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GORGOST-5-ENE-3β,7α,11α,12β-TETRAOL 12-MONOACETATE, A NEW MARINE STEROL FROM THE GORGONIAN *ISIS HIPPURIS*[1]

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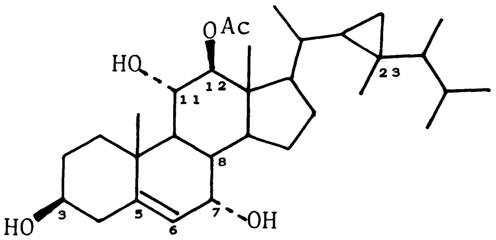
The title compound (1) has been isolated from the gorgonian *Isis hippuris*, and its structure was elucidated by spectral analysis. It is one of the most highly oxygenated marine sterols retaining the C5-C6 unsaturation.

In previous papers[2] we reported several polyoxygenated steroids which we called hippuristanols isolated from the gorgonian coral *Isis hippuris*. They all contained a common skeleton, 24-methyl-22,25-epoxy-5α-furostane, with additional oxygen functions at the 3α, 11β, and 20β positions. We now wish to report that the same animal also contains a new polyoxygenated gorgosterol, gorgost-5-ene-3β,7α,11α,12β-tetraol 12-monoacetate (1), in which the oxygenation pattern is different from those of hippuristanols. Sterol 1 is one of the most highly oxygenated marine sterols retaining the C5-C6 double bond. Although a number of polyoxygenated steroids are known from marine sources,[3] many of them have polyoxygenated structures by being oxygenated at the C5 and/or C6 positions. Gorgosterol (2)[4] was also isolated as a major steroidal constituent of the coral.

The hexane-soluble portion of the 95% ethanol extract of *I. hippuris* collected in Okinawa was chromatographed on silica gel using a hexane-ethyl acetate gradient. A fraction eluted with ethyl acetate was subjected to two more separations on TLC (silica gel, ethyl acetate) to furnish 1, mp 197-200°, in 0.001% yield.

Mass spectrometry indicated no molecular ions but the highest mass peak at m/z 456 (M$^+$-AcOH) and peaks resulted by consecutive loss of water at m/z 438 (found



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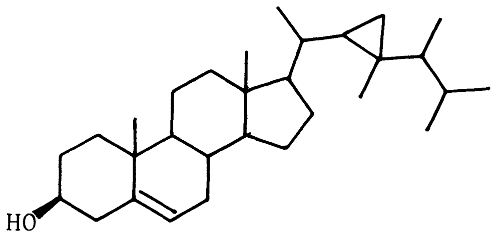

2

438.3486, calcd. for $C_{30}H_{46}O_2$ 438.3496) and 420 (found 420.3431, calcd. for $C_{30}H_{44}O$ 420.3392). The molecular formula $C_{32}H_{52}O_5$ deduced from these mass measurements was confirmed by elemental analysis. The infrared spectrum (KBr, 3430, 2950, 2920, 1715, 1460, 1375, 1255, and 1035 cm^{-1}) revealed features of polyhydroxylated steroids containing an ester function. The presence of an acetoxy group was shown by ^{1}H (δ2.11s, 3H) and ^{13}C NMR spectra (173.3s, 21.5q). The latter spectrum also indicated the presence of a trisubstituted double bond (140.0s and 123.4d) and four methine carbons bearing an oxygen atom (85.0d, 72.8d, 71.2d, 65.1d). Thus, three of the five oxygen atoms must be bound as hydroxyl groups.

The ^{1}H NMR spectrum (360 MHz, $CDCl_3/CD_3OD$) contained signals at δ-0.09 (t, 1H, J=4.8 Hz), 0.21 (m, 2H), 0.44 (dd, 1H, J=4.8, 9.1 Hz), 0.82 (s, 3H, C18-H), 0.86 (d, 3H, J=6.5 Hz), 0.91 (s, 3H,C23-Me), 0.92 (d, 3H, J=8.0 Hz), 0.94 (d, 6H, J=7.0 Hz), 1.12 (s, 3H, C19-H), 1.42 (td, 1H, J=11.7, 3.3 Hz, C8-H), 2.11 (s, 3H, OAc), 2.26 (t, 1H, J=12.5 Hz, C4β-H), 2.32 (dd, 1H, J= 13.5, 5.3 Hz, C4α-H), 2.52 (dt, 1H, J=14.0, 3.3 Hz, C1β-H), 3.43 (m, 1H, Wh/2=22 Hz, C3α-H), 3.79 (t, 1H, J=10.0 Hz, C11β-H), 3.87 (t, 1H, J=3.5 Hz, C7β-H), 4.71 (d, 1H, J=9.2 Hz, C12α-H), and 5.59 (d, 1H, J=5.2 Hz, C6-H). The characteristic high field signals due to a cyclopropyl moiety were virtually identical with those of gorgosterol (2). The methyl signals, four singlets and three doublets (12H), were also consistent with a gorgosterol skeleton containing an acetoxy function. Irradiation of the olefinic proton at δ5.59 collapsed the triplet at δ3.87 to a doublet, indicating the presence of a hydroxyl group at an allylic position. Conversely, irradiation of the latter signal changed not only the olefinic doublet to a singlet, but also a triplet of doublets (δ1.42) to a triplet (J=11.7 Hz) which could be assigned to the axial proton at the C8, thus establishing the positions of the double bond and C7α-OH as indicated in 1. The triplet at δ3.79, which must be an axial proton, was transformed to a doublet by irradiation of the doublet at δ4.71 which in turn was changed to a singlet by the irradiation of the former. This suggested the vicinal relation of the acetoxy and a hydroxyl group which were best accommodated as C11α-OH and C12β-OAc. The remaining hydroxyl group was placed at the usual C3β position, accounting for the seven-lines multiplet at δ3.43 which was nearly identical with that of 2.

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