metal prior to use. ^{11}B NMR spectra were recorded on a Varian FT-80 spectrometer, and all ^{11}B NMR chemical shifts are reported relative to $BF_3{\cdot}OEt_2$ with low field assigned as positive.

GC Analysis. GC analyses were carried out on a Varian Model 1400 FID chromatograph or a Hewlett-Packard 5750 TC chromatograph equipped with a Hewlett-Packard 3390A integrator/plotter. The alcohol products wee analyzed by using a 12 ft × 0.125 in. column of 15% THEED on a 100–120-mesh Supelcoport or 10% Carbowax 20M on 100–120-mesh Supelcoport. Other compounds were analyzed by using a 12 ft × 0.125 in. column of 10% SP 2100 on a 100–120-mesh Supelcoport. All GC yields were determined by using a suitable internal standard and authentic mixtures.

Preparation of Potassium Triisopropoxyborohydride (KIPBH) under Reflux Conditions in THF. An oven-dried, 2-L round-bottomed flask with a side arm, a condenser tube, and an adaptor was attached to a mercury bubbler. The flask was flushed with dry nitrogen and maintained under a static pressure of nitrogen. To this flask was added 60 g of KH (1.5 mol, 50% excess) as an oil dispersion with the aid of a thick double-ended needle. The mineral oil was removed with pentane (3 × 50 mL). To this pure KH was added ca. 400 mL of freshly distilled THF. The suspended KH was kept at room temperature by using a water bath. A total of 188.1 g (1.0 mol) of distilled triisopropoxyborane was added to the KH suspension via a double-ended needle while the mixture was stirred. The ^{11}B NMR spectrum of the reaction mixture showed the formation of 10–15% of a minor compound, $K(i\text{-}PrO)_4B$. To purify the KIPBH reagent, the THF solution of KIPBH was brought to gentle reflux over the excess KH. The ^{11}B NMR spectrum of the mixture after 24 h showed the formation of a >99% pure KIPBH. Hydride

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(13) For previous studies see (a) diborane: Brown, H. C.; Heim, P.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 1637. (b) thexylborane: Brown, H. C.; Heim, P.; Yoon, N. M. *J. Org. Chem.* **1972**, *37*, 2942. (c) disiamylborane: Brown, H. C.; Bigley, D. B.; Arora, S. K.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 7161. (d) 9-BBN: Brown, H. C.; Krishnamurthy, S.; Yoon, N. M. *J. Org. Chem.* **1976**, *41*, 1778. (e) $LiEt_3BH$: Brown, H. C.; Kim, S. C.; Krishnamurthy, S. *Ibid.* **1980**, *45*, 1. (f) $LiAlH_4$: Brown, H. C.; Weissman, P. M.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1458. (g) AlH_3: Brown, H. C.; Yoon, N. M. *Ibid.* **1966**, *88*, 1464. (h) $Li(t\text{-}BuO)_3AlH$: Brown, H. C.; Weissman, P. M. *Isr. J. Chem.* **1963**, *1*, 430. (i) $Li(MeO)_3AlH$: Brown, H. C.; Weissman, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 5614. (j) $LiBH_4$: Yoon, N. M.; Cha, J. S. *J. Korean Chem. Soc.* **1977**, *21*, 108.

(14) Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913.

(15) Brown, C. A.; Krishnamurthy, S. *J. Org. Chem.* **1978**, *43*, 2731.

Table X. Reaction of Potassium Triisopropoxyborohydride with Other Nitrogen Compounds in Tetrahydrofuran at 0 °C

compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
cyclohexanone oxime[d]	1.0	0.01	0.01	0.00
	3.0	0.04	0.04	0.00
	24.0	0.22	0.22	0.00
	48.0	0.30	0.30	0.00
	72.0	0.32	0.32	0.00
phenyl isocyanate	3.0	0.00	0.03	0.03
	48.0	0.00	0.04	0.04
pyridine	72.0	0.00	0.00	0.00
pyridine *N*-oxide	48.0	0.00	0.00	0.00

[a–c] See corresponding footnotes in Table I. [d] A white gel-like precipitate formed gradually.

