

stability constants are largely affected by the solvent medium in the course of the complex formation process. It is thus concluded that the only sources of the inverse secondary equilibrium isotope effects for the complexes are mainly molecular vibrations. From the foregoing discussion, we may therefore characterize the relative importance of the contribution from each vibrational mode and found several modes as the major contributors. These are two positive effects from CH<sub>2</sub> rocking and CH<sub>2</sub> twisting modes, and three negative effects from CH<sub>2</sub> wagging, CH<sub>2</sub>-s-stretching, and CH<sub>2</sub> scissoring modes.

The results demonstrate that theoretical calculations based on the reduced partition function quantitatively support the experimental observations. This preliminary study provides a better understanding on the physical insight of the secondary isotope effects and clarify some vagueness of the molecular properties of metal-olefin complex formation process.

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## Lithium *n*-Butylborohydride. An Excellent 1,2-Selective Reducing Agent of Conjugated Enones

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Lithium *n*-butylborohydride generated from *n*-butyllithium and borane-dimethyl sulfide complex in equimolar ratio in toluene-*n*-hexane is exceedingly effective for selective 1, 2 reductions of enones.

Selective 1, 2 reduction of conjugated ketones with hydride reducing agents is often difficult to achieve in organic synthesis due to the competitive occurrence of 1, 2 and 1, 4 reduction<sup>1</sup>. In general, 1, 4 reduction takes place favorably when the double bond is further conjugated with an aromatic ring or contained in a five- or a six-membered ring.

Although lithium *n*-butylborohydride, a representative monoalkylborohydride reducing agent<sup>2</sup>, was recently utilized for the stereoselective reduction of conjugated enones successfully during the total synthesis of Erythronolide B<sup>3</sup> and (-)-N-methylmaysenine<sup>4</sup> by Corey, the characteristic features of this reducing agent have not fully been explored. On the other hand, it has been demonstrated that the mode of the reduction of lithium, potassium tri-*sec*-butylborohydride (L, K-Selectride) with conjugated cyclohexenones depends critically on the presence or the absence of  $\beta$ -substituent<sup>5</sup>.

In view of these facts, we were encouraged to undertake the reaction of lithium *n*-butylborohydride with acyclic and cyclic enones. The potentially useful results obtained prompt

us to report this communication.

We have observed that treatment of conjugated enones with lithium *n*-butylborohydride, generated from *n*-butyllithium and borane-dimethyl sulfide complex in equimolar ratio<sup>6</sup>, in toluene-*n*-hexane at -78 °C produced high yields of the corresponding allylic alcohols, in most cases uncontaminated with 1, 4 reduction products.

Table 1 summarizes the results for selected model compounds, which demonstrated the synthetic usefulness of this reagent. Reduction was carried out in toluene-*n*-hexane (approximately 15:1) using equimolar amounts of conjugated enones and the reducing agent.

The reduction of acyclic enones (entries 1, 2 and 3) afforded exclusively the corresponding allylic alcohols *via* 1, 2 reduction. It is of interest to note that chalcone (entry 2) was reduced by lithium *n*-butylborohydride in 100% 1, 2-selectivity in contrast with predominant 1, 4 reduction by diisobutylaluminum hydride (1, 2/1, 4:35/65)<sup>7</sup>.

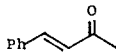
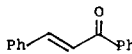
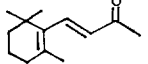

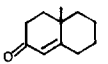
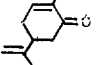
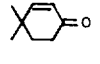


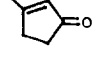
$\beta$ -Substituted cyclohexenones (entries 4 and 5) underwent

exclusive 1, 2 reduction like the case of K-Selectride<sup>5</sup>. However, in sharp contrast with the exclusive 1, 4 reduction with K-Selectride<sup>5</sup>, the reduction of  $\beta$ -unsubstituted cyclohexenones (entries 6 and 7) exclusively afforded the corresponding allylic alcohols in high yields. In case of 2-cyclohexen-1-one, a mixture of 1, 2 and 1, 4 reduction product was obtained in a ratio of 92:8, which was determined by VPC analysis. It seems that the presence of  $\gamma,\gamma$ -dimethyl substituents suppresses 1, 4 reduction because of the steric hindrance at  $\beta$  position.

Reduction of conjugated cyclopentenones occurred less regioselectively: 2-cyclopenten-1-one (entry 9) gave a mixture of 1, 2 and 1, 4 reduction product in a ratio of 65:35 and 3-methyl-2-cyclopenten-1-one (entry 10) gave 1, 2 reduction product as a major product (80 % 1, 2-selectivity).

Even though 1, 2-selectivity is rather low for conjugated cyclopentenones, the excellent 1, 2-selectivity, the easiness of the preparation of the reagent, and high yields obtainable

**TABLE 1: Reduction of Enones with Lithium *n*-Butylborohydride in Toluene-*n*-Hexane at  $-78^{\circ}\text{C}$**

Entry	Enones	Reaction Time (hr)	Allylic Alcohol <sup>a</sup>	Saturated Alcohol	Isolated Yield (%)
1		2	100	0	98
2		2	100	0	99
3		2	100	0	98
4		4	100	0	98
5		3	100	0	99
6		2	100	0	96
7		2	100	0	98
8		2	92	8	84
9		3	65	35	75 <sup>b</sup>
10		3	80	20	96 <sup>b</sup>

Relative percentages of mixture components were determined by vpc (7 ft x 0.125 in. or 12 ft x 0.125 in. 10 % Carbowax 20M on 60/80 mesh Chromosorb W). Identification of reduction products was made by the usual spectral methods (nmr, ir, and vpc) and by comparison with authentic samples; <sup>b</sup>This yield was determined by vpc.

recommend lithium *n*-butylborohydride as an excellent reagent for the selective 1, 2 reduction of acyclic enones and conjugated cyclohexenones, which also can complement other hydride reagents.

The following is a typical experimental procedure. To a dry toluene solution (2 ml) of isophorone (140 mg, 1.0 mmol) under nitrogen atmosphere at  $-78^{\circ}\text{C}$  was added dropwise a slurry of lithium *n*-butylborohydride (4 ml of 0.25 M solution, 1.0 mmol) in toluene-*n*-hexane<sup>8</sup>. The resulting mixture was stirred at  $-78^{\circ}\text{C}$  for 4 hrs and then hydrolyzed with water. After most of the solvent was evaporated, tetrahydrofuran (10 ml) was added. The organoborane was oxidized with 10 % NaOH (3 ml) and 30 % H<sub>2</sub>O<sub>2</sub> (2 ml) by stirring overnight at room temperature. The aqueous layer was extracted with *n*-hexane and the combined organic phases were worked up in the usual manner to afford 139 mg (98 %) of the corresponding allylic alcohol, which was found to be identical with an authentic sample in all respects (nmr, ir, vpc and tlc).

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