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# CHEMICAL STUDIES OF MARINE INVERTEBRATES. XLI (1,2). SIGMOSCEPTRELLIN-A METHYL ESTER A NOR-SESTERTERPENOID PEROXIDE FROM THE SPONGE *SIGMOSCEPTRELLA LAEVIS*.

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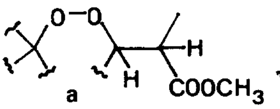
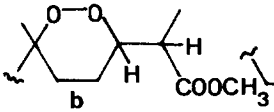
*SUMMARY : Structure 1 has been established for sigmosceptrellin-A methyl ester, a novel ichtyotoxic nor-sesterterpenoid from the sponge S. laevis.*

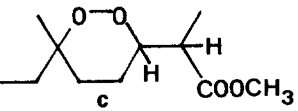
The dichloromethane extract of sun-dried specimens of the sponge *Sigmosceptrella laevis* (Lindgren), collected at Manam Island, off the north coast of Papua-New Guinea, is toxic to the fish *Lebistes reticulatus*. This toxicity has been associated with a two components acidic fraction ($LD_{50}$ : 5mg/l) which on methylation with $CH_2N_2$ yielded two closely related compounds : sigmosceptrellin A (0.6% dry weight) and B (1% dry weight) methyl esters, readily separated by column chromatography. Both methyl esters also appear as minor constituents in the sponge extract.

Sigmosceptrellin-A methyl ester (1, oil, $[\alpha]_D$=54°) has the molecular formula $C_{25}H_{42}O_4$ (by HRMS ; calculated : 406.3083, observed : 406.3101). The spectral properties of 1 indicate the presence of the following functions : 3 tertiary methyl groups ($^1H$ NMR (5) : 3 singlets of 3H each at 0.74, 1.03 and 1.04), 2 secondary methyl groups ($^1H$ NMR : 2 doublets of 3H each at 0.81 (J=5Hz) and 1.10 (J=7Hz)), one exomethylene double bond ($^1H$ NMR : bs 2H 4.51 ; $^{13}C$ NMR : 160.5 s, 102.6 t ; IR : 1640 and 890 $cm^{-1}$) and a COOMe group ($^1H$ NMR : s 3H 3.67 ; $^{13}C$ NMR : 174.2 s, 51.8 q ; IR : 1750 $cm^{-1}$). The $^{13}C$ NMR spectrum of 1 is specially informative. It confirms the presence of 25 carbon atoms, of which only 3 are $sp^2$ ($C=CH_2$ and COOMe group), thus implying the presence of 3 rings. Moreover, only two other carbon atoms ($^{13}C$ NMR : 80.2 s, 81.1 d) bear an oxygen atom , and since the IR spectrum of 1 shows no $\nu_{OH}$ band, the last two oxygen atoms are necessarily part of a peroxide function bonding a quaternary to a tertiary carbon atom ($^1H$ NMR : HC-16 m 4.23). Treatment of 1 with KI in acetic acid yielded diol 2 ($M^+$ 408 ; $C_{25}H_{44}O_4$ ; IR : 3320 $cm^{-1}$ ; $^1H$ NMR : HC-16 m 3.60), confirming the presence of the peroxide and establishing its cyclic nature, since no carbon atom was lost on reduction. It follows that compound 1 is bicarbocyclic.

A 1H quintuplet absorption at 2.56 ppm in the $^1H$ NMR of 1 can be attributed to a proton α to the COOMe group, since it is shifted to high field in the spectrum of 3 ($M^+$ 378 ; $C_{24}H_{42}O_3$ ; IR : 3500 $cm^{-1}$ ; $^1H$ NMR : $H_2C$-18 d 3.58, HC-17 m 2.13), obtained by selective LAH reduction of the COOMe group of 1. Moreover, decoupling experiments established that this proton is coupled to the secondary methyl group at 1.10 ppm and also to the proton at 4.23 ppm leading to partial structure a.


a


b


c

Catalytic hydrogenation of 1 afforded tetrahydroderivative 4 ($M^+$ 410 ; $C_{25}H_{46}O_4$ ; IR : 3300 $cm^{-1}$ ; $^1H$ NMR : HC-16 m 3.60), resulting from the saturation of both exomethylene group and peroxide function. Ratcliffe oxidation [6] of compound 4 yielded the γ-lactone 5 ($M^+$ 322 ; $C_{21}H_{38}O_2$ ; IR : 1780 $cm^{-1}$ ; $^1H$ NMR : $H_3C$-20 s 1.36, $H_2C$-15 m 2.54) whose formation can only be explained if the peroxide is implied in a 6-membered ring (reaction 1). This arrangement also explains the formation of compound 6 ($M^+$ 390 ; $C_{25}H_{42}O_3$ ; IR 1720 and 1640 $cm^{-1}$ ; UV : $\lambda_{max}$ 250 nm (10,000) ; $^1H$ NMR : $H_3C$-19 m 1.80, $H_2C$-14 t 1.83 (J=8Hz), $H_2C$-15 t 3.13 (J=8Hz) ; $^{13}C$ NMR : C-18 170.4 s, C-16 170.1 s, C-17 96.7 s),upon Jones oxidation of 4 (reaction 2).

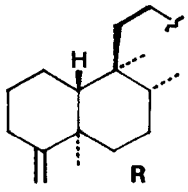
In the NMR spectrum of 6, the C-15 protons appear as a triplet at 3.13 ppm and double irradiation experiments confirm they are coupled to another methylene group. On the other hand, dehydration of the monoacetate 7 ($M^+$ 452 ; $C_{27}H_{48}O_5$ ; IR : 3500 and 1750 $cm^{-1}$ ; $^1H$ NMR : HC-16 m 5.05) yielded a mixture of double bond isomers that was directly submitted to a Lemieux-Johnson oxidative cleavage [7]. Amongst the reaction products, the aldehyde 8 ($M^+$ 236, $C_{16}H_{28}O$ ; IR : 1725 $cm^{-1}$) and the methyl ketone 9 ($M^+$ 264, $C_{18}H_{32}O$ ; IR : $\nu_{C=O}$ 1730 $cm^{-1}$, $^1H$ NMR : s 3H 2.15) were isolated, the latter establishing the partial structure b.

