

## Aminoborohydrides. 2. Regiospecific Reductions of $\alpha,\beta$ -Unsaturated Carbonyl Compounds with Lithium Pyrrolidinoborohydride. A Facile Conversion of $\alpha,\beta$ -Unsaturated Aldehydes and Ketones to the Corresponding Allylic Alcohols in High Purity

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**Summary:** Lithium aminoborohydrides ( $\text{LiABH}_3$ ), obtained by the reaction of  $n\text{-BuLi}$  with amine-boranes, are powerful reducing agents for the reduction of  $\alpha,\beta$ -unsaturated aldehydes and ketones to the corresponding allylic alcohols. Thus, lithium pyrrolidinoborohydride ( $\text{LiPyrrBH}_3$ ) reduces cinnamaldehyde and cyclohexenone to give exclusively cinnamyl alcohol and 2-cyclohexen-1-ol respectively. This 1,2-reduction appears to be general and ester groups are tolerated. The yield of allylic alcohols from this procedure is essentially quantitative.

The regioselective reduction of  $\alpha,\beta$ -unsaturated ketones and aldehydes to the allylic alcohols is a very important process in organic chemistry.<sup>2-11</sup> It has been shown that reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds using sodium borohydride or lithium aluminum hydride yields mixtures predominating in either 1,2- or 1,4-reduction products depending on the substituents of the substrate used.<sup>11-14</sup> Quite a number of new hydride reducing agents have been investigated in the recent years for the reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds. However, the applicability of these reagents depends on the particular substrate under study.<sup>15-18</sup>

Recently, we showed that  $\text{LiPyrrBH}_3$  is a powerful yet stable reducing agent and can be prepared readily from  $n\text{-BuLi}$  and pyrrolidine-borane (eq. 1).<sup>19</sup> In the process of systematically characterizing the reducing properties of  $\text{LiPyrrBH}_3$ , it was found that it regioselectively reduced cyclohexenone to 2-cyclohexen-1-ol exclusively (eq. 2). Encouraged by this finding, we studied the reduction of a wide variety of  $\alpha,\beta$ -unsaturated carbonyl compounds using  $\text{LiPyrrBH}_3$ .  $\text{LiPyrrBH}_3$  reduced all the  $\alpha,\beta$ -unsaturated aldehydes and ketones used in this study in exclusive 1,2 fashion to the corresponding allylic alcohols. The results for the reductions of representative  $\alpha,\beta$ -unsaturated aldehydes and ketones with  $\text{LiPyrrBH}_3$  are shown in Table 1.

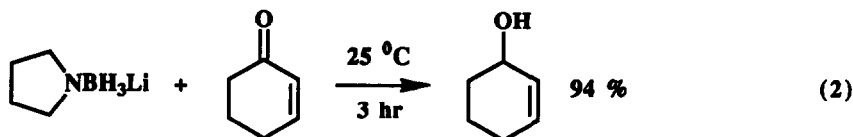
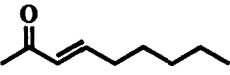
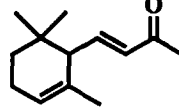
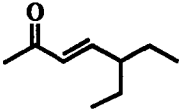
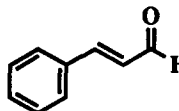
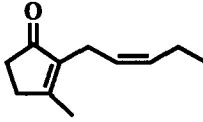
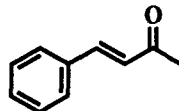
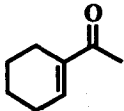
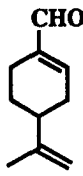
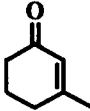
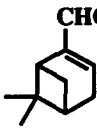
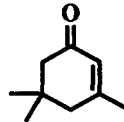
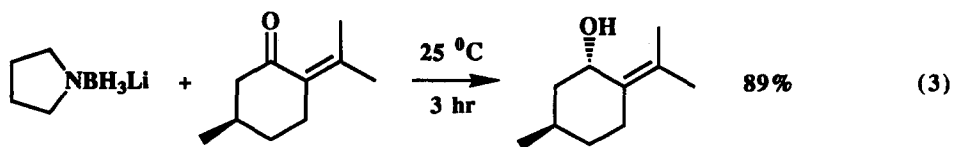


Table 1. Reduction of  $\alpha,\beta$ -Unsaturated Carbonyl Compounds with Lithium Pyrrolidinoborohydride

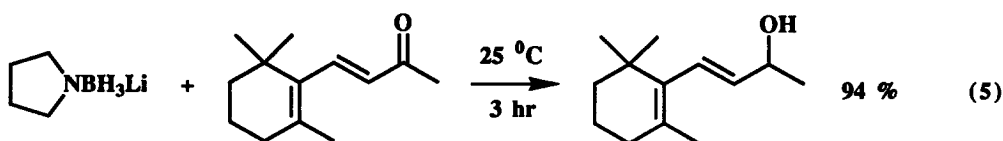
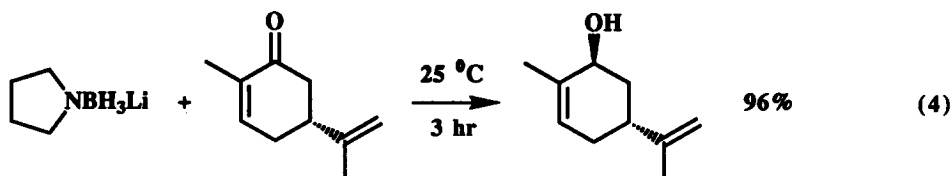
substrate	1,2: 1,4 <sup>a</sup>	yield, % <sup>b</sup>	substrate	1,2: 1,4 <sup>a</sup>	yield, % <sup>b</sup>
	>99:0	96		>99:0	94
	>99:0	90		>99:0	91
	>99:0	98		>99:0	95
	>99:0	89 <sup>c</sup>		>99:0	97
	>99:0	92		>99:0	89
	>99:0	92 <sup>c</sup>			

