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FURANOSESQUITERPENOIDS IN SPONGES - IV*: MICROCIONINS FROM *MICROCIONA TOXYSTILA*

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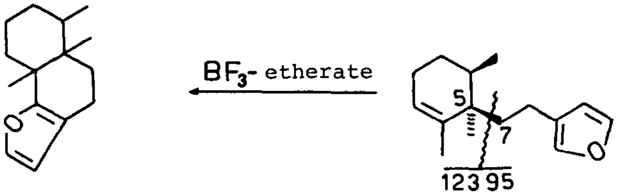
The sponges continue to yield an array of furanosesquiterpenoids. Recently we reported the occurrence of ten furanosesquiterpenes from *Disidea pallescens*[1] and three from *Pleraplysilla spinifera*[2,3], most of them biogenetically interesting, since the resultant sesquiterpene rings were unknown.

Acetone extraction of fresh specimens of the marine sponge *Microciona toxystila* followed by ether-water partition of the residue and chromatography on $AgNO_3$-treated silica gel (light petroleum and increasing amounts of benzene) of the ether soluble fraction has now yielded four additional furanosesquiterpenes, microcionin-1 (1, 0.04% of the dry weight of animal), -2 (2, 0.18%), -3 (3, 0.42%) and -4 (4, 0.20%) and this report concerns with their structures.

All compounds, oils homogeneous on SiO_2-$AgNO_3$ t.l.c. and g.l.c. (3% SE-30 at 130°) and giving positive test with Ehrlich reagent, were isomeric and analyzed for $C_{15}H_{22}O$ (accurate mass measurements).



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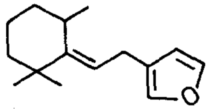
* Part III : G. Cimino, S. De Stefano, A. Guerriero and L. Minale, *Tetrahedron Letters*, 1426 (1975).



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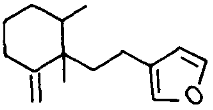

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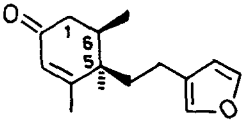
Microcionin-2 (2), $\{\alpha\}_D$ -58.3°, λ_{max}^{MeOH} 210 nm (ε 10,500), $\nu_{max}^{CCl_4}$ 3090, 1162, 1025 and 875 cm^{-1}, and microcionin-4 (4), $\{\alpha\}_D$ $+98.3^{\circ}$, λ_{max}^{MeOH} 212 (ε 14,200), $\nu_{max}^{CCl_4}$ 3090, 1635 and 895 (exocyclic double bond) cm^{-1}, are double bond isomers as shown by the identity (t.l.c. and g.l.c.-m.s.) of their dihydroderivatives, obtained by metal-catalysed transfer-hydrogenation, using decalin and Pd-C under reflux for 2 h[4]. The n.m.r. spectrum (CCl_4) of the less polar microcionin-2 revealed the presence of a β-substituted furan ring (b singlets of 1H at 7.24, 7.12 and 6.14 ppm), of an olefinic proton (m at 5.40 ppm) and three methyl groups: one secondary (d with J 7 Hz at 0.99 ppm), one tertiary (s at 1.08 ppm) and the remaining one on an olefinic bond (1.64 ppm, d with J 1.5 Hz converted to a s on irradiation at 5.40 ppm). These structural components can be readily accomodated in a rearranged mono-cyclofarnesane skeleton as indicated in 2. The presence of a furano-ethyl side chain is further indicated by the mass spectrum which is marked by intense ions at m/e 123 (base peak, M^+-95) and 95 (45%) originating by cleavage of C_5-C_7 bond (2). Oxidation of microcionin-2 with CrO_3-pyridine reagent slowly produced the enone 5, M^+/e 232, $\{\alpha\}_D$ -86.7°, λ_{max}^{MeOH} 238 nm (ε 13,900), $\nu_{max}^{CCl_4}$ 1660 cm^{-1}, which exhibited resonances attributable to a methylene group α to the ketone at about 2.17 ppm (C_6D_6) overlapped by resonances due to



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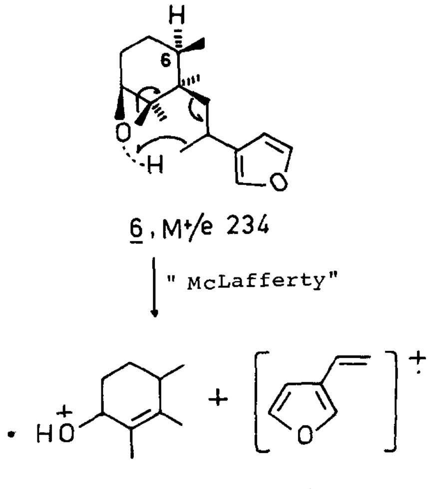

