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REGIOSELECTIVE OPENING OF RING E IN SPIROSTAN SAPOGENINS [1]

A G González, C G Francisco, R Freire, R Hernández,
J A Salazar and E Suárez

Department of Organic and Biochemistry, University of La Laguna,
Instituto de Química de Productos Naturales, C S I C, Tenerife, Spain

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The acid-catalyzed reaction of spirostan sapogenins (1) with Ac_2O, affording furostene derivatives (2) ("pseudo-sapogenins") is well-known [2], because of the usefulness of 2 in the synthesis of steroid hormones [3]. A number of acids have been used and, in all cases, the opening of ring F is recorded [4].

In the course of our research, we treated 25R-5α-spirostan (1) with Ac_2O containing BF_3 (200 mg of 1 in 100 ml Ac_2O and 0.01 ml BF_3) at room temperature for 1 hour and, surprisingly, got 3 in high yield (90%), together with a small quantity of 4. This anomalous opening of the spiro-ketal side chain has not previously been reported.

Compound 3, $C_{31}H_{48}O_4$, M^+ 484, $[\alpha]_D$ + 16 °, $\nu_{max}^{CHCl_3}$ 1720, 1690, 1660, 1570 cm^{-1}, λ_{max}^{EtOH} 276 nm, NMR signals at δ 5.15 (1H, m, H-C_{16}), 4.0 (2H, m, $W_{1/2}$ = 25 Hz, H-C_{26} and H-C_{20}), 3.46 (1H, m, $W_{1/2}$ = 22 Hz, H-C_{26}), 2.20 (3H, s, COMe), 1.84 (3H, s, C_{16}-OAc), 1.17 (3H, d, J = 7 Hz, Me-C_{20}), 0.97 (3H, d, J = 7 Hz, Me-C_{25}), 0.90 (3H, s, Me-C_{13}) and 0.80 (3H, s, Me-C_{10}).

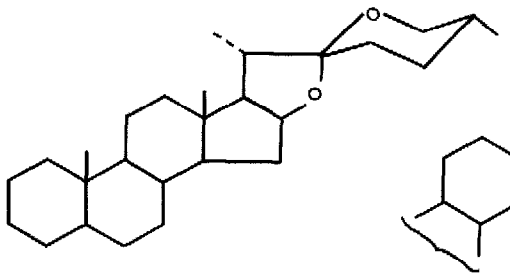
Zderic *et al* [5] and Uhle [6] performed the above reaction under similar conditions and they obtained a compound (15-45%) with the physical and spectroscopical properties of 3, for which they proposed structure 5. This structure

does not agree with our NMR spectrum, where the expected doublet for the H_2-C_{26} is missing, contrary to what occurs in the case of the "pseudo-sapogenins"; instead, there are two complex multiplets indicative of two magnetically non-equivalent protons such as are present in andesgenin [7].

Moreover, several chemical proofs support our structure: treatment of 3 with KOH/MeOH (3%) at reflux for 3 hrs gave the 23-acetyl derivative 6, mp 218-219° (MeOH). Ozonization of 3 and cleavage of the ozonide with Jones' reagent yielded a dinor-acid acetate which was characterized by its methyl ester 7, $C_{30}H_{48}O_6$, M^+ 504, mp 106-108 ° (MeOH), $[\alpha]_D$ +50 °, NMR signals at δ 3.85 (2H, m, $W_{1/2}$ = 10 Hz, H_2-C_{26}), 3.68 (3H, s, COOMe) and 1.93 (3H, s, C_{16}-OAc). Its MS fragments are in accordance with the structure proposed. The presence of an acetate group at C_{16} and the C_8 side chain in this compound rules out structure 5. Saponification of 7 with $NaHCO_3$/MeOH at reflux for 2 hrs yielded the already-known lactone 8 [8].

The NMR spectrum of 4 [$C_{31}H_{50}O_5$, M^+ 502, mp 158-161 ° (MeOH), $[\alpha]_D$ + 56 °] shows signals at δ 1.92 (3H, s, C_{16}-OAc), 2.02 (3H, s, C_{26}-OAc), 3.89 (2H, d, J = 5 Hz, H_2-C_{26}) and 4.95 (1H, m, $W_{1/2}$ = 28 Hz). On saponification with KOH/MeOH (10%), compound 4 rendered the starting material 25R-5α-spirostan 1.

In addition to the catalytic action of BF_3, that of BCl_3 and BBr_3 on the acetolysis of 1 was also studied. Treatment with BCl_3 in Ac_2O at reflux for 1 hour resulted in a mixture of 2 and 3, whereas with BBr_3, the "pseudo-sapogenin" 2 was the only product obtained. The difference in the behaviour of the Lewis acids can be explained by the fact that tetrahydrofuranic oxygen is at the same time more basic and sterically more hindered than tetrahydropyranic oxygen [9]. So, in the case of the smallest boron halide, BF_3 interacts with the tetrahydrofuranic oxygen, while in that of the bulky BBr_3, the steric factor governs the reaction.



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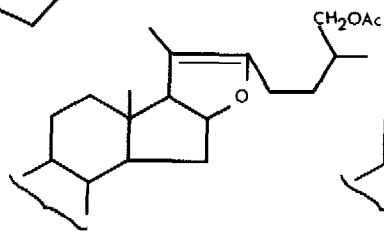

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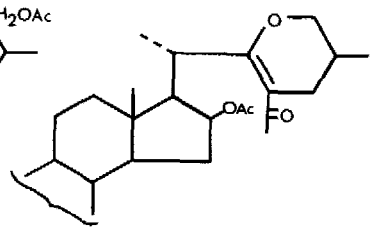

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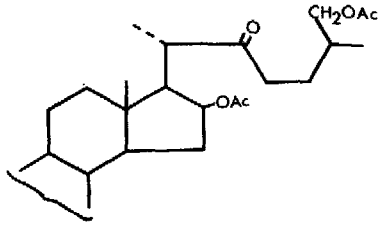

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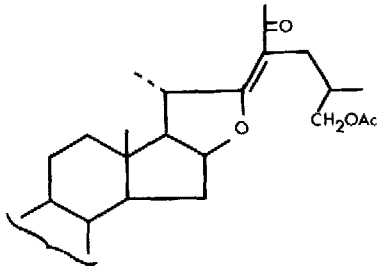

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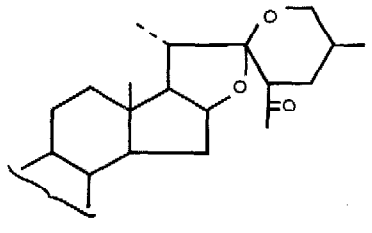

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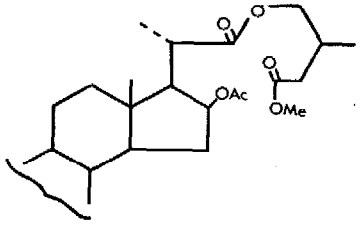

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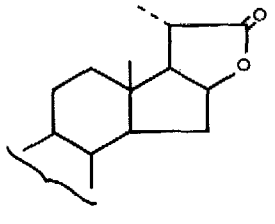

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All new compounds gave correct elemental analyses. Optical activities were measured in $CHCl_3$ and NMR spectra in $CDCl_3$ (60 MHz).

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