The MS of compounds 1, 2 and 3 show a prominent fragment peak at m/e 191, observed at m/e 193 in 4, 5, 6 and 7, where the $C=CH_2$ group has been hydrogenated. In the case of 1, it has been shown by HRMS that this ion corresponds to the molecular formula $C_{14}H_{23}$. This is consistent with the loss of fragment b + $C_2H_4$ from the molecular ion. The obtention of aldehyde 8 implies that the $C_2H_4$ fragment is a two methylene unit ($CH_2$-$CH_2$). Partial structure b can thus be extended to c.

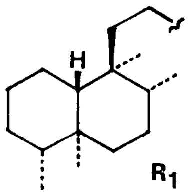
At this stage, a crystalline derivative 10, suitable for X-ray diffraction analysis was obtained by $OsO_4$ treatment of 1 followed by p-bromobenzoylation. Crystals of compound 10 belong to the space group $P2_1$ with a=11.197, b=22.177, c=6.601 Å, β=91.98° and Z=2 (radiation MoKα, $2\theta_{max}$=42°). The structure was solved using the MULTAN 78 [8] programs and the refinements were realized using the SHELX 76 [9] programs. $R_{final}$=0.077. A computer generated drawing of 10 is reproduced in fig. I. Accordingly sigmosceptrellin-A methyl ester has structure 1 (relative configuration).

Although many sesterterpenoids have been isolated from marine and terrestrial sources [10,11], sigmosceptrellin-A methyl ester is of particular interest since it is the first example of a nor-sesterterpene. It has a non-isoprenic carbon skeleton whose bicarbocyclic part is identical to that of avarol [12].

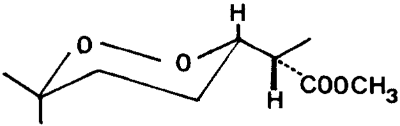
The structural study of the closely related sigmosceptrellin-B methyl ester is now being completed in our laboratory.



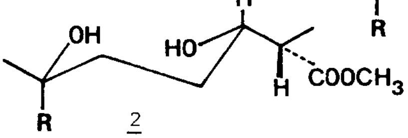
R



$R_1$



1



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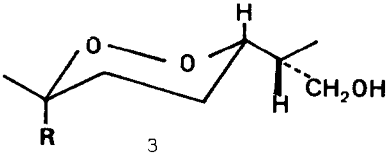

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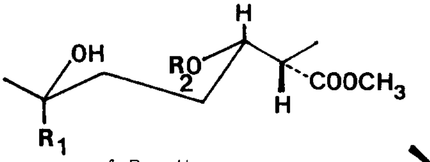
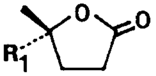


4 $R_2$= H

7 $R_2$= $COCH_3$



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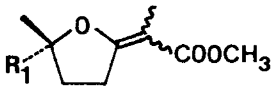
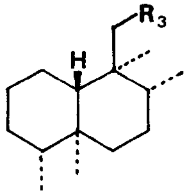
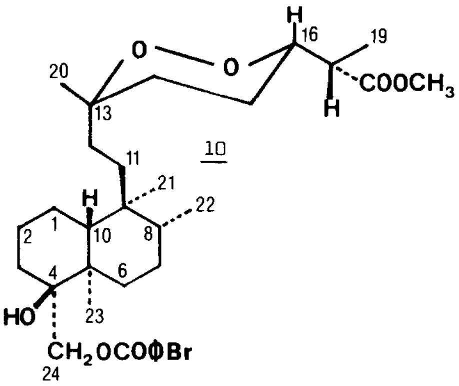


6

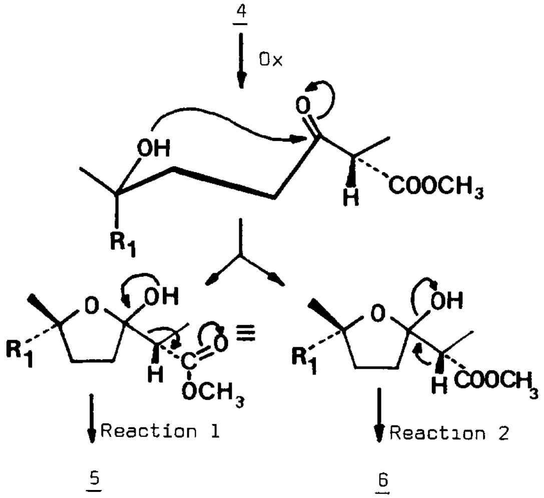
8 $R_3$= CHO

9 $R_3$= $CH_2COCH_3$





10



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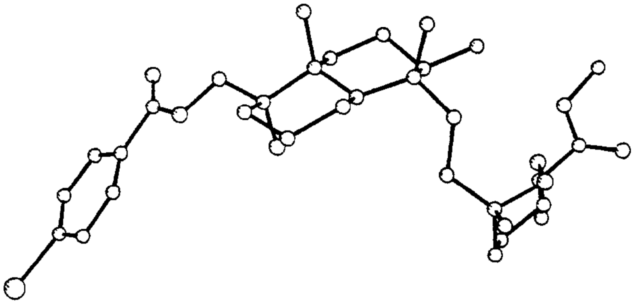

Figure I : Computer generated drawing of compound 10.

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