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SIPHONELLINOL, A NEW TRITERPENE FROM THE MARINE SPONGE SIPHONOCHALINA SIPHONELLA

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Abstract

The structure of siphonellinol (3), a novel tricyclic triterpene containing the trans-decahydrobenzoxepine ring system isolated from the Red Sea sponge Siphonochalina siphonella, was elucidated from spectral and chemical evidence.

In the course of bioactive and structural studies of metabolites in sponges[1], we have recently reported the isolation of two new triterpenes, sipholenol-A (1) and sipholenone-A (2) (Scheme 1) of marine origin from Siphonochalina siphonella (from the Gulf of Eilat the Red Sea)[2]. Subsequently, we investigated the minor components of the above sponge and succeeded in the isolation of ten additional sipholanes[1,3], another new triterpene designated siphonellinol (3), which is the subject of this report, and two other triterpenes belonging to yet another unknown group[4].

Siphonellinol (3) was isolated as an amorphous material (0.05%, dry weight), m.p. 109° - 111°C, $[\alpha]_D$ - 52° (c,3.8 $CHCl_3$), ν_{max} 3460(OH), 2905,1450,1375,1160,1080(-O-), and 900 cm^{-1}. The molecular formula $C_{30}H_{52}O_4$ was established by ^{13}C-NMR and HRMS.

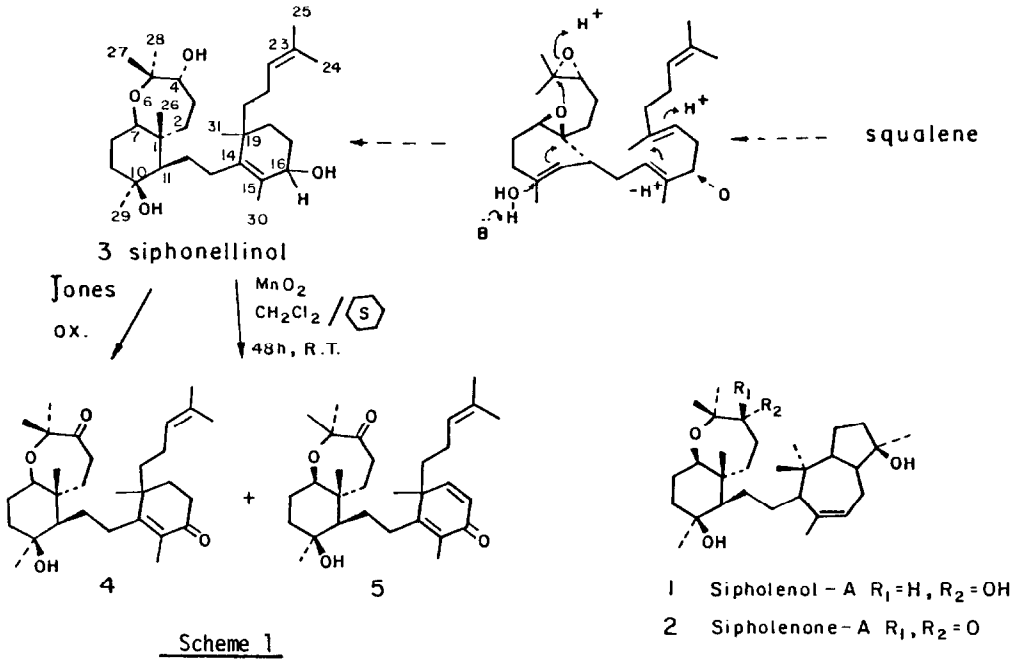
According to the elemental composition of 3 (5 unsaturations) and its ^{13}C-NMR spectrum, siphonellinol contains two double bonds[5] and three rings. The ^{13}C-NMR spectrum[5] reveals also five oxygen bearing carbon atoms; one tertiary and two secondary alcohol groups (confirmed by addition of trichloroacetylisocyanate, TAI, to the NMR tube)[6] and an ethereal bridge.

Two out of the three rings of compound 3 could readily be accounted for. As mentioned above, we have isolated from the petrol-ether extract of S.siphonella a group of new triterpenes, the sipholanes, characterized by the trans-decahydrobenzoxepine and cis-octahydroazulene moieties (see compounds 1 and 2). Comparison of the ^1H and ^{13}C-NMR spectra of compound 3 with the NMR data of compound 1 strongly suggested that the benzoxepine system of 1 is also part of compound 3:

C	1	4	5	7	9	10	11
1	42.78	77.14	77.83	76.54	39.24	72.44	55.87
3	42.96	77.11	77.85	76.48	39.42	72.32	56.02

H	4	7	Me-26	27	28	29
1*3.77d(J=6.5)		3.46dd (J=11.7, 4.4)	0.99	1.24	1.13	1.25
3 3.81d(J=6.7)		3.52dd (J=11.4, 4.4)	0.98	1.23	1.12	1.26

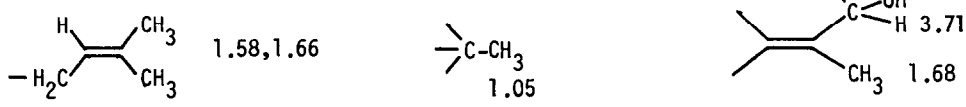
(* numbers according to compound 3)



Scheme 1

Finally, the hydrobenzoxepine moiety of 3 was confirmed by a HRMS (Scheme 2) and by Jones oxidation to give the 4,16-dioxo derivative of 3, compound 4. Thus, the NMR data of the characteristic protons of the bicyclic moiety of 4[7] were in full agreement with those of sipholenone-A (2)[3] (e.g. δ 2.93 dd (J=12 & 4.4 Hz) and δ 2.90dd (J=11.4 & 3.8 Hz) for H-7 in compounds 4 and 2 respectively).

