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SIPHONODIOL, A NEW POLYACETYLENIC METABOLITE FROM THE SPONGE <u>SIPHONOCHALINA TRUNCATE</u>

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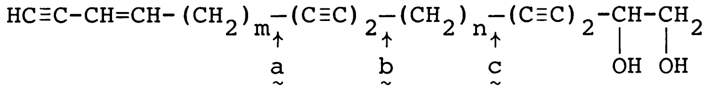
A new C23 polyacetylene diol was isolated from the marine sponge *S. truncata* and its structure was elucidated mainly on the basis of its spectral data.

Polyacetylene compounds from marine organisms have been found only during the past several years.$^{1-4)}$ In the course of our continuing studies to find bioactive marine metabolites, we isolated an antifungal and antibacterial polyacetylene diol, named siphonodiol (**1**), from the marine sponge *Siphonochalina truncata*.

The frozen sponge sample (dry weight after extraction 6.8 g) was immersed in dichloromethane and the organic layer was subjected to silica gel chromatography followed by successive preparative HPLC (10ϕ x 250 mm glass columns packed with Nucleosil 10C$_{18}$ and LiChrosorb 60 10 um). The pure **1** obtained (25 mg) mp 31-32°C, $[\alpha]_D$ -6.7° (c 0.5, MeOH), $C_{23}H_{24}O_2$ (M^+ 332.1760), was very labile at room temperature even at 0°C but rather stable at -20°C. Acetylation of **1** gave diacetate (**2**) (IR and ^{1}H-NMR). Catalytic reduction of **1** gave the perhydro compound (**3**) (M^+ 356 $C_{23}H_{48}O_2$), suggesting an unsaturation number of 12 for **1**.

The presence of hydroxyl, disubstituted and terminal acetylene, and olefin functions was inferred from the IR spectrum (3580, 3380, 3300, 2250, 2090, 1620 cm^{-1}). The UV spectrum showed enyne [228 nm (ε 15100)] and ene-diyne unsaturation [215 (ε 69700), 241 (ε 11300), 254 (ε 13900), 268 (ε 19300), 284 (ε 14900)].$^{5)}$ In the ^{1}H-NMR spectrum of **1**, proton signals were well separated: δ6.05 (d-t, J = 11 and 7 Hz), 5.99 (d-t, J = 11 and 7 Hz), 5.48 (2H, d-m), 4.50 (X part of ABX), 3.73 (AB part of ABX), 3.08 (d, J = 2 Hz, $-C\equiv CH$), 2.46 (4H, $-C\equiv C-CH_2$), 2.35 (4H, $=C-CH_2$), 1.78 (2H, quint. J = 7 Hz), 1.45 (4H, quint. J = 7 Hz). The terminal groups of **1** are thus $HC\equiv C-$ and the diol system $-CH(OH)-CH_2OH$. Irradiation of the methine signal of the diol system caused no change on the other signals indicating that the diyne group is adjacent to the diol system.

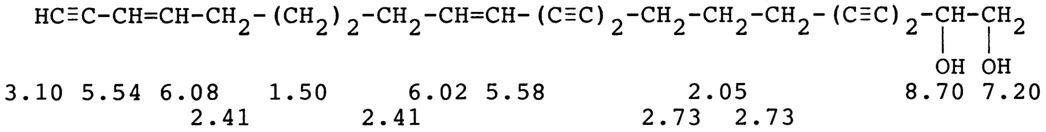
According to the above data, the gross structure 1 can be represented by Formula A. An additional vinyl group -CH=CH- must be inserted at position a or b or c. The configuration of double bonds may be cis in consideration of J-values.



$$HC\equiv C\text{-}CH{=}CH\text{-}(CH_2)_m\underset{\underset{a}{\uparrow}}{-}(C\equiv C)_2\underset{\underset{b}{\uparrow}}{-}(CH_2)_n\underset{\underset{c}{\uparrow}}{-}(C\equiv C)_2\text{-}\underset{\underset{OH}{|}}{CH}\text{-}\underset{\underset{OH}{|}}{CH_2}$$

Formula A: m = 4, n = 3 or m = 3, n = 4

The lanthanide-induced shift (LIS) experiment combined with the spin-decoupling experiment was very useful for determining the numbers of m and n, as well as the position of the additional vinyl group.



$$\underset{3.10}{HC}\equiv C\text{-}\underset{5.54}{CH}{=}\underset{6.08}{CH}\text{-}\underset{2.41}{CH_2}\text{-}\underset{1.50}{(CH_2)_2}\text{-}\underset{2.41}{CH_2}\text{-}\underset{6.02}{CH}{=}\underset{5.58}{CH}\text{-}(C\equiv C)_2\text{-}\underset{2.73}{CH_2}\text{-}\underset{2.05}{CH_2}\text{-}\underset{2.73}{CH_2}\text{-}(C\equiv C)_2\text{-}\underset{8.70}{\underset{\underset{OH}{|}}{CH}}\text{-}\underset{7.20}{\underset{\underset{OH}{|}}{CH_2}}$$

LIS experiment: Siphonodiol 1 with 0.5 equiv. of $Eu(fod)_3d_{27}$

Besides the diol system, the 4H signal shifted largely (δ 2.46 to 2.73) and the 2H quintet also shifted (δ 1.78 to δ 2.05) much more than the 4H quintet (δ 1.45 to δ 1.50). Irradiation of the signal at δ 2.41 caused decoupling of the olefinic proton signals to a doublet and the 4H quintet to a singlet. By irradiation of the δ 2.73, only the 2H quintet was decoupled to a singlet. These results confirmed that m = 4 and n = 3, and the additional double bond must be situated at position a in Formula A.

Siphonodiol 1 showed weak activity against Trichophyton asteroides (MIC 25.0 µg/ml) and medium activity against Staphylococcus aureus (MIC 12.5 µg/ml) and Streptococcus pyogenes C-203 (MIC 6.2 µg/ml).

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References

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