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VARIABILIN, AN ANTIBIOTIC FROM THE SPONGE, *IRCINIA VARIABILIS*

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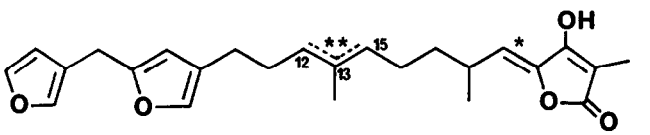
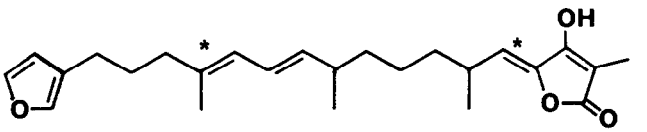
During the past year, three closely related sesterterpenes have been isolat from sponges of the genus *Ircinia*. Ircinin-1 1 and ircinin-2 2 from *Ircinia oro* were found to be isomeric linear difurano-sesterterpenes containing an unusual conjugated tetronic acid moiety. Fasciculatin 3 from *Ircinia fasciculata* was sho to be a closely related monofurano-sesterterpene. We wish to report the isolati and structural elucidation of a fourth linear sesterterpene, variabilin 4.

A single sample (30g dry weight) of the sponge, *Ircinia variabilis* (Schmidt was shown to contain an ethanol soluble antibiotic, active *vs. Staphylococcus aur* Chromatography of the ether soluble material on silica gel plates gave the pure antibiotic, variabilin 4 in 0.2% yield.



1 $\Delta^{12,13}$

2 $\Delta^{13,15}$



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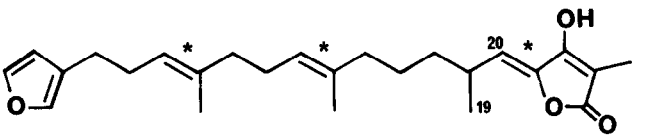

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*stereochemistry of olefin unknown.

Variabilin 4, $C_{25}H_{34}O_4$, was so similar to fasciculatin 3 that most of the structural features could be assigned on the basis of spectral similarities. The ultraviolet spectrum of variabilin (λ_{max}(MeOH) 255mμ) underwent a base shift

(λ_{max}(MeOH-OH^-) 249, 309mμ), characteristic of the conjugated tetronic acid moiety. Furthermore, ir bands at 1730 and 1630 cm^{-1} and the nmr signals at δ 1.81 (s, 3H) and 5.41 ppm (d, 1H, J = 8Hz) add considerable weight to this assignment. Irradiation at 2.79 ppm caused the doublets at 1.05 and 5.41 ppm to collapse to singlets, indicating the relationship between the C-19 methyl group and the unsaturated tetronic acid moiety. The β-substituted furan ring was indicated by the presence of signals at 6.25, 7.18 and 7.31 ppm (broad singlets, 1H each) in the nmr spectrum and ir bands at 1030, 880 and 765 cm^{-1}.

Having defined the functional groups at each end of the molecule, there remains the problem of placing two unsaturations within a polyisoprenoid chain. The remaining methyl groups must be attached to trisubstituted olefinic bonds, since the nmr spectrum shows two characteristic vinyl methyl signals at 1.62 and 1.67 ppm together with a 2 proton multiplet at 5.08 ppm. The location of the olefinic bonds was determined by ozonolysis, followed by oxidative work-up and treatment with ethereal diazomethane solution, to obtain dimethyl succinate, methyl levulinate and methyl 2-methyl-6-oxoheptanoate.[4] Each component was shown to be identical (glpc retention time and mass spectrum) to authentic samples.

The occurance of sesterterpenes in geographically separated species of *Ircinia* strongly supports the previous taxonomic classification of this sponge. Assuming a normal polyisoprenoid biosynthesis for this series of compounds, variabilin may be regarded as a likely precursor of both the oroidins and fasciculatin.

Acknowledgement

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References

1. G. Cimino, S. De Stefano, L. Minale, and E. Fattonesso, Tetrahedron, 28, 333 (1972)

2. F. Cafieri, E. Fattonesso, C. Santacroce, and L. Minale, Tetrahedron, 28, 1579 (1972)

3. The sponge was identified from the description of a sample collected by Ricketts in the same location and identified by de Laubenfels. J. Steinbeck and E.F. Ricketts, "Sea of Cortez", P.P. Appel, Mamaroneck, N.Y. p.324.

4. An authentic sample was obtained by ozonolysis of 1,3-dimethylcyclohexene followed by methylation.