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A NEW SESQUITERPENE FROM THE SPONGE DYSIDEA HERBACEA

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Three previous reports on metabolites of the sponge Dysidea herbacea have been published[1-3]. A collection from the Caroline Islands in the Pacific yielded brominated diphenyl ethers[1] and some Barrier Reef collections have also produced this class of compound[4]. Other Barrier Reef collections have given chlorinated metabolites derived from amino-acid precursors.

A new collection of D. herbacea from the Gladstone area of Queensland was freeze-dried and extracted with dichloromethane to yield a 2.5% extract which contained two major compounds. Chromatography on silica gel gave a new sesquiterpene acetate, spirodysin (1), and the diketopiperazine (2)[5] in dry weight yields of 0.3% and 1.2% respectively. We now report evidence for the structural assignment of (1) for spirodysin.

Spirodysin (1) was isolated as an unstable colourless oil $[\alpha]_D^{20}$ +24° (c = 1, $CHCl_3$) and the formula $C_{17}H_{24}O_3$ was established by high resolution EI mass spectrometry (12eV). The ^{13}C n.m.r. spectrum of (1) in $CDCl_3$ showed all 17 carbon atoms as follows:- 169.8(s), 142.5(d), 132.9(s), 125.0(d), 107.1(d), 99.3(d), 63.0(s), 46.9(s), 44.6(d), 36.0(t), 35.3(d), 28.6(t), 23.8, 23.0, 21.8, 21.3, 21.0. The signal at 169.8 suggested an ester carbonyl and the presence of an acetate was established by the ^1H n.m.r. spectrum (δ1.98, 3H, s) and the loss of AcOH from the molecular ion in the 70 eV EI m.s. of (1) to give the first observable ion at m/e 216 ($C_{15}H_{20}O$). Other downfield signals of the ^{13}C n.m.r. indicated the presence of one disubstituted and one trisubstituted double bond, together with a methine carbon bearing two oxygen atoms. The presence of an acetate demanded the structural unit -O-CH-OAc and, because (1) must be tricyclic, the nonacetate oxygen must be part of a cyclic ether.

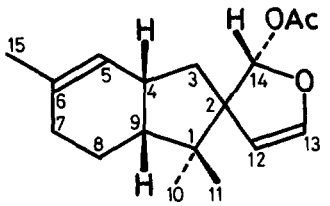
The ^1H n.m.r. of (1) in CCl_4 showed resonances at δ6.25 (1H, s); 6.12 (1H, d, J 2.5Hz), 5.20 (1H, bs), 4.70 (1H, d, J 2.5Hz), 1.98 (3H, s), 1.58 (3H, bs), 0.89 (3H, s) and 0.80 (3H, s). The chemical shifts of the proton doublets at δ6.12 and 4.70 and the carbon doublets at δ142.5 and 107.1 were very similar to those reported for 2,3-dihydrofurans[6,7] and the presence of a -O-CH-OAc unit in the molecule suggested the partial structure (3) with remaining structural features, including two quaternary methyl groups and a -C(Me)=CH-CH- grouping. Several regular isoprenoid structures incorporating these features could be written.

Treatment of (1) with BF_3-etherate in benzene gave a 1:1 mixture of (4) and (5), two sesquiterpenes recently isolated from a Dysidea species collected near Sydney, Australia[8]. Also pyrolysis of (1) gave a mixture in which (4) and (5) were dominant. The gross structure of spirodysin as (1) was therefore established in which the AB ring junction must be cis.

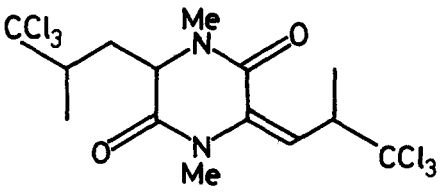
The stereochemistry about the spiro-ring junction and the acetoxy-group was inferred from ^{13}C and ^1H n.m.r. studies with various lanthanide shift and broadening reagents. The unexceptional positions of the two quaternary methyl groups in the ^1H n.m.r. spectrum of (1) suggested that the acetoxyl group exerted no effect and was therefore anti to these two groups. This was

supported by a $Eu(fod)_3$ shifted ^1H n.m.r. spectrum which showed relative shift rates C3-H_A > C3-H_B ~ C4-H > C1-Me. The stereochemistry of the acetoxyl-group was further supported by $Pr(fod)_3$ shifted ^{13}C n.m.r. spectra of (1) which showed that the relative shift rate of C3 was very much greater than that of both C1-methyls, and a 20% NOE between C14-H and a C1-Me in the ^1H n.m.r. of (1) confirmed this stereochemical assignment. However stereochemical assignment about the spiro ring junction was not possible.

Spirodysin (1), a regular isoprenoid sesquiterpene, is an attractive precursor for the formation of both furodysin (4) or the rearranged sesquiterpene furodysinin (5). D. herbacea has yielded many halogenated metabolites[1-5] and (1) is the first terpene to be characterised from a collection of D. herbacea. The co-occurrence of (1) and (2) in this collection suggests that each metabolite is derived from a different biological source and the presence of significant amounts of blue-green algae in the sponge matrix[5] would indicate that (2) is a metabolite of the symbiotic algae, whilst (1) is a metabolite of the sponge.



(1)



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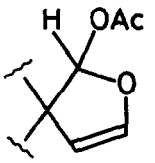

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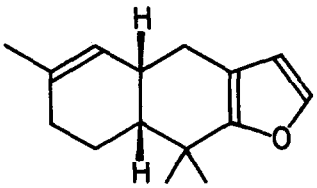

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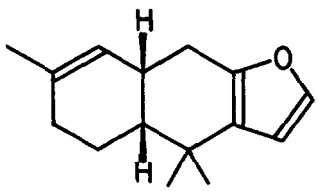

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