

Selective Hydroboration of Terminal Alkenes in the Presence of Aldehydes and Ketones

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Abstract: The hydroboration of olefinic ketones and aldehydes with dicyclohexylborane gives the corresponding hydroxy aldehydes and ketones in good yields after oxidation with sodium perborate.

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Boron hydride reagents have been utilized extensively in organic synthesis. They have proven to be valuable for the selective reduction of carbonyl compounds as well as for the stereoselective hydroboration of alkenes and alkynes.¹² Because of the effectiveness of borane reagents in reducing aldehydes and ketones, hydroboration reactions involving substrates containing these functional groups are often carried out by either converting the carbonyl group to a less reactive functionality³ or modifying the hydroborating agent.⁴ Otherwise, reduction of the carbonyl moiety might compete with the desired hydroboration reaction. For example, α,β -unsaturated aldehydes and ketones are reduced rapidly and quantitatively to the corresponding allylic alcohols by 9-BBN.⁵ Similarly, Molander reported that the hydroboration of allyl ketones with diisopinocampheylborane produced enantiomerically enriched 1,4-diols via an intramolecular reduction.⁶ Diols are also the final products (after oxidation) when olefinic ketones are reduced by either borane or thexylborane.⁷ However, these latter reports, and related examples such as one involving a hydroboration with catecholborane in the presence of Wilkinson's catalyst⁸, indicate that it might be possible to selectively hydroborate alkenes in the presence of aldehydes and ketones. We wish to report the preliminary results of a study focused on the selective hydroboration of terminal alkenes in the presence of ketones and aldehydes.

Brown and his coworkers have carried out extensive research on the reactions of alkenes and carbonyl compounds with a variety of boron hydrides.⁹ Analysis of their kinetic data reveals that unhindered borane reagents such as 9-BBN are more reactive toward aldehydes than they are toward alkenes but that certain alkenes should react faster with 9-BBN than with ketones. We felt that these reactivity differences might be amplified if more hindered borane reagents were utilized. As a probe, we allowed 1-octene and 2-heptanone (as model substrates) to react with a variety of common borane reagents at various temperatures, (0 °C, 25 °C, 68 °C). The

mixtures were then oxidized with sodium perborate;¹⁰ the results of the study are presented in Table 1.

Table 1. The Reaction of 1-Octene and 2-Heptanone with Various Borane Reagents: A Competitive Study^a

Entry	Rx temp (°C)	Borane Reagents	Ratio of 1-octanol to 2-heptanol ^{b,c}
1	0	BH ₃ ·THF	97:3 ^d
2	25	BH ₃ ·THF	99:1 ^d
3	68	BH ₃ ·THF	98:2 ^d
4	0	BMS	96:4 ^d
5	25	BMS	97:3 ^d
6	25	9-BBN	93:7
7	68	9-BBN	89:11
8	0	(<i>c</i> -C ₆ H ₁₁) ₂ BH	100:0
9	25	(<i>c</i> -C ₆ H ₁₁) ₂ BH	100:0
10	0	Sia ₂ BH	96:4
11	25	Sia ₂ BH	97:3

^a Reactions were carried out using one equivalent each of hydride, alkene and ketone.
^b Ratios obtained by GC analysis after aqueous sodium perborate oxidation. ^c Overall combined yields ranged from 90-100%. ^d 2-Octanol was also formed in small quantities.

Analysis of the data in Table 1 indicates that a terminal alkene can be successfully hydroborated in the presence of a ketone utilizing essentially all of the common hydroborating agents. As anticipated from earlier studies, 9-BBN is less chemoselective than the more hindered hydroborating reagents (entries 6-11); dicyclohexylborane is quite effective at hydroborating a terminal alkene in the presence of a ketone. Also noteworthy is the fact that temperature had little effect on the selectivity of the reagents (entries 1-5).