In addition to the bicyclic system, the NMR[8] spectra also allowed the definition of the following structure units:



a b c

The proposal of an allylic alcohol was based on the relatively low-field signal of the CHOH proton and was confirmed by oxidation of 3 to the corresponding α.β -unsaturated ketone (4).

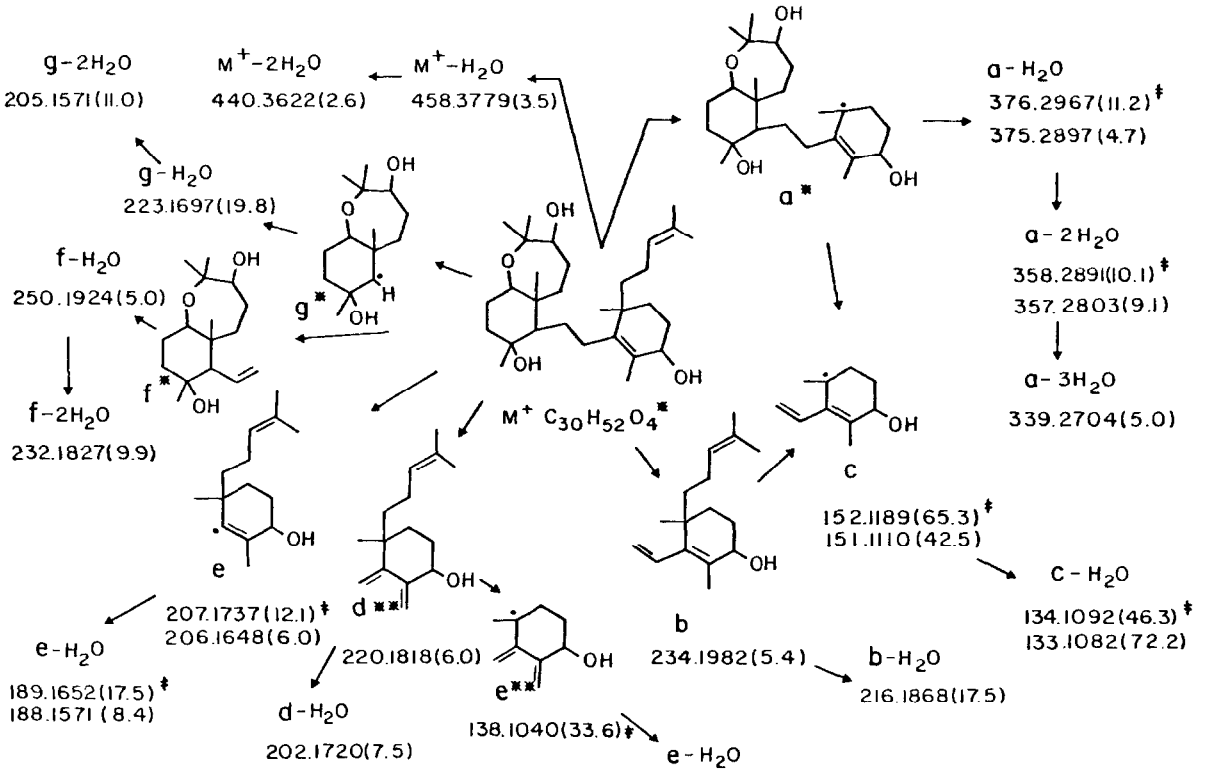
Furthermore, the 9.4Hz (Jaxax) and 3.8 Hz (Jaxeq) coupling constants of the CHOH proton strongly suggest the allyl alcohol to be part of a small ring system.

Most indicative for the structure elucidation of the molecule's second half, containing moieties a - c, was the mass spectrum fragmentations (Scheme 2). Loss of 83 m.u. (C_6H_{11}) from various fragments of 3 suggest for this part of the molecule, the substituted cyclohex-

-14-en-16-ol structure. The proposed structure is in full agreement with the suggested biogenesis (Scheme 1). Finally, the substituted cyclohexene moiety was confirmed by oxidation of 3 to the corresponding 14, 17-dien-16-one derivative (5)[9]. As expected the Me_{30}- signal which was shifted from δ1.68 in 3 to δ1.80 in 4 moved further down to δ2.01 in 5 and most characteristic also was the AB system of H-17 and H-18 (δ5.99d and δ6.89d, J=9.8 Hz, respectively) pointing to a double substituted C-19. Attempts to prepare compound 5 by DDQ oxidation failed. Surprisingly, however, activated MnO_2 not only oxidised the allyl alcohol but also dehydrogenated the system to give the desired dienone. At the same time the 4-OH group was also transformed to a ketone[10].

