## NEW DITERPENES FROM SPONGIA OFFICINALIS

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<u>Abstract</u> - Four new dilerpenes has been isolated from <u>Spongia</u> <u>officinalis</u> and their structures determined on the basis of spectral and chemical evidence

Following the earlier isolation<sup>1</sup> of isoagatholactone (1), a growing group of tetracyclic diterpenes has been recently isolated from *Spongia officinalis*<sup>2,3</sup>, whose carbon skeleton may be formally derived from the hypothetical skeleton spongian<sup>2</sup>. These findings prompted also some synthetic work<sup>4,5</sup>

We report here the isolation of a new diterpene (2) of the spongian type and, in addition, the isolation of three new tricyclic diterpenes<sup>6</sup> (5, 7, 8) which could be structurally considered precursors of spongian diterpenoids.

The diethyl ether solubles (5.5 g) from an acetone extract of the fresh sponge (150 g dry weight) were chromatographed repeatedly over silica gel using various combinations of diethyl ether-petrol, benzene-diethyl ether and/or dichloromethane to give, besides isoagatholactone (1; 0 05% dry weight) 2, 5, 7, 8 and several other compounds<sup>7</sup>.

 $15\alpha, 16\alpha$ -diacetoxyspongian (2, 0.08%)  $C_{24}H_{38}O_5$ , m p  $151-53^{\circ}C$  (dec.),  $[\alpha]_D - 23^{\circ}$  (c 1.1 CHCl<sub>3</sub>), did not give the molecular ion in the mass spectrum, the highest ion being observed at m/z 286 (M<sup>+</sup>-2CH<sub>3</sub>COOH; 100%). The presence of two acetyl groups was evident from the p.m.r. spectrum (singlets at  $\delta$  2.05 and 2.11, each 3H) which also contains methyl singlets at  $\delta$  0.80, 0.84 (6H), 0.96 and two signals at  $\delta$  6.10 (s) and 6.11 (d, J 8 Hz) accounting for the CHOAc protons. The above spectrum was strongly reminiscent of the spongian diterpene aplysillin (3)<sup>8</sup>, also in the stereo-chemical details.

Moreover the close similarity, where relevant, of the c.m.r. spectra of 2<sup>9</sup> and 3<sup>8</sup>, suggested that 2 differs from aplysillin in lacking the acetyl group at C-12.

Confirmation of the proposed structure was obtained by heating 2 in benzene solution in the presence of a catalytic amount of silica gel, whereupon the previously known<sup>3</sup> furan derivative 4 was obtained in good yield. The relative stereochemistry at the ring D has been tentatively assigned as depicted in 2 on the observation that the coupling constants of the protons at C-15 and C-16 in the p.m.r. spectrum





2



3

1





4

7





5







6

of 2 are exactly the same of those of 3, whose relative stereochemistry was established by X-ray analysis.

ent-isocopal-12-en-15,16-dial (5; 0.53%),  $C_{20}H_{30}O_2$  (M<sup>+</sup>, 302; M<sup>+</sup>-28, 274, base peak; M<sup>+</sup>-28-15, 259); m.p. 139-42°C (dec.);  $[\alpha]_D$  + 48°(c 1.5, CHCl<sub>3</sub>), shows i.r. (1670 and 1710 cm<sup>-1</sup>) and u.v. absorptions  $[(\lambda_{max} (MeOH) 230 \text{ nm}, \varepsilon 7600)]$  corresponding to two aldehyde groups, one being  $\alpha,\beta$ -unsaturated.

8

The p.m.r. spectrum showed four singlet methyl signals at  $\delta$  0.83, 0.88, 0.93 and 0.95, indicative of a diterpene skeleton, a proton multiplet at  $\delta$  2.83 (-CH-CHO), one olefinic proton ( $\delta$  7.12, m) and two aldehyde protons at  $\delta$  9.45 (s) and 9.55 (d, J 4 Hz), this latter being compatible<sup>10</sup> with an equatorial orientation of the 14-CHO group.

The carbon resonances of the c m.r. spectrum<sup>11</sup> of 5 were easily assigned when compared with those of similar C-15<sup>12</sup> and C-25<sup>13</sup> dialdehydes.

