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5α-CHOLESTA-9(11),17(20),24-TRIENE-3β,6α-DIOL, A MINOR GENIN FROM THE STAR FISH <u>ACANTHASTER PLANCI</u>

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Recently[1] we reported the isolation of the two novel steroids 5α-pregn-9(11)-ene-3β,6α-diol-20-one (XI) and 5α-cholesta-9(11),20(22)-diene-3β,6α-diol-23-one (XVII) from the starfish <u>A. planci</u>. We now describe the isolation from the same source and structure determination of two additional minor genins: 5α-cholesta-9(11),17(20),24-triene-3β,6α-diol (I) and 24ξ-methyl-5α-cholesta-9(11),20(22)-diene-3β,6α-diol[2] (XV). These genins are of interest because of their unusual structures and probable role in the biosynthesis of the 23-oxygenated marine steroids XVII and XVIII.[3] The presence of 17(20) and 20(22) double bonds in genins I and XV suggests their likely origin from the corresponding 20α-hydroxy steroids possibly during acid hydrolysis of the saponin.

The nmr spectrum ($CDCl_3$) of genin I [mp 138-140° (needles from aqueous methanol), $[\alpha]_D^{21}$ ($CHCl_3$) 43.2±3°, M^+ 398.31665 calculated for $C_{27}H_{42}O_2$ 398.31840, λ_{max} (KBr) 3425 cm^{-1} (OH)] depicted two quaternary methyl [C-18 CH_3, 0.72(s, 3H), C-19 CH_3, 0.90(s, 3H)], three olefinic methyl [C-21,26,27 CH_3, 1.56, 1.62 (s, 9H)], two carbinol methine [3.50 (c, 2H) shifted to 4.60-5.0 (c, 2H) in the diacetate II] and two olefinic methine [C-24 H, 5.04 (c, 1 H), C-11 H, 5.30 (c, 1 H)] protons. Its mass spectrum displayed significant peaks at <u>m/e</u> 329.245117 [$C_{22}H_{33}O_2$, $M^+-(CH_3)_2C{=}CH{-}CH_2$], 311.23706 [$C_{22}H_{31}O$, 329-$H_2O$], 293.226807 [$C_{22}H_{29}$, 311-$H_2O$], 211.14866 [$C_{16}H_{19}$, ring D Cleavage + 2 x H_2O, therefore one double bond in rings A,B or C], 111.0800 [$C_7H_{11}O$, one hydroxyl in ring A], 95.086736 [C_7H_{11}] and 69.070206 [C_5H_9].

Hydrogenation of a mixture of the oily diacetates II and XVI furnished a mixture which by glc analysis and comparison with authentic reference compounds appeared to consist of III,IIIa,

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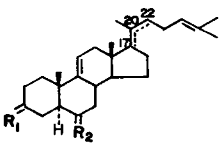
XIX and XIXa. Since the small quantity of material precluded further chemical work and the presence of the nuclear bond was assumed only by analogy, the structure of I was established by synthesis from 5α-pregn-9(11)-ene-3β,6α-diol-20-one diacetate (XII).

Hydrobromic acid treatment of 1,1-dimethyl cyclopropyl carbinol[4] (IV) led to 1-bromo-4-methyl-3-pentene (VI) (b.p. 155-156°, M$^+$ 162,164) which on subsequent conversion to the Grignard complex and reaction with XII[5] furnished the crystalline triol IX [mp. 153-154°, $[\alpha]_D^{21}$ (CHCl$_3$) 21.5±5°, mp. 115-117° (needles; slow crystallization from hexane-ethyl acetate after optical rotation) λ_{max} (KBr) 3380 cm^{-1}, nmr (CDCl$_3$) C-18 CH$_3$ (0.77, s, 3H each), C-19 CH$_3$ (0.95, s, 3H), C-21 CH$_3$ (1.28, s, 3H), C-26,27 CH$_3$ (1.60, 1.66, s, 3H each), two carbinol methine [3.57, c, 2H shifted to 4.50-5.10 (c, 2H) in the 20α-hydroxy diacetate X] and two olefinic protons (C-24 H, 5.10 and C-11 H, 5.30), m.s. 398 (M$^+$-H$_2$O), 347 (M$^+$-C$_5$H$_9$), 315 (398-C$_6$H$_{11}$), 287 (M$^+$-side chain + 2H),[6] 109 (C$_8$H$_{13}$), 95 (C$_7$H$_{11}$), 82 (C$_6$H$_{10}$), and 69 (C$_5$H$_9$)]. Acetylation of IX to the diacetate X followed by dehydration (POCl$_3$/Py) of the tertiary hydroxyl function gave II [glc, ir, nmr, ms identical to that of the natural genin diacetate] and IIa (M$^+$ 482). Saponification of the dehydration mixture followed by separation via preparative glc furnished I [mp. 141-2°, $[\alpha]_D^{21}$ (CHCl$_3$) 40.0±5°, glc, nmr, ir, and ms identical to that of the natural genin I] and Ia [M$^+$ 398].

