# Chemistry of Sponges, XI. 22-Deoxyvariabilin, a New Sesterterpene from the Sponge Thorecta sp.

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# CHEMISTRY OF SPONGES, XI.[1] 22-DEOXYVARIABILIN, A NEW SESTERTERPENE FROM THE SPONGE *THORECTA* SP.

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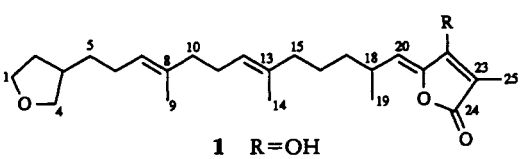
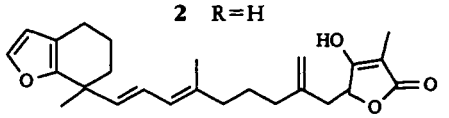
ABSTRACT.—In addition to the known linear sesterterpene furospinulosin 1 [**6**], the new compound 22-deoxyvariabilin [**2**] was isolated from the marine sponge *Thorecta* sp.

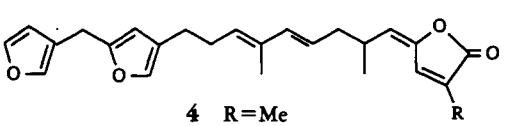
Linear sesterterpenes containing terminal furan rings and tetronic acid moieties are common natural products of marine sponges of the genera *Ircinia*, *Psammocinia*, and *Sarcotragus* (Order Dictyoceratida, Family Thorectidae). For example, variabilin [**1**] (1) has been reported to be the major cytotoxic component in all New Zealand collections of sponges of these genera (2). It appears that there are other genera within the Thorectidae that contain related metabolites. Okinonellin A [**3**] is a tetronic acid containing a terminal dihydrotetronic acid from a marine sponge that was originally assigned to the genus *Spongionella* (Family Dysideidae) (3) but has been reexamined and found to be a species of *Fasciospongia* (Family Thorectidae). Okinonellin A was also isolated under the name hippospongin from an Okinawan sponge identified as *Hippospongia* (Family Spongiidae) (4); however, there are no other reports of *Hippospongia* from Okinawan waters, and it is likely that this sponge has been misidentified. The two unsaturated butenolides **4** and **5** were isolated from a marine sponge that was initially identified as *Thorecta marginalis* (5) but which has subsequently been revised to *Taonura marginalis* (6). We recently obtained a specimen of an undescribed *Thorecta* sp. (Order Dictyoceratida, Family Thorectidae) from a collection in



**1** R=OH
**2** R=H



**3**



**4** R=Me
**5** R=$CH_2OH$

with a novel carbon skeleton that is related to the linear furanosesterterpenes by the formation of an additional carbocyclic ring. Okinonellin A was isolated along with a linear furanosesterterpene

[1]For Part X, see M. Kernan, R.C. Cambie, and P.R. Bergquist, *J. Nat. Prod.*, **53**, 1353 (1990).

the Bay of Islands, New Zealand. This is the first report of a collection of the genus *Thorecta* from New Zealand (6). A $CH_2Cl_2$ extract of this sponge had antimicrobial properties. We now report the isolation and structure elucidation of 22-deoxyvariabilin [**2**] as the major $CH_2Cl_2$-soluble bioactive metabolite of this sponge.

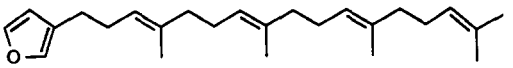
Extensive cc and plc of the $CH_2Cl_2$ extract led to the isolation of **2** along with the known furanosesterterpene furospinulosin 1 [**6**] (7) which was identified by comparison of its spectral parameters with literature values (7). Variabilin [**1**] was not detected in either the crude $CH_2Cl_2$ extract or in any of the fractions from cc.

