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STRUCTURE OF SOLANOCAPSINE

Synthesis of 3β-acetoxy-22,26-acetylepimino-16α,23-epoxy-5α,22αH,25β H-cholestan-23β-ol

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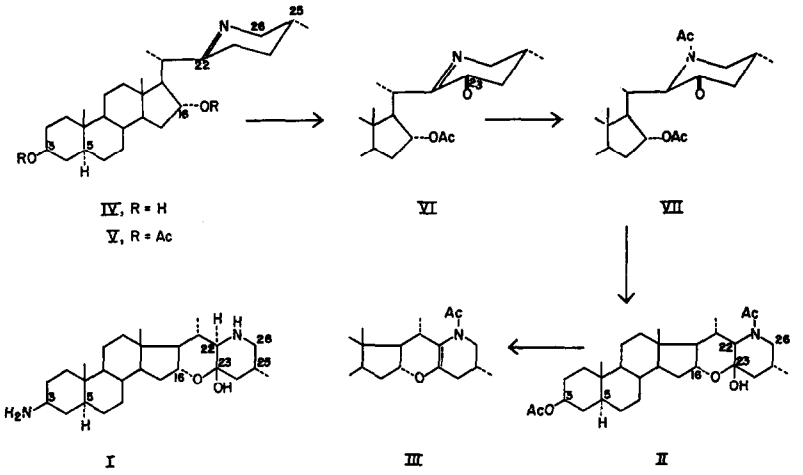
In a recent publication Ripperger and Schreiber[2] reported the synthesis of 3β-amino-22,26-epimino-16β,23-epoxy-5α,22αH,25βH-cholestan-23β-ol (16β-isomer of solanocapsine) and further submitted evidence (NMR, molecular rotation differences) in support of the presence of a 16α-epoxy linkage in place of the 16β in the molecular structure of solanocapsine (I). We have now been able to confirm the correctness of their observation by synthesizing the key solanocapsine derivatives II and III.

Starting from solafloridine[3] [IV, (25R)-22,26-epimino-5α-cholest-22(N)-ene-3β,16α-diol] a minor constituent of Solanum congestiflorum now available synthetically[4], the synthesis consists in the acetylation of IV-HCl to the 3,16-diacetyl derivative (V), $C_{31}H_{49}NO_4$, m.p. 173-175°, $[\alpha]_D$ - 56.6°, IR (CCl_4) 1740, 1734, 1240 (OAc), 1658 cm^{-1} (C=N-), oxidation of V to the 23-oxo compound, VI, $C_{31}H_{47}NO_5$, m.p. 196-198.5°, $[\alpha]_D$ - 27.5°, IR (CCl_4) 1740, 1736, 1247 (OAc), 1708 (C=O), 1631 cm^{-1} (C=N-) and reduction of VI followed by acetylation to the 22,26-acetylepimino compound, VII, $C_{33}H_{51}NO_6$, m.p. 194.5-196.5° $[\alpha]_D$ - 37.7°, IR (CCl_4) 1741, 1738, 1243 (OAc), 1724 (sh, C=O), 1661 cm^{-1} (NAc), NMR (δ,$CDCl_3$) 0.82 ($2CH_3$), 2.03 ($2CH_3CO$-O-), 2.15 (CH_3CON), MS 557 (Weak M^+, $C_{33}H_{51}NO_6$), 497, 454, 437, 394, 343, 283, 182, 155. Hemiketalization of VII with base and reacetylation afforded the 3-deamino-3β-acetoxy-N'-acetylsolanocapsine (II)(3β-acetoxy-22,26-acetylepimino-16α,23-epoxy-5α, 22αH,25βH-cholestan-23β-ol), m.p. 202-205° (lit. m.p. 174-176°[5]), IR ($CHCl_3$) 3570 (OH), 1726 (OAc), 1630 cm^{-1} (N-Ac), MS 515 (M^+,$C_{31}H_{49}O_5N$), 497 (M^+-H_2O). Compound II agreed in properties (m.p., mixture m.p., IR, TLC) with an authentic sample of II prepared from solanocapsine[5,6]. For confirmation II was further converted into the unsaturated product (III) by refluxing in glacial acetic acid. Its properties, m.p. 262-266°, $[\alpha]_D$ 10.4°, (lit. m.p. 245°, $[\alpha]_D^{19}$ 12.4°[2]) were also in agreement (m.p., mixture m.p., IR, TLC) with an authentic specimen[2,5]. Barring an unlikely isomerization (C-20

and/or C-22), the synthesis of II and III from solafloridine thus proves the correctness of the structure ascribed to solanocapsine (I).

For the acetylation of IV to V in the above synthesis, an acetylating mixture consisting of acetic anhydride, acetic acid and zinc chloride was utilized. It avoided the formation of the undesirable Δ^{22}-NAc compound[3]. Manganese dioxide[3] in



chloroform proved to be the reagent of choice for the oxidation of V to VI (77% yield). The reduction of the C=N bond in VI was effected with zinc and acetic acid. While the carbonyl moiety remained intact during the reduction, some aromatization of the side chain occurred and the product after acetylation was contaminated with slight amounts of 3β,16α-diacetoxy-20-[2-(5-methylpyridyl)]-5α-pregnane[3,7]. An alcoholic KOH base containing water was used in the hemiketalization of VII.

Finally an identical sequence of reactions was also applied to 5,6-dihydropseudosolasodine B diacetate[8], the 16β-isomer of V, for conversion into the 16β-isomers of II and III. The properties of the compounds obtained thereby were essentially in agreement with those as reported by Ripperger and Schreiber[2] in their conversion procedure.

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