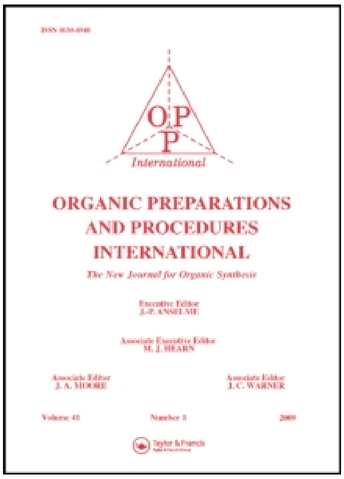

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B-HYDROXYDIISOPINOCAMPHEYLBORANE AS A MILD, CHEMOSELECTIVE REDUCING AGENT FOR ALDEHYDES

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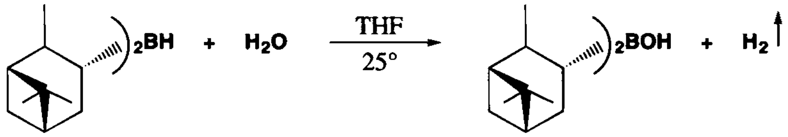
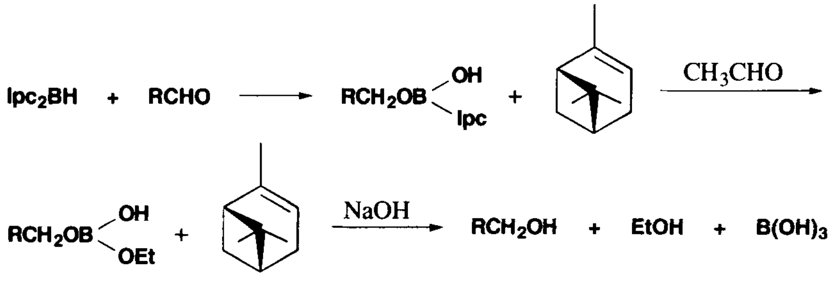
The chemoselective reduction of aldehydes to primary alcohols in the presence of ketones and other readily reducible groups affords a very useful methodology in organic synthesis. Consequently in recent years, numerous reagents have been proposed to accomplish this objective.[1,2] However, an ideal reagent for the completely selective reduction of aldehydes in the presence of keto and all other reducible functional groups still eludes organic chemists. In the course of exploring the reducing action of *B*-hydroxydiisopinocampheylborane (Ipc_2BOH), we observed that the reagent is extremely mild and effectively reduces aldehydes under mild conditions. Herein we report the application of this newly synthesized reagent, Ipc_2BOH, for the selective reduction of aldehydes in the presence of other reducible functional groups. The reagent is conveniently prepared by a simple reaction between diisopinocampheylborane (Ipc_2BH) and water in THF solution (Eq 1).



(1)

(Ipc_2BH) (Ipc_2BOH)

The reagent is very effective for the reduction of aldehydes at 25° in pentane. As in the case of diisopinocampheylchloroborane (Ipc_2BCl),[3] the formation of an intermediate alkoxyborane is accompanied by the liberation of α-pinene. The treatment of the reaction mixture with excess acetaldehyde (elimination of the second α-pinene) followed by addition of aqueous sodium hydroxide provides the alcohol[4] (Eq 2). The usual alkaline hydrogen peroxide oxidation of the intermediate organoborane[6] is also applicable. However, prior addition of a solution buffered at pH 7 is desirable to suppress the undesired side-reaction during the oxidation.



(2)

TABLE 1. Reduction of Aldehydes to Alcohols with Ipc_2BOH in Pentane at 25°[a]

Product	Time (hrs)	Yields (%)[b]
$CH_3(CH_2)_2CH_2OH$	6	100
$CH_3(CH_2)_4CH_2OH$	12	100 (71)
$C_6H_5CH_2OH$	12	100 (73)
p-$ClC_6H_4CH_2OH$	24	100
p-$CH_3OC_6H_4CH_2OH$	24	100
$C_6H_5CH{=}CH_2OH$	12	100

a) Ten percent excess reagent was utilized. Reaction mixture were *ca.* 1 M in substrates. b) Determined by GC using internal standard. Numbers in parenthesis indicate isolated yields.

