Cyclization of Polyenes; VIII*.  
Asymmetric Cyclization of Optically Active Esters of Homogermanic Acid

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It is well known that cyclic terpenoids having several asymmetric centers are biosynthesized from the corresponding acyclic polyenes which have no asymmetric carbon. Cyclization of polyenes is considered to be caused, in vivo, by an enzyme affording optically active terpenoids, while optically inactive compounds are obtained by a biogenetic-type synthesis in the laboratory.

From the outset of our work on biogenetic-type syntheses of terpenoids, we were interested in the asymmetric cyclization of polyenes in order to obtain optically active terpenoids in a laboratory operation.

This paper describes the partial asymmetric cyclization of esters of homogermanic acid (4,8-dimethylnona-3,7-diene-oic acid). Homogermanic acid was esterified with optically active alcohols (see Table) and the esters (1) were treated with stannic chloride in anhydrous benzene solution to afford cis-tetrahydronoctilifilide (3)*, the natural form of which is reported to have +64.5° (CHCl₃). As shown in the table, the lactone thus obtained is partially optically active and is levorotatory in the three cases in which the original alcohols are levorotatory. Exclusive formation of the cis-lactone suggests that the cyclization proceeds via a nonconcerted mechanism and cation 2 could be an intermediate.

\[
\text{COOR} \rightarrow \begin{array}{c}
\text{1} \\
\text{2} \\
\text{3}
\end{array}
\]

**Homogermanic Acid l-Mentyl Ester:**
A solution of homogermanic acid chloride (1.37 g, 6.78 mmol), l-menthol (1.01 g, 6.50 mmol), and pyridine (0.1 ml) in anhydrous benzene (30 ml) was stirred for 5 hr at room temperature. The solvent was then evaporated, the residue extracted with ether.
the extract washed with aqueous sodium hydrogen carbonate and water, and dried with magnesium sulfate. Evaporation of the solvent afforded the crude ester, which was purified by chromatography on silica gel (benzene/isopropyl ether 4:1 used as an eluent); yield: 1.54 g (70%).

An analogous procedure was used to obtain the other esters listed in Table 1.

Cyclization of Homogenic Acid l-Methyl Ester:
To a solution of the l-methyl ester (700 mg) in anhydrous benzene (30 ml) was added tin(IV) chloride (3 ml) and the reaction mixture was stirred for 4 hr at room temperature. The mixture was then poured into ice water and extracted with ether. The ether solution was washed with aqueous sodium hydrogen carbonate and water, and was dried with calcium chloride and evaporated to give the crude lactone 3. The product was purified by chromatography on silica gel (using benzene/isopropyl ether 4:1 as an eluent) to give cis-transhydroactinidiolide; yield: 147 mg.

Purity of Lactone 3:
l-Menthol (1, 3, and 5%) was mixed with an authentic sample of the lactone obtained by catalytic reduction of dihydroactinidiolide. Each mixture was analyzed by G.L.C. (5% PDEGS) to give the G.L.C. references of l-menthol versus lactone. The purity of the lactone obtained by cyclization was analyzed using these references.

Table. Conversion of Homogenic Acid Esters (I) into cis-Tetrahydroactinidiolide (3)

<table>
<thead>
<tr>
<th>R</th>
<th>Purity of 3 (%)</th>
<th>$[\alpha]_{D}^{CHCl_3}$</th>
<th>Optical yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1,2,5,6-di-O-isopropylidene-x-d-glucosynase</td>
<td>100</td>
<td>$-13.4^\circ$ (c = 2.17)</td>
<td>20.8</td>
</tr>
<tr>
<td>l-menthol</td>
<td>99.0</td>
<td>$-7.5^\circ$ (c = 1.74)</td>
<td>11.6</td>
</tr>
<tr>
<td></td>
<td>99.6</td>
<td>$-7.9^\circ$ (c = 2.64)</td>
<td>12.3</td>
</tr>
<tr>
<td>l-isobornol</td>
<td>99.0</td>
<td>$-4.3^\circ$ (c = 1.88)</td>
<td>6.7</td>
</tr>
</tbody>
</table>

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