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# SIPHOLENOL AND SIPHOLENONE, TWO NEW TRITERPENES FROM THE MARINE SPONGE SIPHONOCHALINA SIPHONELLA (LEVI).

U. Shmueli*, S. Carmely, A. Groweiss and Y. Kashman*
Department of Chemistry, Tel-Aviv University, Tel Aviv 69978, Israel.

## Abstract

Several squalene-derived triterpenes possessing a hitherto unknown ring system were isolated from the Red Sea Sponge, Siphonochalina siphonella. The structure of one of the new compounds, sipholenol (1a), was determined by spectroscopic methods including a full x-ray diffraction analysis.

Terpenes are the most abundant, nonsteroidal secondary metabolites isolated and characterized to date from marine sponges[1]. Among the higher members of this class are two major groups; the $C_{21}$-furanoterpenes (possessing four prenyl units of which one or two cyclize into a furane ring, most common in the sponge terpenoids), and the $C_{25}$-sesterterpenes which are formed by successive head-to-tail additions of five isoprenoid units to give tetracyclic compounds[1-3]. Although a $C_{30}$ compound, mokupalide[4], a hexaprenoid, was isolated from a sponge, to the best of our knowledge, until now no triterpene has been reported aside from squalene[1].

We now report the isolation and characterization of squalene derived metabolites from the sponge Siphonochalina siphonella (Levi, 1965)[5], collected in the Gulf of Eilat (The Red Sea). Extraction of the freeze-dried sponge (petrol ether) and subsequent chromatography (silica gel; elution with ethylacetate petrol ether), yielded several crystalline compounds. Sipholenol (1a) m.p. 169°-171°, one of the purified compounds, was found by NMR to possess: one trisubstituted double bond, one sec. alcohol, two tert. hydroxy groups and an oxygen bridge between a methine and a tert. carbon atom[6]. The molecular formula of 1a was inferred from HRMS to be $C_{30}H_{52}O_4$. According to sipholenol's unsaturations it must be tetracyclic (including the ether ring). In addition, some 8 methyl groups were resolved, by NMR, strongly suggesting a terpenoid structure[7].

The structure of 1a was determined by x-ray crystallography of its mono acetate 1b[8]. X-ray diffraction studies were first carried out on a monoclinic modification of sipholenone 2[9,10]. However, poor quality of the crystals, erratic recrystallization behavior and perhaps also intrinsic structural reasons precluded the refinement of the trial structure ($R \approx 0.2$) which, in retrospect, displayed a correct picture of the sipholane framework (Kashman & Shmueli, unpublished) Much better crystals were obtained from the acetylated compound 1b; Crystals of sipholenol acetate (1b) are tetragonal, space group $P4_1$, with four molecules of $C_{32}H_{54}O_5$ in a unit cell of dimensions: $a$ = 10.373(1)Å and $c$ = 29.732(5)Å. Intensity data were collected on a CAD4 diffractometer using nickel filtered Cu radiation in the range $2° < \theta < 75°$, in the $\theta/2\theta$ scanning mode. The crystal was stable throughout the measurement which gave 3128 unique reflections with non-negative intensities. The structure was solved with the aid of the MULTAN 78[11] system and was refined by the least squares method. Anisotropic refinement of the 37 non-H atoms resulted in $R=0.089$ for 2562 reflections with $I > 3\sigma$ and 333 parameters, and in an acceptable molecular geometry. A projection of the molecule onto a plane forming an angle of ∿20° with the "best" plane of sipholenol acetate is shown in Figure 1. Sipholenol acetate (1b) consists of a *cis*-fused cyclopentane-cycloheptene system, linked via a dimethylene bridge to a *trans*-fused cyclohexane-oxepane system, with methyl, hydroxyl and acetyl substituents. The molecules appear to be stabilized in the crystal by hydrogen bonds involving the hydroxyl and carbonyl oxygens. Further study of the structure, its packing arrangement and the relationship of the latter to the rather low specific gravity ($D_{meas}$ = 1.06 g/cm$^3$, $D_{calc}$ = 1.07 g/cm$^3$), is in progress.

Interesting is the finding of a polyoxygenated squalene derivative, thyrisiferol from a *Laurencia* sp., however, in contrast to 1a the latter compound contains only cyclic ether rings[12].