Table XI. Reaction of Potassium Triisopropoxyborohydride with Representative Sulfur Derivatives in Tetrahydrofuran at 0 °C

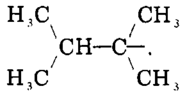
compound[a]	time, h	hydrogen evolved[b,c]	hydride used[b,c]	hydride used for reduction[b,c]
di-*n*-butyl disulfide[d]	0.25	0.03	0.33	0.30
	1.0	0.05	0.50	0.45
	3.0	0.07	0.74	0.67
	6.0	0.10	0.90	0.80
	24.0	0.13	1.16	1.03
	48.0	0.15	1.17	1.02
	1.0[e]	0.47	1.07	0.60
	3.0[e]	0.73	1.59	0.86
	6.0[e]	0.86	1.83	0.99
	24.0[e]	0.98	1.99	1.01
diphenyl disulfide[f]	0.25[g]	0.24	1.24	1.00
	1.0	0.28	1.28	1.00
	3.0	0.31	1.32	1.01
dimethyl sulfoxide	48.0	0.00	0.00	0.00
diphenyl sulfone	48.0	0.00	0.01	0.01
methanesulfonic acid	1.0	0.26	0.26	0.00
	3.0	0.32	0.32	0.00
	6.0	0.39	0.39	0.00
	24.0	0.66	0.66	0.00
	48.0	0.78	0.78	0.00
	72.0	0.85	0.85	0.00
p-toluenesulfonic acid, monohydrate[h]	0.5	0.64	0.64	0.00
	1.0	0.78	0.78	0.00
	6.0	1.04	1.04	0.00
	24.0	2.21	2.21	0.00
	48.0	2.38	2.38	0.00
	72.0	2.44	2.44	0.00
cyclohexyl tosylate	1.0	0.00	0.01	0.01
	6.0	0.00	0.11	0.11
	24.0	0.00	0.23	0.23
	48.0	0.00	0.26	0.26

[a–c] See corresponding footnotes in Table I. [d] A white precipitate was formed gradually. [e] Reduction at room temperature. [f] Each value was determined by the batch system. [g] A white gel-like precipitate formed immediately. [h] A white precipitate formed gradually.

Table XII. Reaction of Potassium Triisopropoxyborohydride with Dialkylhaloborane in the Presence of Olefins

R_a and R_b of R_aBR_bCl	alkene C	product	yield,[a] %
R_a = Thx[b] R_b = *n*-octyl	1-decene	1-decanol	99
R_a = Thx R_b = *n*-octyl	6-chloro-1-hexene	6-chlorohexanol	89
R_a = R_b = cyclopentyl	1-octene	*n*-octanol	98
R_a = R_b = *n*-pentyl	1-octene	*n*-octanol	99

[a] GC yields. [b] Thx =



measurement was done by calculating the number of moles of hydrogen evolved after the reagent was quenched with a mixture of THF, glycerine, and 2 *N* HCl. A 1.56 *M* concentration of hydride was observed. The above reagent was kept over the unused portion of potassium hydride (ca. 50% excess). No disproportionation was detectable after 1 year.

General Procedure for Determination of Rate and Stoichiometry. To a 100-mL flask fitted with a side arm and capped by a rubber septum was added 32.05 mL of a solution of KIPBH in THF (50 mmol in hydride). The flask was immersed in an ice bath. The reaction mixture was diluted with 17.9 mL of THF containing 12.5 mmol of the compound to be reduced. This made the mixture 1.0 *M* in hydride and 0.25 *M* in the compound under investigation. At different time intervals, 4-mL samples were withdrawn and quenched in a THF–glycerine–2 *N* HCl hydrolyzing mixture. The hydrogen evolved was measured volumetrically. The reaction was stopped when two or more analyses indicated that no more hydride was taken up. The solutions were transferred by means of a hypodermic syringe. For reaction of compounds with active hydrogen, the reaction flask was attached to a gas meter.

The reduction of anthraquinone is described here as a representative procedure. After a 30-min reaction time at 0 °C, hydrolysis of a 4-mL aliquot of the reaction mixture indicated 2.83 mmol of residual hydride, which means 1.17 mmol of hydride per mol of anthraquinone had been consumed. After 24 h, the analysis showed 1.98 mmol of residual hydride (after correction for hydrogen evolution), which indicated 2.02 mmol of hydride per mol of the compound had been consumed.

