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Ircinianin Sulfate from the Marine Sponge *Ircinia (Psammocinia) wistarii*

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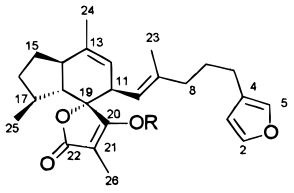
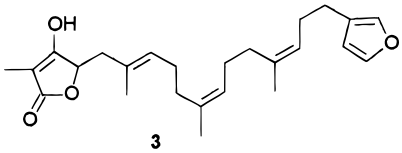
Extraction of *Ircinia (Psammocinia) wistarii* Wilkinson from Lamont Reef, Great Barrier Reef, with MeOH has yielded the very unstable sulfate ester (**1**) of the known sesterterpene ircinianin (**2**).

Marine sponges of the order Dictyoceratida have attracted interest for their unusual sesterterpene secondary metabolites. The genus *Ircinia* in particular has yielded many linear sesterterpenes, which contain both furan and tetronic acid moieties, for example, palominin (**3**).[1] The most unusual of the *Ircinia* sesterterpene metabolites, however, has been the tetracyclic furanoterpene ircinianin (**2**), first reported from *Ircinia wistarii* by Hofheinz and Schonholzer,[2] and its pentacyclic isomer wistarin (**4**), more recently isolated[3] by Gregson and Ouvrier from one of a number of specimens of *I. wistarii* collected at various locations around Australia.



1 R = SO_3^-
2 R = H



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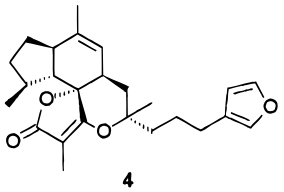

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Extraction in our laboratory of a specimen of *I. wistarii* Wilkinson (Irciniidae) collected from the Great Barrier Reef resulted in isolation of a polar, very unstable, major secondary metabolite. This compound had better stability when the sponge was extracted with MeOH, and because it decomposed immediately when dissolved in $CHCl_3$, NMR spectra were obtained in CD_3OD solutions. Rapid step-gradient column chromatography on Si gel of the Et_2O-soluble portion of the MeOH extract gave ircinianin sulfate (**1**) as a light yellow gum. Smaller amounts of the known compounds ircinianin and wistarin were also recovered from earlier column fractions and identified by comparison of their ^{1}H- and ^{13}C-NMR spectra with those reported in the literature.[2,3]

The ^{1}H- and ^{13}C-NMR spectra of **1** showed a sesterterpene containing furan (β-substituted) and tetronic acid functionalites, with the DEPT135 spectrum indicating a probable ten degrees of unsaturation, six of which had already been accounted for. An additional two degrees of unsaturation were satisfied by carbon−carbon double bonds, implying a tetracyclic structure for **1**. The presence of an oxygenated quaternary carbon at 87.7 ppm suggested a possible spiro ring junction at C-19. Comparison of the spectra of **1** with those reported for ircinianin (**2**) revealed close similarities. Assignments for **1** (e.g., C-8 and C-17), which differ significantly from those reported[3] for **2**, are supported by DEPT135 and COSY, HMBC, and HMQC 2D-NMR correlations, and by comparison with the ^{13}C- and DEPT135-NMR spectra of **2** in MeOH and CD_3CN in our laboratory. We believe the anomalies between the ^{13}C spectra of **1** and **2** are due to assignment errors rather than to any differences in structure. Assignments of the ^{13}C-NMR spectrum of **1**, and our partial reassignment of signals for **2**, are shown in Table 1.

The greater separation of the C-20 and C-22 carbon signals in **1**, and the downfield shift of C-26, are typical of C-20 esters of the tetronic acid moeity. However, as there are no more carbons in **1** than in **2**, an inorganic ester, most likely a sulfate, is required. This was confirmed by the negative ion HRMS of **1**, which gave a molecular ion at m/z 475 for $C_{25}H_{31}O_7S$.

The rarity of sesterterpene sulfate esters was noted by Faulkner[4] in his paper describing the isolation of the halisulfates. Our finding that ircinianin occurs as a tetronic acid sulfate may indicate that the linear sesterterpene compounds such as **3** are also present in the living sponge as very unstable sulfate esters.

Our study of ircinianin sulfate also casts some doubt on the true status of both ircinianin and wistarin as natural products. Although Gregson and Ouvrier noted[3] that wistarin might arise from ircinianin during isolation, they reported that ircinianin did not cyclize to wistarin with either acid, base, or Lewis acid catalysis. We have observed, however, that, although only trace amounts of wistarin are isolated directly from the sponge, it can be isolated in 18% yield from the decomposition of ircinianin sulfate in $CHCl_3$, and hence both wistarin and ircinianin could be formed from ircinianin sulfate during extraction of *I. wistarii*. The

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Table 1. Comparison of ^{13}C Spectra of **1** and **2**

carbon	**1** (CD_3OD)	**2** (CD_3CN)	carbon	**1** (CD_3OD)	**2** (CD_3CN)
2	143.9	143.8	15	27.4	26.8 (C-7)[c]
3	112.4	112.0	16	34.0	33.0 (C-8)[c]
4	126.9	126.2	17	33.5	32.7 (C-15)[c]
5	140.4	139.9	18	52.6	50.9
6	25.8	24.8	19	87.7	85.1
7	29.4	29.0 (C-16)[c]	20	177.8	174.3[a]
8	40.8	40.1 (C-17)[c]	21	102.9	98.2
9	137.4[a]	136.7	22	171.2	176.2[a]
10	124.2[b]	124.2	23	16.6	16.3
11	50.1	48.2	24	20.6	20.5
12	124.4[b]	123.0	25	21.1	20.5
13	137.3[a]	137.5	26	9.6	6.4
14	46.6	45.7			

[a,b] Signals may be interchanged. [c] Previous assignments.[3]

true status of wistarin and ircinianin may have to await examination of the living animal.

