rather difficult to obtain suitable crystals of the β form for single crystal work and its space group has not yet been established. The solution of the structures will be pursued.


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Preliminary Note on the Configuration at C₂₂ of Solanum Alkaloids

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Tomatinidine and 5α-solasodanol-(3β) are generally believed to represent two types of Solanum alkaloids (aminoketal alkaloids) related to each other in the same manner as the "neo" and "iso" steroid sapogenins, i.e., they differ in configuration at C₂₂ by having an axial C₃₅-methyl group (structure II) and an equatorial C₃₅-methyl group (structure I), respectively.

Recently, Schreiber 1 and later Toldy 2 have suggested, however, that the two compounds differ in configuration at C₃₅. According to their formulation, tomatidine is a 22β-compound (structure III) and 5α-solasodanol-(3β) a 22α-compound (structure I). This difference in configuration at C₂₂ will cause the methyl groups at C₃₅ in both compounds to be equatorial.

The work submitted in this preliminary note supports the idea that tomatidine and 5α-solasodanol-(3β) in fact differ in configuration at C₂₂. It was found that tomatidine forms an N-bromo as well as an N-chloro derivative, whereas 5α-solasodanol-(3β) only forms an N-chloro derivative.

With the object of estimating the space requirements for binding a halogen atom to the nitrogen atom of ring F the hydrogen-halogen separation distances were measured on Dreiding molecular models. These measurements indicate that the distance between the N-halogen atom and two of the hydrogen atoms of the C₃₅-methyl group in structure I is 2.4 Å. In structure III the distance between the N-halogen and the hydrogen atom at C₃₅ is 2.6 Å.

Assigning a van der Waals radius of 1.0 Å to hydrogen and radii of chlorine and bromine of 1.8 Å and 1.95 Å, respectively, the distances H ↔ Cl and H ↔ Br can be estimated to 2.8 Å and 2.95 Å, respectively. Although the measured distances H ↔ Hlg in structure I and III only are 2.4 Å and 2.6 Å, respectively, one can easily see, remembering the experimental facts, that the difference in the measured distances is of an order of magnitude allowing the formation of an N-chloro derivative, but not the formation of an N-bromo derivative in the case of 5α-solasodanol-(3β). Furthermore, small distortions of the bond angles in rings E and F may increase the H ↔ Hlg separation distances to values estimated using the van der Waals radii. Such distortions of bond angles are quite common 3.

Table 1. Halogen derivatives of Solanum alkaloids.

<table>
<thead>
<tr>
<th>Derivative</th>
<th>Halogen content *</th>
<th>M. p., °C **</th>
<th>[α]D 24 (CHCl₃)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-Chlorosolasidine</td>
<td>7.92</td>
<td>153</td>
<td>−114°</td>
</tr>
<tr>
<td>N-Chloro-5α-solasadonol-(3β)</td>
<td>7.89</td>
<td>183</td>
<td>−59°</td>
</tr>
<tr>
<td>N-Chlorotomatidine</td>
<td>7.89</td>
<td>175</td>
<td>+ 35°</td>
</tr>
<tr>
<td>N-Bromotomatidine</td>
<td>16.17</td>
<td>208 ***</td>
<td>+ 51 ***</td>
</tr>
</tbody>
</table>

* The halogen content determined by iodometric titration.

** The m. p. reported are corrected. All four compounds melt under decomposition.

*** Toldy reports the m. p. 202–205°C and [α]D 20 −8.6 (dimethylformamide). However, N-bromotomatidine is quite unstable and decomposes to tomatidine hydrobromide ([α]D 24 −8.0 (CH₃OH)).

Fieser and Fieser have suggested that 22β-steroid sapogenins are destabilized by steric interference between the two hydrogens at C₂β and the hydrogens of the C₃β-methyl group, these being only 1.8 Å apart. However, similar model considerations by the present author on a 22β-steroid sapogenin and a 22β-aminoketal alkaloid indicate that the above mentioned hydrogens are in fact 2.0 Å apart. This last distance is a permissible hydrogen-hydrogen separation distance.

Further details of this work will be submitted shortly.


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