General Procedure for Stereoselective Study. The reduction of 2-methylcyclohexanone is representative. To a 100-mL, round-bottomed flask fitted with a side arm and capped by a rubber septum was added a 2.0-mL solution of KIPBH in THF (3.12 mmol in hydride). The flask was kept at 0 °C with the aid of an ice bath. To this was added 1.0 mL of a 2-methylcyclohexanone solution in THF (1.56 *M* in ketone). The reaction mixture was kept at 0 °C for 3 h (3 days at −25 °C). It was then hydrolyzed by addition of 2 mL of 2 *N* HCl solution. The aqueous layer was saturated with anhydrous potassium carbonate, and the organic layer was analyzed by GC. The results are summarized in Table III.

General Procedure for Stepwise Hydroboration with Haloboranes. The reaction of *n*-octylthexylchloroborane is representative. A 100-mL, round-bottomed flask equipped with a nitrogen inlet and a magnetic stirring bar was charged at 0 °C with 1.0 mL of *n*-dodecane (0.75 g, 4.40 mmol), the internal standard, and 1.57 mL of 1-octene (1.12 g, 10.0 mmol). Then 5.0 mL of 2.0 *M* cold thexylchloroborane methyl sulfide (10.0 mmol) in CH_2Cl_2 was added. After 5 min at 0 °C, the ice bath was replaced with a water bath and the mixture was stirred at 25 °C for 1 h. After cooling to 0 °C, 1.90 mL of 1-decene (1.40 g, 10.0 mmol) was added. Then 6.41 mL of 1.56 *M* KIPBH (>99% purity) in THF was added dropwise by using a syringe over a 3–5-min period. A white precipitate was formed immediately. The resulting mixture was stirred for 1 h at 0 °C and then oxidized by adding 10 mL of THF, 12 mL of 6 *N* NaOH, 10 mL of absolute ethanol, and 6 mL of 30% aqueous hydrogen peroxide (dropwise). After being stirred at 0 °C for 1 h, the mixture was heated at 55 °C overnight and cooled to room temperature. Absolute Et_2O (10 mL) was added and the aqueous layer was saturated with anhydrous potassium carbonate. GC analysis of the organic layer showed the formation of 10.0 mmol of 1-decanol. The results are summarized in Table XII. A full experimental section for carbonylation and cyanidation reactions has been described elsewhere.[16]