Several representative example of successful transformations of aldehydes are presented in Table 1. A wide variety of aldehydes are reduced completely in less than 24 hrs at 25° in pentane. α,β-Unsaturated aldehydes are reduced cleanly to the corresponding allylic alcohols. Competition experiments carried out by adding one equivalent of the reagent to an equimolar mixture of aldehyde and ketone in pentane reveals that the reagent is highly selective toward aldehydes (Table 2). Even more remarkable is the chemoselective discrimination between an aldehyde and a more reactive ketone, cyclohexanone. Thus, a wide variety of aldehydes can be selectively reduced in the presence of cyclohexanone. In addition, various representative functional groups, such as ester, lactone, amide, nitrile, alkene, alkyne, and anhydride, are not affected by Ipc_2BOH. Carboxylic acids and water do not react at all. Furthermore, even epoxides and acid chlorides are inert to the reagent. Consequently, the reagent permits the selective reduction of aldehyde groups in the presence of all other functional groups. Such a remarkable inertness toward most of the functional groups, combined with a high selectivity for the reduction of aldehydes, has not been realized with any previously described reagent. Very recently, Ipc_2BCl has been reported to be superior to all of the earlier reported reagents in its ability to distinguish effectively between carbonyl compounds.[2] However, the reducing power of this reagent is much stronger than that of Ipc_2BOH and reacts with epoxides[5] and water.

TABLE 2. Selective Reduction of Aldehyde Groups in the Presence of Keto and Other Functional Groups with Ipc_2BOH in Pentane at 25°[a]

Starting mixture	Time (hrs)	Ratio of reduction products[b]
Butanal / Cyclohexanone	6	100 : 0
Hexanal / Cyclohexanone	12	100 : 0
Hexanal / 2-Heptanone	12	100 : 0
Hexanal / Acetophenone	24	100 : 0
Hexanal / Benzophenone	24	100 : 0
Benzaldehyde / Cyclohexanone	12	100 : 0
Benzaldehyde / 2-Heptanone	12	100 : 0
p-Anisaldehyde / Cyclohexanone	24	85 : 15
	48[c]	95 : 5
Hexanal / Hexanoyl chloride	12	100 : 0
Hexanal / Benzoyl chloride	12	100 : 0
Hexanal / 1,2-Butylene oxide	12	100 : 0

a) Reaction mixture were *ca.* 1 M in substrates. One equivalent of reagent was utilized for competitive reduction of equimolar mixture of two carbonyl compounds. b) Normalized ratio determined by GC with appropriate internal standard; the total yields of product alcohols were ≥ 99.9%. c) At 0°.

EXPERIMENTAL SECTION

All glassware used dried thoroughly in an oven, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reactions and manipulations of air- and moisture-sensitive materials were carried out using standard techniques for handling air-sensitive materials.[6] All chemicals were commercial products of the highest purity which were purified further by standard methods before use. Pentane was bubbled with dry nitrogen, dried with molecular sieve (4Å) and distilled. Borane-methyl sulfide (BMS) was purchased from the Aldrich Chemical Company. GC analyses were performed on a Hewlett-Packard 5790 A FID chromatograph equipped with a Hewlett-Packard 3390 A integrator/plotter, using 12 ft. X 0.125 in. column of 10% Carbowax 20M on 100-120 mesh Supelcoport. ^1H NMR Spectra were recorded on a Varian EM-360 A instrument. ^{11}B NMR spectra were recorded on a Bruker AMX-300 spectrometer, and chemical shifts are with reference to $BF_3{\bullet}OEt_2$.

Preparation of *B*-hydroxydiisopinocampheylborane (Ipc_2BOH) in Pentane. - To an oven-dried, 250-mL flask with a side-arm and a reflux condenser leading to a mercury bubbler were added 10 mL of BMS (10M, 100 mmol) and 96 mL of THF. It was cooled to 0°, and 35 mL (220mmol) of α-pinene was added dropwise with stirring. After the addition of α-pinene, the stirring was stopped and the flask was stored at 0° for 12 hrs. The supernatant solution was decanted by using A double-ended needle. The residue crystalline lumps of Ipc_2BH were broken up and washed with ethyl ether (3 X 12 mL).

The crystalline Ipc_2BH (90 mmol) was suspended in THF (40 mL) and cooled to 0°. To this 1.7 mL of water (95 mmol) was added dropwise with stirring. The solid disappeared as hydrogen evolved. After the addition of water, the mixture was warm to room temperature and stirred for 1 hr.

The volatile materials were evaporated. The viscous Ipc_2BOH was diluted with pentane to 2M using a mass cylinder. The 11B NMR spectrum of the solution showed a broad singlet at δ 52.4 ppm.

Reduction of Aldehydes.- The following procedure for the reduction of butanal is representative. An oven-dried 50-mL flask, fitted with a side arm and a bent adapter connected to a mercury bubbler, was charged with 2.5 mL of 2M butanal solution (5 mmol) in pentane and dodecane as an internal standard. The solution was maintained at 25° in a water bath. To this solution was added 2.75 mL of a 2M Ipc_2BOH solution (5.5 mmol) in pentane with stirring, and reaction mixture was stirred for 1 hrs at 25°. Acetaldehyde (0.39 mL, 7 mmol) was added dropwise to the reaction mixture and the mixture was stirred for 6 hrs. Sodium hydroxide (6N, 5 mL) was added to the mixture. The aqueous layer was then saturated with potassium carbonate and thoroughly extracted into pentane. The combined pentane extract was dried over magnesium sulfate. Gas chromatographic analysis showed 100% 1-butanol.

