133. Ircinianin, a Novel Sesterterpene from a Marine Sponge

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Summary

Ircinianin (**2**), a new furano-sesterterpenetetronic acid, has been isolated from a marine sponge of the genus *Ircinia*. Structure **2** has been established by X-ray diffraction methods.

Until quite recently sesterterpenes formed a rare group of natural products¹). However, during the past five years, sesterterpenoid compounds of diverse and novel structural types from marine sponges of the order *Dictyoceratida* have been reported in increasing numbers [2]. The genus *Ircinia* has yielded a group of closely related linear sesterterpenes characterized by a β-substituted furan and a tetronic acid ring as terminal units [3]. A typical example is fasciculatin (**1**) from *Ircinia fasciculata* [4]. We now wish to report the isolation and structure elucidation of a new sesterterpene, ircinianin (**2**) from an undescribed *Ircinia species*²) found on *Wistari Reef* near *Heron Island* on the *Australian Great Barrier Reef*. Ircinianin is the first polycyclic sesterterpenetetronic acid.

Ircinianin (**2**) crystallized in *ca.* 2% yield from a crude petrol ether extract; m.p. 165–167°, $[\alpha]_D^{25} = -232°$ ($c = 0.5$, $CHCl_3$). The molecular formula $C_{25}H_{32}O_4$ was established by MS. and corresponds with the results of elemental analysis. The presence of a tetronic acid unit [5] could be inferred from following properties:

- **2** is strongly acidic with $pK_{a_{MCS}} = 6.7$ (measured in methyl-cellosolve/water 4:1), comparable to benzoic acid;
- the UV.-spectrum of **2** (λ_{max} (ethanol) 208 nm) undergoes a base shift (λ_{max} (ethanol/NaOH), 264 nm);
- on methylation with diazomethane or with methyliodide/$NaHCO_3$ in DMF two oily methyl ethers **3** and **4** are formed. The structures could be assigned on the basis of spectral similarities with the known methyl ethers of simple tetronic acids [6]: **3** is characterized by IR.-bands at 1744 and 1665 cm^{-1} and a UV.-maximum at 208 nm with shoulder at 238 nm, **4** by a strong IR.-band at 1610 cm^{-1} and a UV.-maximum at 265 nm.

A β-substituted furan ring was indicated by broad one-proton singlet signals at 6.26, 7.20 and 7.34 ppm in the NMR.-spectrum of **2** and IR.-bands at 1022, 865 and 751 cm^{-1}.

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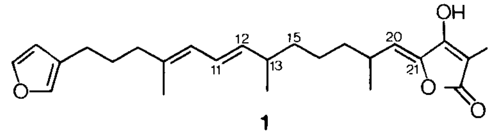
¹) For a review on sesterterpenes s. [1].

²) We are obliged to Professor Dr. *P. Bergquist*, Department of Zoology, University of Auckland, New Zealand, for the taxonomic classification.



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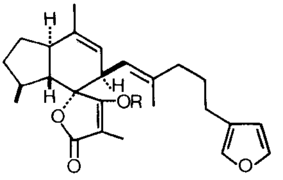
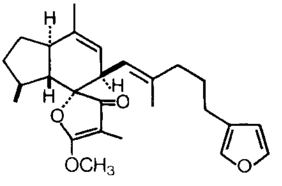


2 R=H

3 R=CH₃



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Signals of three methyl groups on unsaturated carbon atoms could be observed in the NMR.-spectrum. One of these, a singlet at 1.68 ppm could be assigned to the α-methyl group of the tetronic acid unit, and the remaining two doublet signals at 1.62 and 1.68 ppm (1.58 and 1.68 ppm in the spectrum of **3**) together with one-proton multiplets at 5.12, 5.05, and 3.14 ppm, to the unit $-C(CH_3){=}CH{-}\underset{|}{C}H{-}CH{=}C(CH_3)-$. Spin decoupling confirmed the latter assignment.

