A Stereoselective Synthesis of Allylic Alcohols via the Reduction of z,β-Unsaturated Epoxides with Diborane

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In spite of the many methods for the synthesis of allylic alcohols described in the literature, recent reviews reflect a constant search for new stereoselective reactions leading to these compounds. We recently reported that cyclic z,β-unsaturated epoxides are transformed by diborane into allylic alcohols with excellent yields. The reaction is highly stereoselective involving borane attack on the double bond from the cis-direction with regard to the epoxide ring.

Here we wish to report the results of our study on the reaction of diborane with representative aliphatic z,β-unsaturated epoxides. Determination of the stoichiometry carried out in our laboratory

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\begin{align*}
\text{H}_3\text{C}-\text{CH}_2-\text{CH}==\text{CH}-\text{CH}_2-\text{OH} & \xrightarrow{\text{BH}_3/\text{THF}} \text{H}_3\text{C}-\text{CH}_2-\text{CH}==\text{CH}-\text{CH}_2-\text{O}-\text{B}^\text{H} \\
\text{H}_3\text{C}-\text{CH}_2-\text{CH}==\text{CH}-\text{CH}_2-\text{O}-\text{B}^\text{H} & \xrightarrow{\text{BH}_3/\text{THF}} \text{H}_3\text{C}-\text{CH}_2-\text{CH}==\text{CH}-\text{CH}_2-\text{O}-\text{B}^\text{H} \xrightarrow{1. \text{BH}_3} \text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}==\text{CH}_2 & \text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{O}^\text{H} + \text{H}_3\text{C}-(\text{CH}_2)_2-\text{CH}-\text{CH}_2-\text{OH} \\
\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}==\text{CH}_2 & \xrightarrow{2. \text{NaOH}/\text{H}_2\text{O}_2} \text{H}_3\text{C}-(\text{CH}_2)_2-\text{CH}_2-\text{OH} + \text{H}_3\text{C}-(\text{CH}_2)_2-\text{CH}-\text{CH}_2-\text{OH}
\end{align*}
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94% 6%

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### Table. Allylic Alcohols 6–10 from α,β-Unsaturated Epoxides 1–5 by Diborate Reduction

<table>
<thead>
<tr>
<th>Epoxide&lt;sup&gt;a&lt;/sup&gt; No. Structure</th>
<th>Allylic Alcohols&lt;sup&gt;b,c,d&lt;/sup&gt; No. Structure</th>
<th>Yield&lt;sup&gt;e&lt;/sup&gt; [%]</th>
<th>b.p. (Lit. b.p.)</th>
<th>η&lt;sub&gt;η&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt; (Lit. n&lt;sub&gt;η&lt;/sub&gt;)</th>
<th>Molecular formula&lt;sup&gt;f&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(Z)-6</td>
<td>66</td>
<td>137–138° (135–137°)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>1.4370 (1.4350)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>C₆H₁₂O₂</td>
</tr>
<tr>
<td>2</td>
<td>(Z)-7</td>
<td>40</td>
<td>120–121° (63–65°C/70 torr)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>1.4280 (1.4301)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>C₆H₁₂O₂</td>
</tr>
<tr>
<td>3</td>
<td>(Z)-8</td>
<td>64</td>
<td>136–137° (136–136.5°)&lt;sup&gt;20&lt;/sup&gt;</td>
<td>1.4410 (1.4427)&lt;sup&gt;20&lt;/sup&gt;</td>
<td>C₆H₁₂O₂</td>
</tr>
<tr>
<td>4</td>
<td>(Z)-9</td>
<td>43</td>
<td>139–140° (140–141°C)&lt;sup&gt;21&lt;/sup&gt;</td>
<td>1.4430 (1.4376)&lt;sup&gt;21&lt;/sup&gt;</td>
<td>C₆H₁₂O₂</td>
</tr>
<tr>
<td>5</td>
<td>(Z)-10</td>
<td>95%</td>
<td>138–139° (92%)</td>
<td>1.4330 (1.4376)&lt;sup&gt;21&lt;/sup&gt;</td>
<td>C₆H₁₂O₂</td>
</tr>
</tbody>
</table>

<sup>a</sup> Epoxides 1, 2, 3 were prepared according to the literature procedures<sup>7,8</sup>, 4 was obtained by the peracetic acid oxidation of (Z)-3-methyl-1,3-pentadiene<sup>6</sup>, 5 was prepared in the same way from a mixture of geometric isomers of 2,4-hexadiene obtained by dehydration of (E)-2-hexen-4-ol<sup>17</sup> with 48% aqueous hydrobromic acid.

<sup>b</sup> All products were identified by comparison (1H-NMR, G.L.C.) with authentic samples prepared as follows: (E)-7, by the Grignard reaction<sup>17</sup> of crotonaldehyde with CH₂MgCl; (Z)-7 and (Z)-10, by the catalytic hydrogenation of 3-pentyn-2-ol and 3-hexyn-2-ol, respectively; (Z)-6, (E)-6, (Z)-8, (E)-8, (Z)-9, (E)-9, (E)-10, by Al₂H₃ reduction of (Z)-2-pentenoic<sup>12</sup>, (E)-2-pentenoic<sup>12</sup>, (Z)-2-methylbutenoic<sup>14</sup>, (E)-2-methylbutenoic<sup>14</sup> acids. (Z)-3-methyl-2-penten-4-one, (E)-3-methyl-2-penten-4-one, and (E)-3-hexen-2-one, respectively. The ketones were obtained by the reaction of methyllithium with (Z)-2-methylbutenoic, (E)-2-methylbutenoic, and (E)-2-pentenoic acids, respectively.