Siponellinol (3) possesses a new carbocyclic skeleton for which we suggest the name siphonellane[11]. The proposed biogenesis of 3 exhibits the close relationship of 3 to the squalene derived sipholanes (1 or 2) and further supports the suggestion of two independent cyclisations of the two farnesyl halves of squalene to give these compounds[3].

Acknowledgement: Thanks are due to Y. Abudi for her excellent technical assistance



Scheme 2 HRMS of compound 3

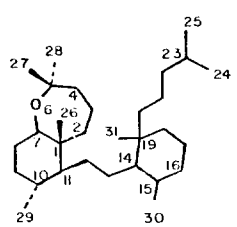
* Invisible because of easy loss of H_2O.

** Other structural isomers possible.

‡ Hydrogen atom transfer or loss of OH rather than H_2O affords the M +1 peak.

References and notes

1. Y. Kashman, A. Groweiss, S. Carmely, Z. Kinamoni, D. Czarkie and M. Rotem, Pure & Appl. Chem. 54, 1995 (1982).
2. U. Shmueli, S. Carmely, A. Groweiss and Y. Kashman Tetrahedron Lett. 22, 709 (1981).
3. S. Carmely and Y. Kashman, J. Org. Chem. in press.
4. The structure of these compounds will be the subject of a forthcoming report.
5. ^{13}C-NMR of compound 3 (75.46 MHz, $CDCl_3$)δ: 135.80s, 128.58s, 124.92d, 77.11d, 76.66s, 76.48d, 72.32s, 71.66d, 56.02d, 43.38s, 42.96s , 131.30s.
6. ^{1}H-NMR (300 MHz, $CDCl_3$)δ:0.97 (3H,s;Me-26), 1.13 (3H,s; Me-31), 1.24 (3H,s; Me-28), 1.26 (3H,s; Me-27), 1.55 (3H,s; Me-29), 1.66 (3H,brs; Me-24), 1.69 (3H,s; Me-25) 1.70 (3H,s; Me-30), 3.79 (1H,dd, J=4.4, 11.4 Hz; H-7), 5.00 (1H,t,J=6.3Hz; H-22) 5.06 (1H,dd,J=4.3, 10.3 Hz; H-16), 5.11 (1H,d,J=6.4 Hz, H-4), 8.20 (1H,s; NH), 8.39 (1H,s; NH), 8.53 (1H,s; NH).
7. Compound 4, m/e 454($M-H_2O$), an oil, $\nu_{max}^{CHCl_3}$ 3460,2930,1705,1685,1445,1375,1250,1230,1175, 1140,900,870 cm^{-1}. ^{1}H NMR (270MHz, $CDCl_3$)δ1.15 (3H,s), 1.18 (3H,s), 1.24 (3H,s), 1.27 (3H,s), 1.32 (3H,s), 1.54 (3H,brs), 1.64 (3H,brs), 1.80 (3H,s), 1.92 (1H,ddd; J=1.8, 6.8, 10.8Hz; H-3), 2.31 (2H,m) 2.40 (1H,dd, J=14.4, 6.4 Hz; H-17), 2.51 (1H, dt, J=14.4, 8.4 Hz; H-17'), 2.93 (1H,dd, J=4.4, 12.0Hz; H-7), 3.24 (1H,ddd, J=13.8, 10.8, 2.4 Hz; H-3'), 4.99 (1H, brt, J=6.7 Hz; H-22).
8. ^{1}H-NMR of compound 3 (270 MHz) δ 1.05s (Me-31), 1.58s, 1.66s & 1.68s (three vinyl Me's 24, 25 & 30), 3.71 (1H,dd, J=9.4, 3.8, H-16) and 5.06 (1H,t,J=6.2, H-22).
9. Compound 5, m/e 452 ($M-H_2O$), an oil, $\nu_{max}^{CHCl_3}$ 3500,2970,2930,1707,1657,1625,1450 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$)δ 6.89 (1H,d,J=9.8Hz, H-18), 5.99 (1H,d,J=9.8 Hz, H-17), 4.92 (1H,t, J=6.2 Hz, H-22), 3.24 (1H,ddd, J=13.6, 10.9, 2.7 Hz, H-3), 2.94 (1H,dd, J=3.9, 11.7 Hz, H-7), 2.01 (3H,brs), 1.61 (3H,brs) 1.48 (3H,brs), 1.33 (3H,s) 1.27 (6H,s), 1.22 (3H,s), 1.14 (3H,s).
10. Prolonged treatment (48 hrs) of compound 3 in a 1:1 mixture of CH_2Cl_2-cyclohexane at r.t. with activated MnO_2 (18 hrs. at 130°) gave as major products compounds 4[7] and 5.[9]
11. Siphonellane:



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