The molecular formula of 22-deoxyvariabilin [**2**] was determined as $C_{25}H_{34}O_3$ from the hrms, and the structure of the compound was determined from spectroscopic studies. Thus, the ir spectrum of **2** suggested the presence of an α-methyl-γ-butenolide group (ν max 1769 $cm^{-1}$), and its presence was confirmed from the nmr spectra [$^1H$ δ 6.95 (br s, H-22), 1.99 (s, Me-25); $^{13}C$ see Table 1]. A $^1H$-$^1H$-COSY spectrum showed a correlation between the signals at δ 6.95 and the signal at δ 1.99. A signal at δ 4.95 (br d, $J$ = 10 Hz, H-20) that was coupled to a methine proton signal [δ 2.86 (m, H-18)] was also coupled to the signal at δ 6.95. The signal at δ 2.86 was also coupled to signals of a methyl group [δ 1.03 (d, Me-19)] and a methylene group [δ 1.28 (q, $J$ = 7 Hz, H-17)]. The remainder of the $^1H$-nmr spectrum was very similar to that of variabilin [**1**], and all remaining signals were assigned by analysis of the COSY and decoupling experiments. Comparison of the $^{13}C$-nmr data (Table 1) of **2** with those of **1** (8) and palinurin [**7**] (9) provided further support for structure **2**. The vinyl methyl groups (C-14 and C-9) of **2** had $^{13}C$-nmr chemical shifts of δ 16.0 and 15.8, which indicated that the

TABLE 1. $^{13}C$-nmr Chemical Shifts of Variabilin [**1**], 22-Deoxyvariabilin [**2**], and Palinurin [**7**] ($CDCl_3$).

| Carbon | Compound | | |
|---|---|---|---|
| | **1**[a] | **2** | **7**[b] |
| C-1 | 142.5 | 142.5 (d) | 142.5 |
| C-2 | 111.1 | 11.1 (d) | 110.9 |
| C-3 | 125.0 | 124.9 (s) | 124.9 |
| C-4 | 138.8 | 138.8 (d) | 138.7 |
| C-5 | 25.0 | 25.0 (t) | 24.4 |
| C-6 | 28.4 | 28.4 (t) | 28.2 |
| C-7 | 123.7 | 123.7 (d)[c] | 39.3 |
| C-8 | 135.7 | 135.8 (s)[d] | 135.7 |
| C-9 | 16.0 | 15.8 (q)[e] | 16.7 |
| C-10 | 39.6 | 39.5 (t)[f] | 125.3 |
| C-11 | 26.6 | 26.5 (t)[g] | 125.2 |
| C-12 | 124.4 | 124.3 (d)[c] | 137.8 |
| C-13 | 134.8 | 134.8 (s)[d] | 36.9 |
| C-14 | 15.8 | 16.0 (q)[e] | 20.8 |
| C-15 | 39.7 | 39.7 (t)[f] | 37.1 |
| C-16 | 25.7 | 25.7 (t)[g] | 26.0 |
| C-17 | 36.6 | 36.4 (t) | 129.3 |
| C-18 | 31.0 | 31.3 (d) | 129.0 |
| C-19 | 20.6 | 20.8 (q) | 16.5 |
| C-20 | 117.2 | 120.6 (d) | 41.6 |
| C-21 | 143.0 | 128.9 (s) | 78.4 |
| C-22 | 162.5 | 137.9 (d) | 177.9 |
| C-23 | 99.1 | 125.3 (s) | 96.8 |
| C-24 | 172.5 | 170.1 (s) | 176.2 |
| C-25 | 6.1 | 10.5 (q) | 5.9 |

[a]Data in this column are from Manes *et al.* (8).
[b]Data in this column are from Barrow *et al.* (9).
[c–g]Signals are interchangeable.



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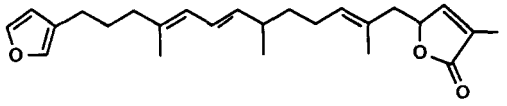

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double bond geometry must be *E* (8). In NOEDS experiments, irradiation at δ 6.95 (H-22) showed an enhancement of the signal due to H-20 (δ 4.95, 2%), irradiation at δ 5.10 (H-12) showed an enhancement of the signal due to H-15 (δ 1.94, 4%), and irradiation at δ 5.15 (H-7) showed an enhancement of the signal due to H-10 (δ 1.98, 6%). The relative stereochemistry of the double bonds in **2** is thus as shown. There was insufficient material to determine the stereochemistry at C-18 in **2**.

