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CHEMICAL STUDIES OF MARINE INVERTEBRATES XXXII (1). ISODYSIDENIN, A FURTHER HEXACHLORINATED METABOLITE FROM THE SPONGE *DYSIDEA HERBACEA* (2).

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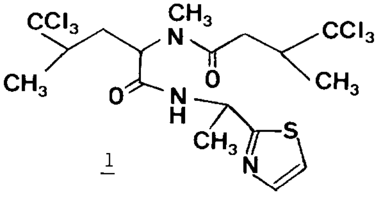
The isolation and structure determination of dysidenin (1), an hexachlorinated metabolite from the sponge *Dysidea herbacea* Keller, collected on the Great Barrier Reef, were recently described by KAZLAUSKAS et al.(5). No data are available concerning the relative and absolute configuration of this remarkable molecule, which constituted the major metabolite of the sponge

In contrast, specimens of the same species collected at Laing Island (North Coast of New Guinea) consistently yielded, besides small amounts of dysidenin (m.p.,[α], IR, UV, ^{1}H NMR, MS identical with published data (5)) much larger amounts (more than 2% dry weight) of a novel, toxic (6) stereoisomer for which the name isodysidenin was coined.

Isodysidenin (amorphous, $C_{17}H_{23}Cl_6N_3O_2S$ by high resolution mass spectrometry, $[\alpha]_D^{22}$ +47° (c=0.88,$CHCl_3$)) exhibits spectral properties (UV(CH_3OH):238 nm(3.52); IR(film):3320,1688,1630 and 1530 cm^{-1}; MS:identical to that of dysidenin(5); NMR(270 MHz,$CDCl_3$/TMS,δ(ppm),J in Hz) : 1.36(d,J=6,H_3C-1),1.39(d,J=6.5,H_3C-8),1.49(m,H_aC-6),1.65(d,J=7,H_3C-14),2.51(dd,J=16 and 9.5, H_bC-3),2.68(m,HC-7),2.94(m,H_bC-6),2.98(s,H_3C-10),3.08(dd,J=16 and 2,H_aC-3),3.30(m,HC-2),5.34 (dd,J=4.5 and 9,HC-5),5.43(dq,J=8 and 7,HC-13),6.97(bd,J=8,NH),7.31(d,J=3.5,HC-17),7.70(d,J= 3.5,HC-16)) which are very similar to those of dysidenin. Treatment of isodysidenin with diborane-THF complex (7),followed by iodomethylation (CH_3I/CH_3CN) of the resulting tertiary amine afforded a crystalline derivative (2, m.p. 220° dec.) that was submitted to X-ray diffraction analysis. Compound 2 crystallises in the space group P $2_12_12_1$ with a = 19.49, b = 13.52, c = 10.39 Å, Z = 4. The absolute configuration of the molecule was established from the measurement of several Friedel pairs and is that depicted in formula 2.



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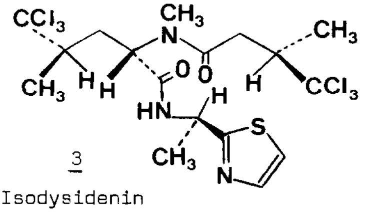
Dysidenin



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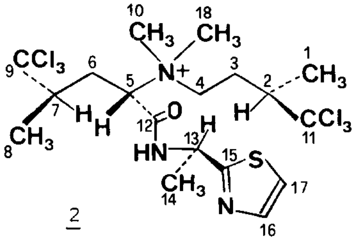
Isodysidenin

Since compound 2 arises from isodysidenin by a selective reduction of the tertiary amide function, the structure and absolute configuration of isodysidenin are necessarily as depicted in 3, the asymmetric carbon atoms C-2, C-5, C-7 and C-13 being R,S,R and R respectively.

In the NMR spectrum of dysidenin, KAZLAUSKAS et al.(5) did attribute the signal at 2.5 ppm to the two C-3 protons and the signals at 1.94 and 3.10 ppm to the two protons at C-6. Extensive decoupling experiments at 270 MHz on dysidenin and isodysidenin forced us to modify these assignments. In fact, the protons at C-3 appear in the NMR spectrum of 1 respectively at 2.51 (dd,J=16.5 and 8.5,1H) and 3.15 ppm (dd,J=16.5 and 3,1H) while the protons at C-6 appear at 1.94 (m,1H) and 2.64 ppm (ddd,J=15,11 and 2,1H). Furthermore it can be seen that in the NMR spectra of 1 and 3, all the corresponding protons have practically identical chemical shifts except for the protons at C-5, C-6 and C-7. This strongly suggests that dysidenin is the C-5 epimer of isodysidenin.

Dysidea herbacea is known to live in symbiosis with the blue-green alga *Phormidium spongeliae* (Cyanophyceae)(8). In addition, like many marine sponges, it is probably associated with bacteria. At this time it is not known which of the symbionts is responsible for the synthesis of these unusual hexachloroderivatives.



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