Furan ring, tetronic acid and two olefinic bonds accounted for 8 of 10 double bond equivalents of $C_{25}H_{32}O_4$. The remaining two consequently had to be attributed to carbocyclic rings. Since little information on the structure of this ring system could be gained from spectroscopic data, a single-crystal of ircinianin was subjected to X-ray diffraction studies. The result is given in *Table 1* listing the atomic coordinates and in *Figure 1* showing relative configuration, numbering of the atoms, bond lengths, and bond angles. A stereoprojection [7] showing one of the two possible enantiomeric structures of ircinianin is depicted in *Figure 2*. All bond distances and

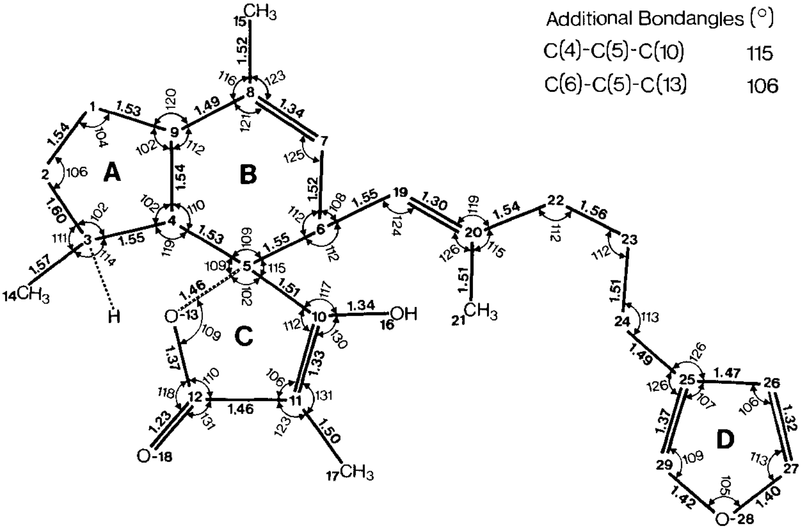

Fig. 1. *Structure of ircinianin with numbering of atoms, bond lengths* (Å) *and bond angles*

angles agree well with generally accepted values. Calculations of 'best planes' through the ring atoms show rings C and D to be practically planar, the r.m.s.-deviation of the ring atoms from the planes being 0.011 Å and 0.019 Å resp. Rings A and B are non planar and best described as half chairs. A short intermolecular O(16)–O(18) distance of 2.63 Å points to a fairly strong intermolecular hydrogen bond in the crystal.

Ircinianin although differing markedly from the usual linear sesterterpenes of most *Ircinia species* by its polycyclic structure, is evidently closely related to fasciculatin (**1**): it can be imagined as being biosynthetically derived from a $\Delta^{13,15}$-dehydrofasciculatin by intramolecular 4+2 cycloaddition. This relationship supports the assumption, that furano-sesterterpenetetronic acids are specific chemotaxonomic markers for the genus *Ircinia.*

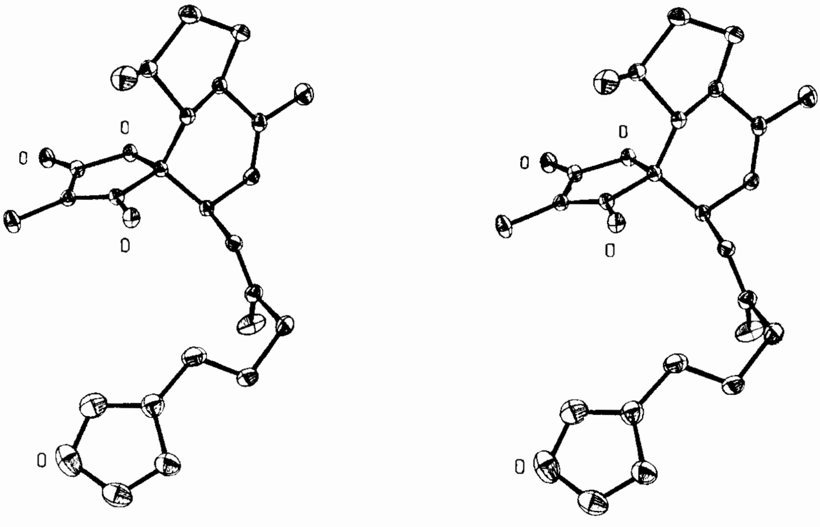

Fig. 2. *Stereoprojection of Ircinianin*

Table 1. *Coordinates of the Atoms* (Standard Deviations × 10,000)