<sup>c</sup> G.L.C. analyses were performed on a Chrom 4 (flame ionization) chromatograph (conditions: 10% diglycerol on Chromosorb P, 90°C).

<sup>d</sup> 1H-N.M.R. spectra were recorded on a Tesla instrument at 80 MHz, TMS as internal standard. The spectrum of (Z)-9 (CCl₄); δ = 1.15 (t, 3H, CH₃–C–O–), 6.25 (s, 1H, OH); 4.66 (4.15 ppm (1H, –CH–O–), J = 6Hz); 5.12 ppm (1H, –CH–C–). The spectra of (Z)-8<sup>15</sup>, (E)-7<sup>15</sup>, (Z)-8<sup>15</sup>, and (Z)-10<sup>16</sup> were in accord with the reported data.

<sup>e</sup> Yields of isolated products.

<sup>f</sup> All products gave satisfactory microanalyses (C ± 0.2, H ± 0.2); analyses performed in the Institute of Chemistry, Torun.

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Out with (E)-1-propenylxirane showed fast uptake of 2,4 hydride equivalents per mol of the epoxide. Oxidation of the organoborate intermediate gave a mixture of α- and β-epoxides in 70% yield. The ratio of pentanols suggests formation of 1-pentene and its hydrosilation.

The reaction could be stopped at the allylic boronate stage only if one hydride equivalent per mol of the epoxide was used. Thus, slow addition of borane to the epoxide in tetrahydrofuran at –10°C, followed by alkaline hydrolysis of the intermediate borate ester afforded (Z)-2-penten-1-ol. The results obtained for other epoxides are presented in the Table.

Allylic alcohols with (Z)-configuration of the double bond were obtained in all the cases. Their structures and purity were established by G.L.C. and N.M.R. analysis. The reaction shows high stereoselectivity which does not appear to depend upon the substitution pattern of the unsaturated epoxide intermediate. Its stereochemical course can be explained assuming coordination of borane to the epoxide oxygen atom followed by an intramolecular conjugate reduction.

The intramolecular hydride delivery can effectively operate when the epoxide molecule adopts a conformation having the double bond in a cis-position to the coordinated borane.

In view of the present results, the addition-elimination process proposed earlier<sup>6</sup> seems a less likely reaction mechanism. Formulation of an allylic alcohol in that way requires the addition of borane to the double bond with the boron atom being placed in the z-position to the epoxide ring, followed by a rearrangement of the organoborate to give an allylic borate ester. Consequently, the epoxides 2, 3, and 4 might be expected to give much lower yields of the corresponding allylic alcohols than the epoxides 1 and 5, due to the regiose-
lectivity of borane addition to the terminal double bonds. This was not observed. Moreover, the reaction of 3 with 9-borabicyclo[3.3.1]nonane, a highly regioselective hydroboration agent, gave (Z)-8 in 64% yield. These facts are not compatible with the addition-elimination process. Hence, the conjugate reduction is favoured. This mechanism accounts also for the results obtained in the cyclic series. The reaction described above offers some advantages over the existing procedures for the synthesis of allylic alcohols. It proceeds under mild conditions giving a product of high purity which can be easily isolated. Although the yields in the aliphatic series are only moderate, the procedure can be easily scaled up to molar quantities. Its high stereoselectivity allows a mixture of geometric isomers to be used as a starting material. Alcohols with trisubstituted double bonds which are not available by partial hydrogenation of acetylenes can be obtained in that way.

(Z)-2-Methyl-2-buten-1-ol (Z-8): Typical Procedure:
A solution of borane in tetrahydrofuran (20 mL, 0.033 mol) is added drop-wise to a stirred solution of 2-ethyl-2-methylpropane (3.84 g, 0.1 mol) in tetrahydrofuran (25 mL) at -10°C under nitrogen. The mixture is left for 5 h at room temperature. Water (1 mL) is added at 0°C followed by 3 molar aqueous sodium hydroxide solution (11 mL, 0.033 mol) and the mixture is stirred for 1 h at room temperature. Sodium chloride is added to saturate the mixture and the organic layer is separated. The aqueous layer is extracted with ether. The ether extracts are combined with the tetrahydrofuran solution and dried with magnesium sulphate. The product is isolated by distillation; yield: 5.5 g (64%); b.p. 136-137°C; ν100 1.4410.

1H-N.M.R. (CCl4): δ = 1.60 (d, 3H, CH3, J = 7.0 Hz); 1.72 (s, 3H, CH3); 4.00 (s, 2H, CH2); 4.17 (s, 1H, OH); 5.25 ppm (q, 1H, CH, J = 7.0 Hz).

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1 D. J. Faulkner, Synthesis 1971, 175.