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ACETYL MIGRATION BETWEEN THE 28- AND THE 16-HYDROXYL GROUPS OF PRIMULAGENIN A.

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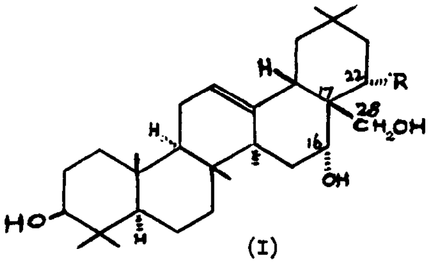
In an examination of methods for the preparation of partially acetylated derivatives of primulagenin A (I, R = H) (1) we observed an acetyl migration between the 28- and the 16α-OH groups. The migration was found to be reversible and to be catalysed by both acids and bases and by contact with chromatographic alumina. Recent publications on the rearrangement of the triacetate of theasapogenol D (2) [identical with dihydropriverogenin A and camelliagenin A (I, R = OH)] on alumina and of dihydropriverogenin A 16-acetate under acid conditions (3) prompt us to report our results in the simpler case of primulagenin A. In this case only the two oxygen functions at C_{16} and C_{28} are involved whereas in the other two examples the rearrangement sequence for the C_{16}, C_{22} and C_{28} functions is not obvious and in particular Tschesche *et al.* (3) discount the possibility of rearrangement between the *trans* di-axially oriented groups at C_{16} and C_{17}.



(I)

The acetyl migration was first observed when primulagenin A 3,28-diacetate[1] in benzene solution was allowed to stand in contact with basic alumina. The product isolated was the known 3,16-diacetate (4), while the expected (5) 3-monoacetate was not obtained in any quantity. When the reaction was performed in cold methanolic potassium carbonate a mixture of 3,16-* and 3,28-diacetates* together with 3-monoacetate was obtained. Treatment of either primulagenin A 3,16-diacetate or 3,28-diacetate with hydrogen chloride/chloroform gave the same mixture of 3,16- and 3,28-diacetates contaminated with the products* of acid catalysed rearrangement (6). In addition primulagenin A

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[1] The purity of all starting materials was carefully checked by t.l.c. The identity of products was usually determined by isolation and comparison with authentic material. Products marked with an asterisk were identified by t.l.c. comparison.

28-monoacetate on treatment with alumina [basic or neutral (Woelm)] was converted into a mixture of 16- and 28-monoacetates and primulagenin A. Similar results were obtained when the 28-monoacetate was treated with hydrogen chloride/chloroform or methanolic potassium carbonate.

Internal migration of the acetyl group from the oxygen at C_{28} to that at C_{16} by the usually accepted mechanism of acetyl migration (7) is obviously impossible with ring D in the chair form. However if ring D changes to a twist boat (from models it appears that ring E accommodates this without any substantial alteration and the stability of the twist boat should be enhanced as the attachment of the double bond to C_{13} of ring D removes some of the usual 1,4-interactions) the 16α-OH group becomes ψ-equatorial and the dihedral angle between C_{16}-O and C_{17}-CH_2O becomes <u>ca</u> 100°. Bridging to form the six-membered cyclic intermediate postulated for acyl migration requires a closer approach of these two units which, because of the <u>cis</u> D-E ring fusion, can be provided by conformational inversion of ring E.

Tschesche <u>et al</u>. (3) observed the conversion of dihydropriverogenin A 16-acetate, under acetonation conditions (sulphuric acid), into the 16,22-isopropylidene-28-acetate, as well as the expected isomer, and suggested that acetyl migration occurred from 16α- to 22α- and thence to 28-OH. A simpler possibility on our observations would be direct migration from 16α- to 28-OH.

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