Atoms	X	Y	Z	Atoms	X	Y	Z
C(1)	0.4894(3)	0.3894(5)	−0.0559(6)	O(16)	0.3274(2)	−0.0016(4)	0.0574(3)
C(2)	0.4101(4)	0.4266(6)	−0.0337(8)	C(17)	0.2129(3)	−0.0510(7)	−0.1498(5)
C(3)	0.3626(3)	0.3054(5)	−0.0489(5)	O(18)	0.3012(2)	0.0596(4)	−0.3579(3)
C(4)	0.4212(3)	0.2043(4)	−0.0473(4)	C(19)	0.4787(3)	−0.0596(5)	0.0364(4)
C(5)	0.4036(2)	0.0794(4)	−0.1009(4)	C(20)	0.5059(3)	−0.1664(5)	0.0591(5)
C(6)	0.4709(3)	−0.0053(5)	−0.0900(4)	C(21)	0.5330(6)	−0.2577(8)	−0.0319(8)
C(7)	0.5410(3)	0.0617(5)	−0.1205(5)	C(22)	0.5139(4)	−0.2068(7)	0.1896(6)
C(8)	0.5477(3)	0.1839(6)	−0.1280(5)	C(23)	0.4582(4)	−0.3086(7)	0.2243(6)
C(9)	0.4831(3)	0.2652(5)	−0.1181(5)	C(24)	0.3814(4)	−0.2608(7)	0.2308(8)
C(10)	0.3336(2)	0.0231(4)	−0.0592(4)	C(25)	0.3266(4)	−0.3590(8)	0.2487(7)
C(11)	0.2874(2)	0.0039(5)	−0.1480(4)	C(26)	0.3290(5)	−0.4561(8)	0.3392(7)
C(12)	0.3223(3)	0.0521(5)	−0.2545(4)	C(27)	0.2708(6)	−0.5233(9)	0.3212(8)
O(13)	0.3905(2)	0.0944(3)	−0.2283(3)	O(28)	0.2256(3)	−0.4759(7)	0.2325(6)
C(14)	0.3051(4)	0.2944(8)	0.0534(8)	C(29)	0.2639(6)	−0.3742(9)	0.1854(8)
C(15)	0.6190(4)	0.2471(8)	−0.1578(8)				

We wish to thank Mr. *C. R. Wilkinson*, Department of Zoology, University of Queensland, Australia, for collection of the sponge and for extracts. We are grateful to our colleagues of the spectroscopy department for providing us with spectra and for many helpful discussions.

Experimental part

General remarks on instrumental techniques s. [8].

Isolation of ircinianin (**2**) *from Ircinia n.sp.* Sponges were collected on *Wistari Reef*, near *Heron Island*, *Queensland*, Australia, and sun dried. Approximately 100 g of crushed sponge was extracted in a Soxhlet apparatus with petrol ether (b.p. 60–80°). On concentrating and cooling the extract, 2.3 g crude crystalline **2** was obtained and twice recrystallized from toluene and acetone; m.p. 165–167°; $[\alpha]_D^{25} = -232°$ ($c=0.5\%$, $CHCl_3$), $pK_{aMCS}=6.7$ (in methylcellosolve/water 4:1). – UV. (in ethanol): 208 (4.36), 238 sh (4.04), 268 sh (3.30); in ethanol/NaOH: 264 (4.26). – IR. (KBr): 3400–2600 br., 1709, 1659, 1620, 1261, 1119, 1022, 865, 751. – CD.: 241 (–22), 222 (+5.6), 203 (–30). – ^1H-NMR. (in $CDCl_3$): 0.88 (*d*, $J=5.5$, 3H); 1.62 (*d*, $J=1.5$, 3H); 1.68 (br. *s*, 6H); 2.12 (*t*, $J=8$, 2H); 2.42 (*t*, $J=7.5$, 2H); 3.14 (*m*, 1H); 5.05 (*m*, 1H); 5.12 (br., *d*, $J=10$, 1H); 6.26, 7.20, 7.34 (br. *s*, 1H each). – MS.: 396.2333 (*M*, $C_{25}H_{32}O_4$, calc. 396.2300, 0.9%), 381 (3.9%), 287.1660 ($C_{18}H_{23}O_3$, calc. 287.1647), 135.1163 ($C_{10}H_{15}$, calc. 135.1173, 17%), 135.0814 ($C_9H_{11}O$, calc. 135.0809, 100%), 81.0340 (C_5H_5O, calc. 81.0340, 60%), 81.0709 (C_6H_9, calc. 81.0704, 40%).

