# Potassium Tri-isopropoxyborohydride. A New Mild Complex Hydride Reducing Agent with High Stereoselectivity for Reduction of Ketones

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*Summary* The readily prepared potassium tri-isopropoxyborohydride exhibits exceptionally mild reducing properties, yet rapidly reduces ketones with high stereoselectivity to the less stable of the corresponding alcohol epimers.

ISOPROPYL BORATE reacts readily with an excess of potassium hydride in tetrahydrofuran (THF) to yield quantitatively potassium tri-isopropoxyborohydride (KTPBH).[1] Unlike trimethoxy- and triethoxy-borohydrides, tri-isopropoxyborohydride does not disproportionate in ethereal solvents.[2] In view of the ease of preparation of this sterically hindered reducing agent, we have examined its reactivity toward a number of systems.

In THF the compound proved to be a very mild reducing agent. Aldehydes and ketones were readily reduced† to alcohols, even at −23°. However, aryl and alkyl halides (except methyl iodide), esters, nitriles, epoxides, and amides, were essentially inert to KTPBH at 0°. Carboxylic acids and alcohols reacted sluggishly only to liberate hydrogen. Surprisingly, isopropyl alcohol was more reactive (100% in 12 h) than hexanoic acid (59% in 24 h).

| Substrate | | Proportion (%) of less stable epimer found with | | | | | |
|---|---|---|---|---|---|---|---|
| | | $NaBH_4$[a,b] | | $LiAlH(OBu^t)_3$[c,d] | | $KBH(OPr^i)_3$[e] | |
| | | 25° | 0° | 0° | −23° | 0° | −23° |
| 2-Methylcyclopentanone[f] | .. | 26 | | 28 | | | 73 |
| 2-Methylcyclohexanone[f,g] | .. | | 31 | 27 | | 92 | 95·5 |
| 3-Methylcyclohexanone[h] .. | .. | 17 | | | 10 | | 85 |
| Norcamphor[i] .. .. | .. | | 89 | 93 | | 98 | |

[a] In MeOH, EtOH, or $Pr^iOH$; [b] J. B. Umland and B. Williams, *J. Org. Chem.*, 1956, **21**, 1302; A. C. Cope, C. H. Part, and P. Scheiner, *J. Amer. Chem. Soc.*, 1962, **84**, 4862, M. G. Combe and H. B. Henbest, *Tetrahedron Letters*, 1964, 404; [c] in ether; [d] ref. 4; [e] in THF; [f] *cis*-alcohol; [g] $LiAlH_4 \rightarrow$ 18—24% *cis*, $LiAlH(OMe)_3 \rightarrow$ 69% *cis*, and $LiBHR_3 \rightarrow$ 96—99% *cis* (W. G. Dauben, G. H. Fonkin, and D. S. Noyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2579; ref. 4; and H. C. Brown and S. Krishnamurthy, *J. Amer. Chem Soc.*, 1972, **94**, 7159; all of these are powerful reducing agents for organic functional groups; [h] *trans*-alcohol; [i] *endo*-norborneol.

In its reducing properties, KTPBH resembles the mild reducing agents lithium tri-t-butoxyaluminohydride (LiTBAH)[4] and sodium borohydride. However, in contrast to these two, KTPBH exhibits a powerful ability to achieve stereoselective reductions of cyclic ketones. Thus reduction of 2-methylcyclohexanone at 0° yields 31% *cis*-alcohol with sodium borohydride, 27% *cis* with LiTBAH,[5] and 92% *cis* with KTPBH. At −23°, KTPBH yields 95·5% *cis*-alcohol. Stereoselective reductions of representative ketones are summarized in the Table.

Thus KTPBH is the first reported complex hydride reducing agent which is both mild and highly stereoselective. It should find considerable use in multistep syntheses of polyfunctional structures.

The mild reducing power of this reagent is unexpected. Garrett and Lyttle[6] report that in reduction of acetone with borohydride, each subsequent hydride transfer is faster than that from $BH_4^-$. This has been explained[2,3] in terms of the weak Lewis acidity of B–O compounds induced by back-bonding; hydride transfer would be more difficult from the stronger Lewis acid $BH_3$ than from $(RO)_3B$. $(RO)_3B$ is a markedly weaker Lewis acid than $R_3B$, yet $R_3BH^-$ is by far a more powerful reducing agent than $BH_4^-$. Evidently, back-bonding is slight in the transition state of reduction with $(RO)_3BH^-$ and the $-I$ effect of the alkoxy-groups predominates, resulting in a more electropositive boron atom in $(RO)_3BH^-$.

We are examining other hindered alkoxyborohydrides, both as synthetic reagents and as probes of mechanism for hydride transfers from boron.

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† Sodium tri-isopropoxyborohydride (prepared at high temperature from NaH and the borate in diglyme) is reported to reduce 3,3,5-trimethylcyclohexanone only slightly.[3]

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[3] H. Haubenstock and E. Eliel, *J. Amer. Chem. Soc.*, 1962, **84**, 2368.
[4] H. C. Brown and P. M. Weissman, *Israel J. Chem.*, 1963, **1**, 4301.
[5] H. C. Brown and H. R. Deck, *J. Amer. Chem. Soc.*, 1965, **87**, 5620.
[6] E. R. Garrett and D. A. Lyttle, *J. Amer. Chem. Soc.*, 1953, **75**, 6051.