Registry No. KIPBH, 42278-67-1; KH, 7693-26-7; $(i\text{-PrO})_3B$, 5419-55-6; $K(i\text{-PrO})_4B$, 84581-08-8; 1-hexanol, 111-27-3; benzyl alcohol, 100-51-6; 3-hexanol, 623-37-0; 3-ethyl-3-pentanol, 597-49-9; phenol, 108-95-2; *n*-hexylamine, 111-26-2; 1-hexanethiol, 111-31-9; benzenethiol, 108-98-5; caproaldehyde, 66-25-1; benzaldehyde, 100-52-7; 2-heptanone, 110-43-0; 2-heptanol, 543-49-7; norcamphor, 497-38-1; norborneol, 1632-68-4; acetophenone, 98-86-2; α-phenylethanol, 98-85-1; benzophenone, 119-61-9; benzhydrol, 91-01-0; cinnamaldehyde, 104-55-2; cinnamyl alcohol, 104-54-1; 3-phenyl-1-propanol, 122-97-4; 2-methylcyclohexanone, 583-60-8; *cis*-2-methylcyclohexanol, 7443-70-1; 3-methylcyclohexanone, 591-24-2; 3-methylcyclohexanol, 591-23-1; 4-methylcyclohexanone, 589-92-4; 4-methylcyclohexanol, 589-91-3; 4-*tert*-butylcyclohexanone, 98-53-3; 4-*tert*-butylcyclohexanol, 98-52-2; 3,3,5-trimethylcyclohexanone, 873-94-9; 3,3,5-trimethylcyclohexanol, 116-02-9; *p*-benzoquinone, 106-51-4; hydroquinone, 123-31-9; anthraquinone, 84-65-1; 9,10-dihydro-9,10-anthracenediol, 58343-58-1; caproic acid, 142-62-1; benzoic acid, 65-85-0; acetic anhydride, 108-24-7; succinic anhydride, 108-30-5; phthalic anhydride, 85-44-9; caproyl chloride, 142-61-0; benzoyl chloride, 98-88-4; ethyl caproate, 123-66-0; ethyl benzoate, 93-89-0; phenyl acetate, 122-79-2; γ-butyrolactone, 96-48-0; phthalide, 87-41-2; isopropenyl acetate, 108-22-5; 1,2-butylene oxide, 106-88-7; styrene oxide, 96-09-3; cyclohexene oxide, 286-20-4; 1-methyl-1,2-cyclohexene oxide, 1713-33-3; caproamide, 628-02-4; benzamide, 55-21-0; *N*,*N*-dimethylbutyramide, 760-79-2; *N*,*N*-dimethylbenzamide, 611-74-5; capronitrile, 628-73-9; benzonitrile, 100-47-0; 1-nitropropane, 108-03-2; nitrobenzene, 98-95-3; azoxybenzene, 495-48-7; azobenzene, 103-33-3; cyclohexanone oxime, 100-64-1; phenyl isocyanate, 103-71-9; pyridine, 110-86-1; pyridine *N*-oxide, 694-59-7; di-*n*-butyl disulfide, 629-45-8; *n*-butyl mercaptan, 109-79-5; diphenyl disulfide, 882-33-7; dimethyl sulfoxide, 67-68-5; diphenyl sulfone, 127-63-9; methanesulfonic acid, 75-75-2; *p*-toluenesulfonic acid, 104-15-4; cyclohexyl tosylate, 953-91-3; *tert*-hexyl-*n*-octylchloroborane, 75052-81-2; dicyclopentylchloroborane, 36140-18-8; di-*n*-pentylchloroborane, 18379-77-6; 1-decene, 872-05-9; 1-decanol, 112-30-1; 6-chloro-1-hexene, 928-89-2; 6-chlorohexanol, 2009-83-8; 1-octene, 111-66-0; 1-octanol, 111-87-5.

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[16] Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, *89*, 5285. Manuscript in preparation: Brown, H. C.; Nazer, B.; Sikorski, J. A.

Organoboranes. 35. Reaction of Alkylthioboronic Esters with Trichloromethyllithium: Preparation of One-Carbon-Extended Carboxylic Acids and Thioacetals from Alkenes via Hydroboration

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Various 2-alkyl-1,3,2-dithiaborolanes, $RB(S_2C_2H_4)$ (**1**), were converted to the corresponding carboxylic acids, RCO_2H (**2**), by using $LiCCl_3$ in THF, followed by oxidation with alkaline hydrogen peroxide. For R = hexyl, a reaction intermediate is converted by solvent into another compound, $C_6H_{13}C(S_2C_2H_4)B[O(CH_2)_4Cl]_2$ (**9a**), characterized spectroscopically. The yields of **2** decreased with increasing bulkiness of the alkyl groups R. Although the configuration of R = *trans*-2-methylcyclopent-1-yl (**1k**) was retained in the product (>98% trans), a significant degree of epimerization took place for R = *exo*-norbornyl (**1j**) during the oxidation (exo:endo = 86:14). More uniquely, the intermediates **9** were easily hydrolyzed by heating the reaction mixture with aqueous NaOH to give the corresponding 2-alkyl-1,3-dithiolanes **3**. Stereochemical integrity was retained in the products derived from **1j** and **1k**. Since **1** was prepared by the hydroboration of alkenes, this sequence provides a new method for introducing oxycarbonyl or thioacetal functionality into alkenes in a regioselective manner, and, in the case of **3**, also with stereocontrol.

Organylboronic esters, $RB(OR')_2$, bearing only one organyl group, would have a major advantage over triorganylboranes, R_3B, in organic synthesis when a single organyl group is to be incorporated into the product.

Recently, a few α-heteroatom-substituted carbanions have been found effective for homologating boronic esters. Thus, as reported by Matteson and co-workers, dichloromethyllithium converts $RB(OR')_2$ to $RCHClB(OR')_2$[1] and