$C_{25}H_{32}O_4$ (396.53) Calc. C 75.73 H 8.13% Found C 76.13 H 8.20%

Methylation of **2**. A solution of 200 mg **2** in 5 ml methanol was treated with 15 ml of a 1% ether solution of diazomethane. The products **3** and **4** were separated by PLC. on silica gel plates with petrol ether/triethylamin 10:1.

3 was obtained as oil (80 mg), Rf 0.23. – UV. (in ethanol): 208 (4.38), 238 sh (4.05). – IR. (in $CHCl_3$): 1744, 1665. – ^1H-NMR. (in $CDCl_3$): 0.88 (*d*, $J=5.5$, 3H); 1.58 (*d*, $J=1.5$, 3H); 1.68 (*d*, $J=1.5$, 3H); 1.96 (*s*, 3H); 2.40 (*t*, $J=7.5$, 2H); 3.06 (*m*, 1H); 3.95 (*s*, 3H); 5.00 (*m*, 1H); 5.05 (br. *d*, $J=10$, 1H); 6.26, 7.21, 7.34 (br. *s*, 1H each). – MS.: 410 (*M*, 2.4%), 395 (1.1%), 135.0798 ($C_9H_{11}O$, calc. 135.0809, 100%), 81 (28%).

4 was also an oil (60 mg), Rf 0.52. – UV. (in ethanol): 265 (4.43). – IR. (in $CHCl_3$): 1610. – ^1H-NMR. (in $CDCl_3$): 0.86 (*d*, $J=5.5$, 3H); 1.51 (*d*, $J=1.5$, 3H); 1.55 (*s*, 3H); 1.73 (*d*, $J=1.5$, 3H); 2.39 (*t*, $J=7.5$, 2H); 3.06 (*m*, 1H); 4.00 (*s*, 3H); 5.04 (*m*, 1H); 5.25 (br. *d*, $J=10$, 1H); 6.27, 7.22, 7.32 (br. *s*, 1H each). – MS.: 410 (*M*, 7%), 168 ($C_9H_{12}O_3$, 100%), 135.0805 ($C_9H_{11}O$, calc. 135.0809, 56%), 81 (60%).

X-ray diffraction studies. Crystals of **2** belong to the orthorhombic space group $P2_12_12_1$, with the cell data $a=18.431$ Å, $b=10.935$ Å, $c=11{,}247$ Å. $Z=4$. $V=2266.8$ Å^3; $\varrho_{calc.}$ 1.17 g/cm^3, $\varrho_{measured}$ 1.13 g/cm^3. X-ray intensities were measured on a four-circle diffractometer with Mo-$K\alpha$ radiation. ω-scan technique was applied with Zr/Y balanced filters for $\Theta=0$–15° and a normal Zr-filter for $\Theta=15$–25°. The strongest reflections which were affected by counting losses were measured with attenuators. No absorption correction was applied. Reflections for which the net count was less than twice the standard deviation of the measurement were considered unobserved. Of 3694 measured reflections 2717 were taken to be observed. The phase problem was solved by direct methods using MULTAN [9]. Isotropic, followed by anisotropic, block-diagonal least squares refinement yielded an *R* value of 9.6%. The determined atomic coordinates are listed in *Table 1*.

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