Genin XV was isolated as the oily diacetate XVI [>90% by glc., M$^+$ 498, nmr (CDCl$_3$:d$_6$ benzene) C-18 CH$_3$ (0.49:0.56, s), C-19 CH$_3$ (1.01:0.80, s), C-26,27,28 CH$_3$ (0.85:0.85, c), olefinic methyl (1.63, broad singlet, therefore $\Delta^{17(20)}$ or $\Delta^{20(22)}$) two acetates (2.03:1.69, 1.71, s), acetate methines (4.50-5.0, c), olefinic protons (5.0-5.36:5.21, c). The relatively higher chemical shift[7] for the C-18 CH$_3$ as compared to that for $\Delta^{17(20)}$ unsaturated model steroids (C-18 CH$_3$ 0.90, ring C saturated) strongly suggested the presence of a $\Delta^{20(22)}$ double bond. The mass spectrum of XVI showed the loss of two moles of acetic acid (*m/e* 438, 378) and significant peaks at *m/e* 363 (378-CH$_3$), 353 (438-C$_6$H$_{13}$), 315, 311 (438-side chain + 2H,[6] therefore C$_9$ unsaturated side chain), 307 (378-C$_5$H$_{11}$), 285 (M$^+$-CH$_3$COOH+C$_{11}$H$_{21}$), 251 (311-CH$_3$COOH), 211 (ring D cleavage + 2 x CH$_3$COOH, therefore one double bond in rings A,B or C), 131, 109, 95, 81 (100%), 71, 55 and 43.

Genin XV (stereochemistry at C$_{24}$ undefined) was synthesized by reaction of 1,1,2-trimethyl cyclopropyl carbinol[8] (V) with HBr to furnish 1-bromo-3,4-dimethyl-3-pentene (VII) which on subsequent hydrogenation (Pt/AcOH) furnished (VIII). Addition of its Grignard complex to XII

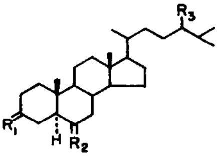


I R_1 = OH H R_2 = OH H 17-20 double bond

II R_1 = OAc H R_2 = OAc H 17-20 double bond

Ia R_1 = OH H R_2 = OH H 20-22 double bond

IIa R_1 = OAc H R_2 = OAc H 20-22 double bond

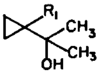


III R_1 = OAc H R_2 = OAc H R_3 = H

IIIa R_1 = OAc H R_2 = OAc H R_3 = H **17,20-iso**

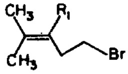
XIX R_1 = OAc H R_2 = OAc H R_3 = CH_3

XIXa R_1 = OAc H R_2 = OAc H R_3 = CH_3 20-iso



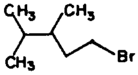
IV R_1 = H

V R_1 = CH_3

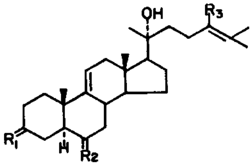


VI R_1 = H

VII R_1 = CH_3



VIII

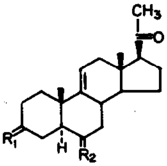


IX R_1 = OH H R_2 = OH H R_3 = H

X R_1 = OAc H R_2 = OAc H R_3 = H

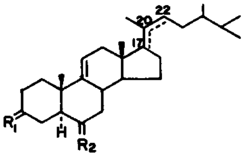
XIII R_1 = OH H R_2 = OH H R_3 = CH_3 24-25 dihydro

XIV R_1 = OAc H R_2 = OAc H R_3 = CH_3 24-25 dihydro



XI R_1 = OH H R_2 = OH H

XII R_1 = OAc H R_2 = OAc H

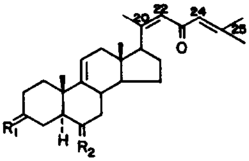


XV R_1 = OH H R_2 = OH H 20-22 double bond

XVI R_1 = OAc H R_2 = OAc H 20-22 double bond

XVa R_1 = OH H R_2 = OH H 17-20 double bond

XVIa R_1 = OAc H R_2 = OAc H 17-20 double bond



XVII R_1 = OH H R_2 = OH H 24-25 dihydro

XVIII R_1 = OH H R_2 = OH H 20-22 dihydro gave XIII which on acetylation and glc purification provided the oily diacetate XIV [nmr ($CDCl_3$) C-18 CH_3 (0.76, s 3H mounted over complex signal due to C-26,27,28 CH_3, 9H), C-19 CH_3 (1.00, s, 3H), C-21 CH_3 (1.26, s, 3H CH_3-C-O), acetates (2.0, s, 6H), acetate methines (4.50-5.0, c, 2H), olefinic hydrogen (C-11 H, 5.36, 1H), m.s. m/e 498 (M^+-H_2O), 438 (498-CH_3COOH), 417 (M^+-C_7H_{15}), 378 (438-CH_3COOH), 363 (378-CH_3), 354 (438-C_6H_{12}), 297 (417-2 x CH_3COOH), 279 (297-H_2O), 254 (314-CH_3COOH), 211 (ring D cleavage + 2 x CH_3COOH)] which on subsequent dehydration led to two products, XVI (M^+ 498) and XVIa (M^+ 498). The former depicted identical glc retention times[2] and m.s. to that of the natural genin diacetate XVI.

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2. Due to very small amounts of both synthetic and natural material only glc retention times using OV 1, OV 17 and OV 25 columns and mass spectral comparison could be made. A total of 4.5 mg of I and 1.5 mg of genin diacetate XVI were isolated from 3 kg of starfish.

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