In a larger scale of reaction, butanal (30 mmol) was treated with Ipc_2BOH (33 mmol) for 1 hr at 25°. Workup as described above, followed by distillation provided 1-butanol in 73% yield : bp 117-119°/761 mmHg. GC analysis showed >99% purity and ^1H NMR spectrum was identical to that of an authentic sample.

Competitive Reduction.- The following procedure for the competitive reaction between hexanal and cyclohexanone is representative. A 50-mL flask was charged with equimolar mixture of hexanal (4 mmol) and cyclohexanone (4 mmol) in 4 mL of pentane. The solution was maintained at 25° in a water bath and 2.0 mL of a 2M solution of Ipc_2BOH (4 mmol) in pentane was added rapidly with vigorous stirring. The reaction mixture was stirred for 12 hrs at 25° and the mixture was then quenched with 3N aqueous sodium hydroxide (2 mL) and dodecane was added as an internal standard. The organoborane derivative was oxidized by addition of buffer solution (pH 7.0, 2 mL) and 30% hydrogen peroxide (0.8 mL), and followed by the reaction mixture being stirred overnight at room temperature. The aqueous layer was then saturated with potassium carbonate and thoroughly extracted into pentane. The combined pentane extract was dried over magnesium sulfate and subjected to GC analysis to show the presence of 100% 1-hexanol and 100% cyclohexanone in total yield of 99.9%.

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REFERENCES

1. a) R. O. Hutchins and D. Kandasamy, *J. Am. Chem. Soc.*, **95**, 6131 (1973); b) G. W. Gribble and D. C. Ferguson, *Chem. Commun.*, 535 (1975); c) C. S. Sell, *Australian J. Chem.*, **28**, 1383 (1975); d) Y. Maki, K. Kikuchi, H. Sugiyama, and S. Seto, *Tetrahedron Lett.*, 263 (1977); e) G. H. Posner, A. W. Runquist, and M. Chapdelaine, *J. Org. Chem.*, **42**, 1202 (1977); f) H. C. Brown and S. V. Kulkarni, *ibid.*, **42**, 4169 (1977); g) N. M. Yoon and J. S. Cha, *J. Korean Chem. Soc.*, **22**, 259 (1978); h) N. Y. M. Fung, P. deMayo, J. H. Schauble, and A. C. Weedorn, *J. Org. Chem.*, **43**, 3977 (1978); i) M. M. Midland and A. Tramontano, *ibid.*, **43**, 1470 (1978); j) P. A. Risbood and D. M. Ruthoven, *ibid.*, **44**, 3969 (1979); k) T. N. Sorrell and P. S. Pearlman, *Tetrahedron Lett.*,

3963 (1980); l) G. W. J. Fleet and P. J. C. Harding, *ibid.*, 675 (1981); m) S. Krishnamurthy, *J. Org. Chem.*, **46**, 4628 (1981); n) N. M. Yoon, G. B. Park, and Y. S. Gyoung, *Tetrahedron Lett.*, 5367 (1983); o) S. Kim, H. J. Kang, and S. Yang, *ibid.*, 2985 (1984); p) S. Kim and S. Yang, *Bull. Korean Chem. Soc.*, **9**, 188 (1988); q) D. E. Ward and C. K. Rhee, *Synth. Commun.*, **18**, 1927 (1988); r) D. E. Ward, C. K. Rhee and W. M. Zoghaib, *Tetrahedron Lett.*, **29**, 517 (1988); s) K. Maruoka, Y. Araki, and H. Yamamoto, *ibid.*, **29**, 3101 (1988); t) B. C. Ranu and R. Chakraborty, *ibid.*, **31**, 7663 (1990); u) D. C. Sarkas, A. R. Das, and B. C. Ranu, *J. Org. Chem.*, **55**, 5799 (1990); v) H. Firouzabadi, B. Tamami, and N. Goudarzian, *Synth. Commun.*, **21**, 2275 (1981).

2. J. S. Cha, E. J. Kim, O. O. Kwon, and J. M. Kim, *Synlett*, In press.

3. H. C. Brown, J. Chandrasekharan, and P. V. Ramachandran, *J. Am. Chem. Soc.*, **110**, 1539 (1988).

4. P. V. Ramachandran, A. V. Teodorovic, M. V. Rangaishenvic, and H. C. Brown, *J. Org. Chem.*, **57**, 2379 (1992).

5. N. N. Joshi, M. Srebnik, and H. C. Brown, *J. Am. Chem. Soc.*, **110**, 6246 (1988).

6. H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, *Organic Synthesis via Boranes*, Wiley-Interscience, New York, NY (1975).

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