<sup>a</sup>Product purity determined by 250 MHz <sup>1</sup>H NMR, <sup>13</sup>C NMR and capillary GC analyses. <sup>b</sup>Isolated overall yield. <sup>c</sup>Reductions were done at 65 °C for 1 h.

Since the lithium aminoborohydrides are not pyrophoric, they can be readily used for large scale reductions. The aminoborohydrides can also be used for the reduction of terpene ketones. Thus, the reduction of pulegone with LiPyrrBH<sub>3</sub> gives the allylic alcohol pulegol (eqs. 3).<sup>20,21</sup>

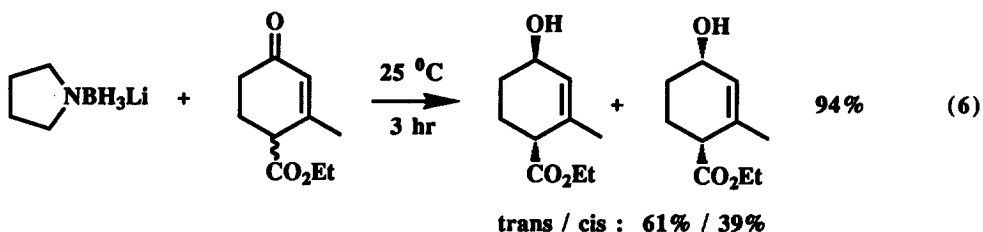


The reductions of carvone and  $\beta$ -ionone with LiPyrrBH<sub>3</sub> yielded the allylic alcohols carveol and  $\beta$ -ionol respectively (eqs. 4 and 5).<sup>21</sup>



The allylic alcohols, from all these reduction reactions, were obtained in both high yield and purity. However, successful product isolations were found to require prior acid hydrolysis to eliminate boron and amine containing side-products.

The results summarized in Table 1 indicate that the reduction of  $\alpha,\beta$ -unsaturated aldehydes and ketones with LiPyrrBH<sub>3</sub> to their corresponding allylic alcohols is a method of general applicability and represents a substantial improvement over other reducing agents currently available for the regioselective 1,2-reduction of  $\alpha,\beta$ -unsaturated aldehydes and ketones.<sup>2-18</sup> The air, moisture, and thermal stability makes LiPyrrBH<sub>3</sub> an ideal reducing agent for large scale reactions, where as the toxic cerium byproducts in Luche's reagent could pose a major environmental concern.<sup>4</sup> Moreover, LiPyrrBH<sub>3</sub> can be used to do a selective 1,2-reduction of an  $\alpha,\beta$ -unsaturated carbonyl compound in the presence of an ester group (eq. 6).<sup>21</sup>



We are actively exploring the use of other aminoborohydrides, including optically active aminoborohydrides, in the regioselective and asymmetric reduction of organic compounds.

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## References and Notes

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- (18). Reduction of 1-octen-3-one gave a mixture of alcohols in the ratio of 80:20 predominating in the expected allylic alcohol. During this reduction the reaction mixture developed a deep blue color indicating a possible single electron transfer process. We are actively exploring the details of this reaction.
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- (20). An oven dried 100-mL round bottom flask with stir bar was charged with pulegone (1.522 g, 10.0 mmol) dissolved in dry THF (20 mL) and held at 25 °C using a water bath. A 1.0 M THF solution of LiPyrrBH<sub>3</sub> (10 mL, 10.0 mmol) was added slowly to the reaction solution with stirring. The reaction was stirred for 1 hr at 25 °C and then cooled to 0 °C using an ice bath. It was then quenched with a slow addition of H<sub>2</sub>O (2 mL), followed by the addition of 6M HCl (7.5 mL) [*Caution: Hydrogen evolution*]. The product(s) were extracted with diethyl ether (2 x 50 mL), washed with H<sub>2</sub>O (3 x 10 mL), and dried over MgSO<sub>4</sub>. The solvent was evaporated at 25 °C under reduced pressure (6 torr). Distillation of the residue yielded pulegol: 1.37 g (89 %) bp 62 °C (0.03 Torr); IR (neat) 3376, 2918, 1640, 1609, 1455, 1370, 1227, 1151, 1026, 948, 896, 842 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 5.67 (d, J=3.0 Hz, 1H), 2.10 (m, 4H), 1.66 (m, 4H), 1.28 (s, 1H), 0.90-0.93 (d, J=7.4 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 143.49, 118.44, 72.86, 33.73, 31.37, 28.90, 28.85, 28.25, 24.74, 21.73; MS (EI) *m/z* 154 (M<sup>+</sup>), 152, 135, 119, 109, 95, 79, 67, 55.
- (21). The stereochemistry of all allylic alcohol products was determined by coupling constants (250 MHz NMR) and capillary CG analyses with internal standards.

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