LiAlH4 reduction of 5 afforded the diol 6 of known absolute stereochemistry<sup>1</sup>, confirming the structure and indicating the absolute stereochemistry of 5 as *ent*--isocopal-12-en-15,16-dial.

The less polar dialdehyde 14-iso-*ent*-isocopal-12-en-15,16-dial (7; 0 02%), m.p. 115-18°C,  $[\alpha]_D$  + 190°(c 1.5,CHCl<sub>3</sub>), shows m.s. fragmentation, i.r. (1670, 1715 cm<sup>-1</sup>) and u.v.  $[\lambda_{max}$  (MeOH) 230 nm, $\varepsilon$  10 000] absorptions very similar to those of 5.

The p.m.r. spectrum showed four methyl singlets at  $\delta$  0.83, 0.85, 0 92, 0.93, a proton multiplet at  $\delta$  3.26 (-CH-CHO), one olefinic proton ( $\delta$  7.10, m) and two aldehyde protons at  $\delta$  9 40 (s) and 9.85 (d, J 3 Hz).

The spectral properties of 7 pointed out for the more stable 14-axial aldehyde, isomeric with 5.

Therefore, isomerization of 5 catalyzed by basic  $Al_2O_3^{12}$  (CH<sub>2</sub>Cl<sub>2</sub>, reflux) afforded in good yield a single product identical with 7 in all respects.

15-acetoxy-ent-isocopal-12-en-16-al ( $\beta$ , 0.02%), C<sub>22</sub>H<sub>34</sub>O<sub>3</sub> (M<sup>+</sup>-CH<sub>3</sub>COOH, 286, M<sup>+</sup>-CH<sub>3</sub>COOH-CH<sub>3</sub>, 271), [ $\alpha$ ]<sub>D</sub> + 4,2<sup>O</sup>(c 3 2, CHCl<sub>3</sub>), contains an  $\alpha$ , $\beta$ -unsaturated aldehyde group (i.r.  $\nu_{ulax}$  1675 cm<sup>-1</sup>; u v.  $\lambda_{max}$  230 nm,  $\varepsilon$  8050) while an additional i r. absorption at 1725 cm<sup>-1</sup> was indicative for the presence of an ester function

Accordingly the p m.r spectrum showed, besides four methyl singlets at  $\delta$  0.82, 0.84, 0.88 and 0.96, an acetyl methyl singlet at  $\delta$  1.96, the AB part of an ABX system centered at  $\delta$  4.51 (-CH-CH<sub>2</sub>-OAc; J<sub>AB</sub> 10 Hz, J<sub>AX</sub> 0.8 Hz, J<sub>BX</sub> 6 Hz) and only one CHO proton singlet at  $\delta$  9.43.

LiAlH<sub>4</sub> reduction afforded the diol  $\beta$ , confirming structure and absolute stereochemistry of  $\beta$ .

Among the products reported here the dialdehyde 5 is the most interesting, since C-15 and C-20 diterpenoids having two aldehydes groups in such a structural arrangement exhibit a number of interesting biological properties and taste very hot to humans<sup>14</sup>. Recently<sup>15</sup> it has been suggested that this biological activity should be related to the ability of these compounds to interact with  $-NH_2$  groups of the taste sense receptors.

However 5 is tasteless, suggesting that the molecular characteristics, together with the functionality, are relevant for the biological activity, probably in connection with the receptor shape.

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11.-  $\delta_{(CDCl_3)}$  39.7 (C-1), 18.2<sup>a</sup> (C-2), 41.6 (C-3)<sup>b</sup>, 33.1 (C-4), 56.2 (C-5), 18.3<sup>a</sup> (C-6), 41.1 (C-7)<sup>b</sup>, 37.0 (C-8)<sup>C</sup>, 53.8 (C-9), 37.5 (C-10)<sup>C</sup>, 24.4 (C-11), 154.2 (C-12), 137.9 (C-13), 60.7 (C-14), 201.9 (C-15), 192.8 (C-16), 15.8 (C-17)<sup>d</sup>, 33.3 (C-18), 21.6 (C-19), 16.0 (C-20)<sup>d</sup>. <sup>a-d</sup> Assignments may be reversed.

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