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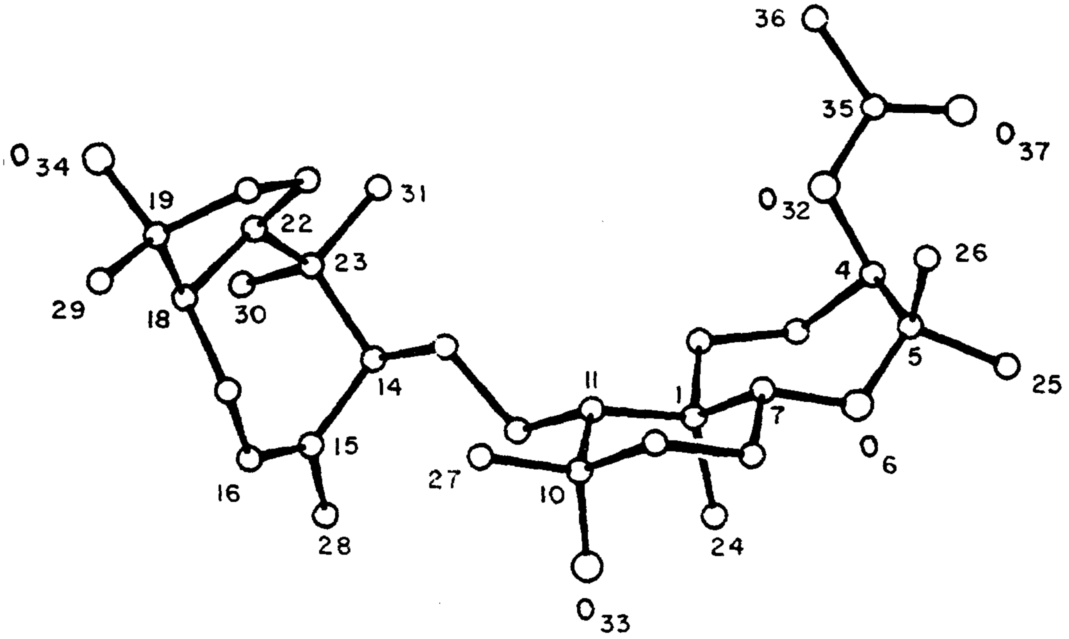

Fig. 1. ORTEP drawing of compound 1b.

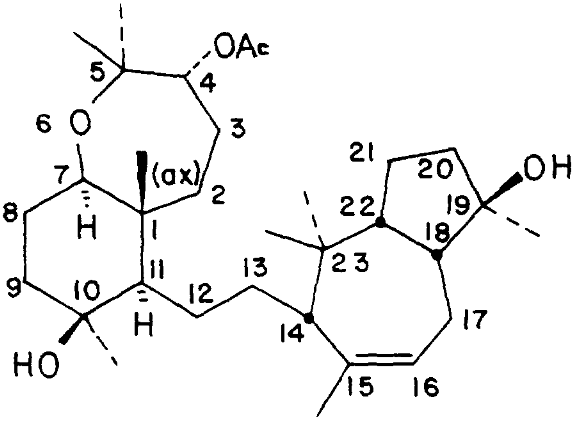

Fig. 2. The structure of 15-sipholen-4,10,19-triol 4-acetate (1b).
(Sipholenone (2) is the 4-keto compound).

## References & Notes

1. L. Minale in "Natural Marine Products", Ed. P.J. Scheuer Vol I, P. 175, Academic Press, N.Y. 1978.
2. The $C_{26}$ and $C_{27}$ alkylated scalarins belong also to the sesterpenes; Y. Kashman and M. Zviely, Tetrahedron Letters, 3879 (1979).
3. Manoalide, most recently isolated by E. Dillep de Silva and P.J. Scheuer, Tetrahedron Letters 21, 1611 (1980), is another new type pentaprenoid.
4. M.B. Yunker and P.J. Scheuer, J. Am. Chem. Soc. 100, 307 (1978).
5. The present sponge,appearing as greyish soft tubes, differs from the *Siphonochalina* sp. from which we have reported the isolation of polyacetylenic compounds; M. Rotem & Y. Kashman, Tetrahedron Letters, 3193 (1979).
6. $^{13}$C-NMR (22.63 MHz, $CDCl_3$,$\delta$): 143.2s & 121.3d (>C=CH), 77.0d (C-4), 82.1s & 72.5s (C-10 and 19), 77.9s (C-5), 76.5d (C-7) and 57.6, 55.7, 52.6 and 48.6 - four doublets (C-11,14,18 and 22
7. $^1$H-NMR (270 MHz, $CDCl_3$,$\delta$): 0.99,1.03,1.08,1.09,1.13,1.24,1.25 and 1.76 - eight 3H-singlets, 2.45m(1H), 3.46dd(J=15.3 and 4.4Hz,1H), 3.77d(J=6.5Hz,1H) and 5.39m(1H); HRMS (EI, 70eV) m/e 476.4893 ($M^+$,$C_{30}H_{52}O_4$, 1.2%).
8. Compound 1b, m.p. 150°-151°, $^1$H-NMR(270MHz,$CDCl_3$,$\delta$) 1.00,1.04,1.10,1.11,1.14,1.19,1.25,1.76 and 2.14 - nine 3H singlets, 3.33dd (J=15.3 & 4.4Hz,1H), 4.98d (J=6.5Hz,1H) and 5.46m(1H), was prepared by r.t. acetylation of 1a with $Ac_2O$/Pyr.
9. Compound 2, m.p. 187°-188°, $\gamma_{max}^{KBr}$ 3450 & 1705 $cm^{-1}$, $^1$H-NMR (270MHz, $CDCl_3$,$\delta$): 1.02,1.09,1.09, 1.15,1.25,1.26,1.31 and 1.76 brs - eight 3H singlets, 2.30dd(J=11.4 and 3.8 Hz,1H), 3.19 ddd (J=13.0, 10.8 & 2.4 Hz,1H) and 5.46m (1H); HRMS (EI,70eV) m/e 456.3613 ($M^+$-$H_2O$, 12.9%).
10. We suggest for the new skeleton the name sipholane; thus,compound 1a is 15-sipholen-4,10, 19-triol and compound 2 15-sipholen-10,19-diol-4-one.
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