We then examined the ability of dicyclohexylborane to selectively hydroborate alkenes in the presence of both aldehydes and ketones (Table 2). The results indicate that hydroxyaldehydes and hydroxyketones can be prepared in good yields, after oxidation. Interestingly, no "simple" reduction products (olefinic alcohols) were detectable in any of the

Table 2. The Hydroboration of Olefinic Carbonyl Compounds with Dicyclohexylborane

Entry	Substrate	Product ^a	Yield (%) ^b
1 ^c			76
2 ^c			77
3 ^d			70
4			80
5 ^e			78
6 ^c			68
7 ^f			50

^aKnown compounds exhibited physical and spectral characteristics in accord with literature values and new compounds were characterized by spectral and elemental analysis or HRMS. ^b Isolated yield. ^c Up to 10% of the corresponding diols were isolated. ^d Acetal formed by the reaction of the crude product with methanol in the presence of TsOH. ^e Two equivalents of dicyclohexylborane were utilized. ^f A trace of 11-undecylenic alcohol was detected by TLC.

reactions except when 11-undecylenic aldehyde was used as the substrate. However, overreduction to the diol product (up to 10%) was observed in some cases.

The synthesis of 6-hydroxy-2-hexanone¹¹ is representative: borane-tetrahydrofuran (5.0 mmol, 5.0 mL of a 1.0 M solution in THF) was placed in a dry, argon-flushed, round-bottomed flask which was then immersed in an ice-water bath. Cyclohexene (10.0 mmol, 0.82 g, 1.0 mL) was added dropwise and the mixture stirred at 0 °C for 1 hour. 5-Hexen-2-one (5.0 mmol, 0.49 g, 0.58 mL) was then added to the slurry of dicyclohexylborane in THF. The cooling bath was removed and the mixture stirred for 2 hours at room temperature. Oxidation was achieved by adding NaBO₃·4H₂O (15 mmol, 2.3 g) and water (5 mL) and stirring the mixture at room temperature for 2 hours. The product was extracted into ether (3 x 15 mL), the solvent removed, and 6-hydroxy-2-hexanone (0.44 g, 76% yield) was isolated by flash chromatography.

We are currently evaluating the ability of various borane reagents to hydroborate alkynes and internal alkenes in the presence of aldehydes and ketones.

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References:

1. Brown, H. C. *Organic Syntheses Via Boranes*; Wiley-Interscience: New York, 1975.
2. Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*, Academic Press, London, 1988.
3. Ruettimann, A.; Englert, G.; Mayer, H.; Moss, G. P.; Weedon, B.C.L. *Helv. Chim. Acta* **1983**, *66*, 1939.
4. Kim, G. P., Yoon, N. M. *Bull. Korean Chem. Soc.* **1986**, *7*, 160.
5. (a) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1975**, *40*, 1864. (b) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 1197.
6. Molander, G.A.; Bobbitt, K. L. *J. Org. Chem.* **1994**, *59*, 2676.
7. (a) Harada, T.; Matsuda, Y.; Imanaka, S.; Oku, A. *J. Chem. Soc. Chem. Commun.* **1990**, 1641. (b) Harada, T.; Imanaka, S.; Ohyama, Y.; Matsuda, Y.; Oku, A. *Tetrahedron Lett.* **1992**, *33*, 5807.
8. Männig, D.; Nöth, H. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 878.
9. (a) Brown, H. C.; Wang, K. K.; Chandrasekharan, J. *J. Am. Chem. Soc.* **1983**, *105*, 2340. (b) Brown, H. C.; Krishnamurthy, S.; Yoon, N. M. *J. Org. Chem.* **1976**, *41*, 1778.
10. (a) Kabalka, G. W.; Shoup, T. M.; Goudgaon, N. M. *J. Org. Chem.* **1989**, *54*, 5940. (b) Matteson, D. S.; Moody, R. *J. Org. Chem.* **1980**, *45*, 1091.
11. Weber, G. F.; Hall, S. S. *J. Org. Chem.* **1979**, *44*, 364.

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