Experimental Section

General Experimental Procedures. ^1H- and ^{13}C-NMR spectra were recorded in CD_3OD with a Bruker AMX-300 NMR at 300 and 75 MHz, respectively, calibrated to 3.5 and 49.3 ppm, respectively. Negative ion LREIMS were recordered on a VG Quattro mass spectrometer and negative ion HRMS on a Bruker BioApex 47e FTMS. FTIR spectra were recorded on a Perkin-Elmer 1600 spectrometer and optical rotations on a Perkin-Elmer 341 polarimeter. Column chromatography was performed on Merck Kieselgel 60 (230−400 mesh).

Animal Material. A specimen of *Ircinia (Psammocinia) wistarii* Wilkinson was collected by scuba diving in about 5 m of water from Lamont Reef in the Capricorn Bunker Group, Great Barrier Reef, in March 1994. The sponge was kept frozen prior to extraction. Voucher specimen QMG306975 has been deposited at the Queensland Museum, South Brisbane, Queensland, Australia.

Extraction and Isolation. A sample (12.5 g) of the frozen sponge was extracted with MeOH (3 × 100 mL) and the extract volume reduced under vacuum to a thick oil. This was suspended in a $NaHCO_3$ solution (40 mL, 30% w/v) and partitioned against Et_2O (3 × 30 mL). The organic phase was dried over Na_2SO_4 and evaporated to dryness. The extract was chromatographed on a Si gel column using step-gradient elution from light petroleum through CH_2Cl_2 to EtOAc. All collection tubes contained a small volume of MeOH to stabilize ircinianin sulfate after elution.

Ircinianin sulfate (1): isolated as a light yellow gum (2.4% by dry wt); mp 138−140 °C (dec); $[\alpha]^{20}_D$ −160 (*c* 0.02, MeOH); IR ν_{max} (thin film) 3150, 3100, 2973, 2870, 1732, 1654, 1501, 1446, 1385, 1332, 1264 cm^{-1}; ^1H NMR (CD_3OD) 1.18 (3H, d, J = 6 Hz, H-25), 1.5 (2H, m), 1.78 (3H, s, H-23), 1.85 (2H, m), 1.89 (3H, s, H-24), 2.05 (2H, m), 2.20 (3H, s, H-26), 2.27 (2H, t, J = 8 Hz, H-8), 2.57 (2H, t, J = 8 Hz, H-6), 2.59 (1H, m, H-14), 3.28 (1H, br d, J = 11 Hz, H-11), 5.21 (1H, br s, H-12), 5.29 (1H, d, J = 10 Hz, H-10), 6.52 (1H, br s, H-3), 7.57 (1H, m, H-5), 7.65 ppm (1H, m, H-2); ^{13}C-NMR data, see Table 1; negative ion HRESIMS *m/z* 475.1810 (calcd for $C_{25}H_{31}O_7S$, 475.1785), 395.2231 (calcd for $C_{25}H_{31}O_4$, 395.2216); negative ion ESIMS *m/z* 475 [M^-] (100), 395 [$M^- - SO_3$] (8).

Ircinianin (2): isolated from the CH_2Cl_2 column fraction as a white solid (0.26%); $[\alpha]^{20}_D$ −167 (*c* 0.004, MeOH); ^{13}C NMR (CD_3OD) 6.2, 16.5, 20.8, 20.9, 25.5, 27.4, 29.7, 33.4, 33.8, 40.7, 46.3, 49.5, 52.2, 87.1, 97.5, 112.2, 123.7, 125.2, 126.7, 136.8, 137.3, 140.4, 144.2, 178.0, 179.5 ppm.

Wistarin (4): isolated in trace amounts from the light petroleum−MeOH column fraction, and from decomposition of **2**, as white solid; $[\alpha]^{20}_D$ +134 (*c* 0.007, MeOH); ^{13}C NMR (CD_3OD) 6.4, 20.9 (C-24), 21.3 (C-25), 24.0 (C-23), 25.4, 26.1 (C-6), 28.0 (C-15), 32.2 (C-17), 33.4 (C-16), 41.5 (C-11), 42.0 (C-10), 43.2 (C-8), 46.6 (C-14), 52.9, 82.9 (C-19), 88.7 (C-9), 108.1, 112.1, 123.1, 126.3, 139.4, 140.5, 144.4, 176.9, 177.9 ppm, other assignments as per Gregson and Ouvrier.[3]

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