A Convenient Procedure for the Synthesis of Secondary Alcohols From 1-Alkynes via the Alkylation of Boron-Stabilized Carbanions

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We recently found that treatment of 1,1-diborylalkanes with 2 equivalents of methylmagnesium bromide followed by reaction with excess ethyl bromide and oxidation with alkaline hydrogen peroxide gives the corresponding secondary alcohols. In the initial work, the 1,1-diborylalkanes were prepared from 1-alkynes by dihydroboration with borane (BH₃) or dicyclohexylborane. 

\[
\begin{align*}
R-\text{C}≡\text{CH} & \quad \xrightarrow{\text{BH}_3} \quad R-\text{C}≡\text{CH} \\
R-\text{CH}_2-\text{C}≡\text{C} & \quad \xrightarrow{\text{NaOH} / \text{H}_2\text{O}_2} \quad R-\text{CH}_2-\text{C}≡\text{C}
\end{align*}
\]

Unfortunately, the conversion of terminal acetylenes into alcohols by the above procedure suffers from several deficiencies. Thus, the dihydroboration products derived from 1-alkynes with borane afford the secondary alcohols in only modest isolated yields (~50%). Also utilization of dicyclohexylborane for the preparation of the germinal diboryl intermediates produces, besides the desired alcohols (~50%), 4 mol of cyclohexanol as a by-product. Finally, with both of these reagents 2 mol of methylmagnesium were required to obtain the above reported yields of alcohols.

In view of the great apparent utility of 1,1-diborylalkanes in organic synthesis, we thus undertook a study to uncover more convenient routes for their preparation. Both 9-borabicyclo[3.3.1]nonane (1) and 3,6-dimethylborepane (2) appeared to be particularly well suited as hydroboring agents for the above process since they are readily available via the hydroboration of the appropriate dienes and afford only 2 mol of high-boiling diols as side-products on oxidation.

Thus, 1-pentyne was dihydroboration at room temperature with 1 and 2. To each of the resultant 1,1-diborylpentanes (3) was added at 0-5° one equivalent of methylmagnesium in ether. The N.M.R. spectra of the reaction mixtures revealed the presence of CH₃ protons at δ = -0.7 (3.1 ± 0.2 H) and δ = -0.8 (3.1 ± 0.2 H), respectively.

The spectra also showed that there was no unreacted methylmagnesium in the reaction mixtures (CH₃Li: δ = -2.1). Addition of ethyl bromide (100%, excess) and heating the organoboranes for 2 hr at 60° resulted in large decreases (to ~15% of the original values) in the high-field CH₃.
Table. Synthesis of Alcohols from 1-Alkynes via Dihydroboration with 3,6-Dimethylborepane

<table>
<thead>
<tr>
<th>Alkyne</th>
<th>Halide</th>
<th>Product</th>
<th>Isolated Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Methyl-1-butyne</td>
<td>α-Butyl bromide</td>
<td>2-Methyl-4-octanol</td>
<td>69</td>
</tr>
<tr>
<td>4-Pentaeny</td>
<td>Isopropyl bromide</td>
<td>2-Methyl-3-heptanol</td>
<td>70</td>
</tr>
<tr>
<td>4-Pentaeny</td>
<td>Alkyl bromide</td>
<td>1-Octen-4-ol</td>
<td>84</td>
</tr>
<tr>
<td>3,3-Dimethyl-1-butyne</td>
<td>Benzyl chloride</td>
<td>4,4-Dimethyl-1-phenyl-2-pentanol</td>
<td>69</td>
</tr>
</tbody>
</table>

proton absorptions. Oxidation of the resultant secondary organoboranes 7 yielded 75%, and 72% of 3-heptanol, respectively.

The data obtained can be interpreted in terms of the mechanism given in Scheme A in which addition of methyl-lithium to 3 gives 4, which is the source of the high-field CH₃ protons. The N.M.R. data suggest that the "site" complexes 4 are only slightly dissociated into the boron-stabilized carbamions 5 and the corresponding methyboranes 6. This conclusion is based on the fact that the intermediates 6 can compete with 3 for methyl-lithium to give the dimethylboranes 8, which should also exhibit the typical high-field CH₃ protons, but would not react with ethyl bromide⁴.

Although boracyclopines 1 and 2 are equally well suited for the conversion of 1-alkynes into secondary alcohols, we report here in detail only the utilization of 3,6-dimethylborepane (2)⁵. The scope of the reaction for the preparation of various alcohols from 1-alkynes is shown in the Table. It should be noted here that this novel procedure using either 1 or 2 requires only one equivalent of methyl-lithium to achieve high yields of secondary alcohols. In several cases, however, utilization of a 20% excess of methyl-lithium afforded somewhat higher yields of alcohols.

It is apparent that boron-stabilized carbamions hold major promise as intermediates for a variety of organic syntheses⁶. In a forthcoming paper we shall report on their reactions with carbonyl compounds.

1-Octen-4-ol
To a solution of 1-pentane (1.7 g, 25 mmol) in tetrahydrofuran (10 ml) contained in a 250-ml flask equipped with a thermometer, a condenser, a septum-capped side arm, and flushed with nitrogen were added sequentially a solution of 3,6-dimethylborepane⁷ in tetrahydrofuran (32 ml of a 1.56 M solution, 50 mmol, 0°C, then 2 hr at 25°C), methyl-lithium in ether (18.3 ml of a 1.64 M solution, 30 mmol, –20°C, then allowed to warm up to 25°C), and allyl bromide (4.6 g, 38 mmol, 2 hr at reflux). The organoborane was oxidized by adding to the reaction mixture 3 N aqueous sodium hydroxide (18 ml) followed by the dropwise addition of 30%, hydrogen peroxide (16.5 ml, 30 min, 30°C). The mixture was saturated with potassium carbonate (K₂CO₃, 1.5 H₂O) and the upper layer formed was decanted. The aqueous phase was extracted twice with ether, the combined extracts were washed once with a saturated solution of sodium chloride, and dried with magnesium sulfate. Distillation in vacuo afforded 1-octen-4-ol; yield: 2.7 g (84%); b.p. 62/7 torr; nₒ²: 1.4365,

5. We have established that lithium methyl-tri-n-hexylborate does not react with ethyl bromide under these reaction conditions.

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