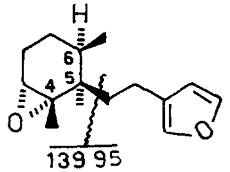

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methylene linked to the furan ring. When the spectrum of the ketone was recorded in the presence of Eu $(fod\text{-}d_9)_3$ the resonances of the methylene α to the ketone separated out giving rise to a 8-line multiplet clearly constituting the AB part of an ABX system with values for J_{AB}, J_{AX} and J_{BX} of 17, 8 and 5 Hz, respectively, thus confirming that C-6 is tertiary and C-5 quaternary. Indication for the relative stereochemistry at C-5 and C-6 in 2 cames from a study of Eu $(fod\text{-}d_9)_3$ induced shifts of the methyl resonances of the epoxides 6,$\{\alpha\}_D$ - 36.5°,$\delta^{C_6D_6}_{H-3}$ 2.66 (bs, $w_{\frac{1}{2}}$ 4Hz) and 7,$\{\alpha\}_D$ - 45.3°,$\delta^{C_6D_6}_{H-3}$ 2.73 (d, J 4Hz), obtained in approximately equal proportions by treatment of 2 with m-chloroperbenzoic acid. The normalized[5] ratios of 10 : 6.14 : 5.65 and 10 : 8.41 : 3.73 for the induced shifts of the C-4, C-5 and C-6 methyl groups in 6 and 7, respectively, are consistent only with a trans-relationship of the methyl groups at C-5 and C-6. In accordance the shift of the H-6 signal in the spectrum of 7 is approximatively four times greater in magnitude than the same signal in the spectrum of 6. Reinforcing evidence for the structure and stereochemistry of the two epoxides cames from their mass fragmentation patterns: the spectrum of 6 is marked by intense peaks at m/e 140 (45%) and 94 (50%)(base peak: 140-Me) originating by a " McLafferty" type process[6], in agreement with the syn-relationship between the oxirane ring an the alkyl chain at C-5; while 7 breaks down without hydrogen transfer giving intense ions at m/e 139 and 95.

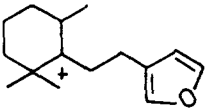
The structure of microcionin-4 was readily established as 4 on chemical interrelation with 2 and n.m.r., which is similar to that of 2 except that the resonances of the olefinic proton and vinyl methyl group are replaced by two b singlets of 1H each at 4.81 and 4.69 ppm ($C = CH_2$). Prominent mass spectral fragments at m/e 124 (45%) and 94 (50%) (base peak: 124-Me), interpreted as originating by a "McLafferty" type rearrangement,support its structure.

Microcionin-1 (1),{α} + 7°, λ_{max} 224 nm (ε 6,600) contains a 2,3-disubstituted furan ring (1H doublets at 7.13 and 6.00 ppm, J 2 Hz) and three methyl groups, two tertiary at 1.07 and 0.84 ppm and one secondary at 0.82 ppm (d, J 6 Hz). The structure of the less abundant component of the sponge was established as 1 by interrelation with 2, which, on treatment with BF_3-etherate, gave a tricyclic compound identical with 1 in SiO_2-$AgNO_3$ t.l.c. and g.l.c.-m.s.

Microcionin-3 (3),$\{\alpha\}_D$ + 36.5°, showed u.v. absorption at 208 nm (ε 9,700). The n.m.r. properties were indicative for a β-substituted furan ring (b singlets of 1H at 7.20, 7.03 and 6.11 ppm), an olefinic hydrogen (5.33 ppm, t, J 6.5 Hz) and three methyl groups, two tertiary and one secondary (singlets at 1.08 and 1.22 ppm and doublet at 1.15 ppm with J 7 Hz). A methylene group in an asymmetric environment located between the furan ring and the double bond was indicated by octet pattern at 3.08 ppm (AB part of an ABX system converted into an ABq, J 16 Hz, on irradiation at 5.33 ppm - X part) partially obscured by the resonance of an allylic methine proton at 2.93 ppm. Irradiation on this latter signal collapsed the Me doublet to a singlet. All these arguments indicate the structure 3. In confirmation oxidative ozonolysis gave 2,2,6-trimethylcyclohexanone, detected in g.l.c.-m.s. by comparison with an authentic sample.

Microcionin-1 (1), -2 (2) and -4 (4) represent the second example of sesquiterpenes with a rearranged mono-cyclofarnesane skeleton after that of ascochlorin and its analogs , sesquiterpenoid phenols recently isolated from the fungus Ascochyta viciae[7].

The co-occurrence of 1, 2 and 4 alongside with 3 suggests that the group is derived from a common biosynthetic precursor, the ion 8.



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