In an antimicrobial assay using the standard disk method, 22-deoxyvariabilin inhibited the growth of *Staphylococcus aureus* at 100 μg/disk, *Bacillus subtilis* at 50 μg/disk, and *Candida albicans* at 100 μg/disk. It is not certain that linear furanosesterterpenes such as furospinulosin 1 are a valid chemotaxonomic marker of sponges in the Dictyoceratida, as these compounds have been found in some, but not all, genera in the families Spongiidae and Thorectidae. However, linear sesterterpenes containing a tetronic acid group such as variabilin are confined to the genera *Ircinia, Sarcotragus, Psammocinia,* and *Fasciospongia* (Family Thorectidae), while linear sesterterpenes containing a terminal unsaturated butenolide or "deoxytetronic acid" as in 22-deoxyvariabilin are confined to the genera *Taonura* and *Thorecta* (Family Thorectidae).

## EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Experimental procedures were as described in Part IX (10).

SPONGE.—The genus *Thorecta* is very common in southeastern Australia and is not reliably known to occur elsewhere. All Australian species have either stalked, fan-shaped flabellate, or vasiform growth form. The present species is the first record of the genus from New Zealand, and while sharing all the generic characters (6) it differs markedly in shape having a stalked, pear-shaped body with a central vestibular cavity opening through a single apical oscule. The internal choanosomal tissue has a dull yellow-green pigmentation, which thus far is unique within the genus although few species are known for living material. Description of this species must await publication of a monograph on the New Zealand Dictyoceratida. The sponge *Thorecta* sp. was collected using SCUBA (−20 m) at the Bay of Islands, New Zealand in December 1988 and stored at −78°. A specimen (voucher number AUZ7-12) has been lodged in the reference collection, Zoology Department, University of Auckland.

ISOLATION OF NATURAL PRODUCTS.—The chopped sponge (7.1 g dry wt) was soaked in MeOH for 72 h, and the concentrated extract was partitioned between $CH_2Cl_2$ (3 × 100 ml) and $H_2O$ (100 ml). The combined $CH_2Cl_2$ fractions (0.24 g) were dried over anhydrous $Na_2SO_4$ and evaporated to give a brown oil that was purified by cc on Si gel [EtOAc-hexane (1:1)] and by plc on a Chromatotron [EtOAc-hexane (5:1 and 1:1), 1 mm plates of Si gel] to give furospinulosin 1 [**6**] (10 mg, 0.14%) and 22-deoxyvariabilin [**2**] (2.1 mg, 0.03%).

22-DEOXYVARIABILIN [**2**].—The compound was obtained as an unstable oil: found $[M]^+$ 382.2481, $C_{25}H_{34}O_3$ requires $[M]^+$ 382.2508; ir ν max (film) 1769, 1667, 1651, 799, 758 $cm^{-1}$; $^1H$ nmr ($CDCl_3$) δ 7.33 (br s, H-1), 7.20 (br s, H-4), 6.95 (br s, H-22), 6.27 (br s, H-2), 5.15 (br t, $J = 7$ Hz, H-7), 5.10 (br t, $J = 7$ Hz, H-12), 4.95 (d, $J = 10$ Hz, H-20), 2.86 (m, H-18), 2.44 (br t, $J = 7$ Hz, H-5), 2.23 (br t, $J = 7$ Hz, H-6), 2.06 (br q, $J = 7$ Hz, H-11), 1.99 (br s, Me-25), 1.98 (br t, $J = 7$ Hz, H-10), 1.94 (br t, $J = 7$ Hz, H-15), 1.58 (s, Me-9), 1.55 (br s, Me-14), 1.34 (m, H-16), 1.28 (q, $J = 7$ Hz, H-17), 1.03 (d, $J = 7$ Hz, Me-19); $^{13}C$ nmr ($CDCl_3$) see Table 1; ms *m/z* (rel. int.) 382 (12), 215 (9), 178 (40), 137 (45), 81 (100), 69 (83), 55 (70), 41 (73).

BIOASSAY PROCEDURES.—The activity of the crude extract was assayed by dipping sterile 6-mm-diameter antimicrobial assay (A) discs into the test sample, draining, and transferring the dry disc to the surface of an agar plate previously seeded with the test organism. Plates were incubated for 24–72 h at 25° and the diameter of the zone of inhibition recorded. A dilution series was assayed for all fractions showing antimicrobial activity. Typical zones of inhibition were 12–16 mm.

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