Chemistry of Sponges. 18.[1] 12-Desacetylfuroscalar-16-one, a New Sesterterpene from a *Cacospongia* sp.

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A new sesterterpene 12-*O*-desacetylfuroscalar-16-one (**1**) has been isolated from the sponge *Cacospongia* sp., and its structure was determined by spectroscopic examination.

Sponges of the genus *Cacospongia* (order Dictyoceratida, family Thorectidae) are an important source of scalarane sesterterpenes, some of which are biologically active.[2] In a continuation of our studies on sponges of the order Dictyoceratida we have examined the constituents of an unnamed *Cacospongia* species collected at Little Barrier Island, New Zealand. Extraction of the freeze-dried sponge with methanol and chromatography of the dichloromethane-soluble portion of the extract on Si gel gave a new sesterterpene, 12-*O*-desacetylfuroscalar-16-one (**1**) (0.01%), and the known sesterterpene, scalarolide[3,4] (0.004%), which was identified by comparison of spectral data with that reported in the literature.

12-*O*-Desacetylfuroscalar-16-one, a colorless solid, was shown to have the molecular formula $C_{25}H_{36}O_3$ by high-resolution desorption electron impact mass measurements (HRDEIMS), indicating eight degrees of unsaturation. The IR spectrum showed absorptions indicative of a hydroxyl group (3360 cm^{-1}) and an α,*β*-unsaturated carbonyl group (1652 cm^{-1}), while the ^1H NMR spectrum (*δ* 6.63, d, J = 2.0 Hz; 7.33, d, J = 2.0 Hz) suggested the presence of a disubstituted furan ring. The ^{13}C NMR spectrum (Table 1) showed five sp^2 carbon signals (*δ* 106.6, 120.5, 142.6, 173.4, and 194.5) accounting for three degrees of unsaturation, and, thus, the compound possessed five rings. The ^1H NMR spectrum (Table 1) indicated the presence of five methyl groups that gave rise to three-proton singlets at *δ*0.82, 0.85, 0.86, 0.98, and 1.27 and that indicated a scalarane sesterterpene. This finding was supported by peaks in the mass spectrum at *m*/*z* 191, 137, and 123, characteristic of scalarane derivatives[5] (Figure 1). Both the ^1H and ^{13}C NMR spectra were similar to those of 12-*O*-desacetylfuroscalarol (**2**).[6,7] The ^{13}C NMR spectrum, however, indicated that one of the hydroxyl groups of **2** was replaced by a keto group (*δ* 194.5). The downfield shift of one of the furanyl carbons (*δ* 173.4) implied that it was part of the α,*β*-unsaturated keto system. This, together with a UV maximum at 260 nm, showed that the keto group had to be linked in a position *β* to the furan ring,[6] thereby localizing its position at C-16. The methyl signal at low field (*δ* 1.27) could be assigned to the C-23 methyl group due to the deshielding effect of the furan ring, while a key HMBC correlation between this signal and that at *δ*173.4 indicated that the furan was fused to ring D at C-17 and C-18. In the ^1H NMR spectrum an ABM coupling system composed of one-proton signals at *δ*2.58, 2.43, and 2.40 assigned to the H-15eq, H-15ax, and H-14 protons respectively, together with HMBC cross peaks between H-14 and C-8, C-13, C-16, C-18, C-21, and C-23 and between H-15 and C-8, C-13, C-14, C-16, and C-17, were in agreement with the partial structure for the D and E rings shown in **1**. Signals at *δ*4.43 (dd, 1H) and 70.8 (d) in the ^1H and ^{13}C NMR spectra, respectively, indicated that the hydroxy group was secondary, and a coupling of the H-23 methyl signal to the carbon signal at *δ*70.8 provided evidence that the hydroxyl group was at C-12. In the $^1H-^1H$ COSY spectrum cross peaks due to couplings of H-12 with H-11ax and H-11eq were observed. Their small coupling constants (J = 2.6, 2.8 Hz) suggested that H-12 was equatorial so that the 12-hydroxyl group was axial, that is, was in an α-position.

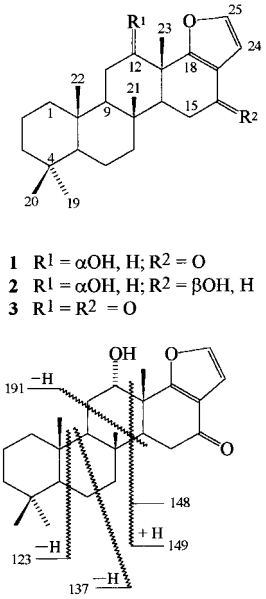

Figure 1.

Further support for structure **1** was obtained from oxidation with Jones' reagent, which afforded a diketone (**3**), mp 217−219 °C, with properties identical to those recorded for the oxidation product of 12-*O*-desacetylfuroscalarol.[6]

Experimental Section

General Methods. ^1H and ^{13}C NMR spectra (COSY, HMQC, HMBC) were recorded on a Bruker DRX-400 spectrometer using $CDCl_3$ as solvent and TMS as internal standard. Multiplicities of ^{13}C NMR peaks were determined from

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Table 1. ^{1}H NMR, ^{13}C NMR, COSY, and HMBC Data for **1** (in $CDCl_3$)

position	δ_C	δ_H (mult, *J* in Hz)	COSY	HMBC (H to C)
1	39.6 t	0.84 (m), 1.66 (m)	H-2ax, H-2eq	C-2, -3, -5, -9, -10
2	18.5 t	1.44 (m), 1.63 (m)	H-1ax, H-2eq	C-3
3	41.9 t	1.13 (m), 1.37 (m)		C-2, -4, -5
4	29.7 s			
5	56.5 d	0.99 (dd, 14.0, 2.2)	H-6ax, H-6eq	C-7, -9, -10, -20, -22
6	18.0 t	1.41 (m), 1.59 (m)	H-5, H-7ax, H-7eq	C-4, -6, -10, -19
7	41.0 t	1.07 (m)	H-6ax, H-6eq	C-5, -6, -8, -9
		1.74 (dt, 12.0, 2.4)		C-14
8	37.0 s			
9	51.5 d	1.54 (dd, 12.0, 4.0)	H-11ax, H-11eq	C-8, -10, -11
10	37.6 s			
11	23.9 t	1.80 (m), 1.84 (m)	H-9, H-12	C-8, -9, -10, -12, -13
12	70.8 d	4.43 (dd, 2.8, 2.6)	H-11ax, H-11eq	
13	43.3 s			
14	49.4 d	2.40 (dd, 13.6, 2.8)	H-15ax, H-15eq	C-8, -13, -15, -16, -18, -21, -23
15	34.7 t	2.43 (dd, 16.4, 13.6)	H-14	C -8, -13, -14, -16
		2.58 (dd, 16.4, 2.8)		C-16, -17
16	194.5 s			
17	120.5 s			
18	173.4 s			
19	33.3 q	0.85 (s)		C-3, -4, -5, -20
20	21.3 q	0.82 (s)		C-3, -4, -5, -19
21	16.7 q	0.98 (s)		C-7, -8, -9, -14
22	16.2 q	0.86 (s)		C-1, -5, -9, -10
23	20.4 q	1.27 (s)		C-12, -13, -14, -18
24	106.6 d	6.63 (d, 2.0)	H-25	C-17, -18, -25
25	142.6 d	7.33 (d, 2.0)	H-24	C-17, -18, -24

DEPT data. Flash chromatography was carried out on Merck Si gel 60, preparative TLC on 1-mm plates of Merck Si gel 60 $PF_{254+366}$, and analytical TLC on Merck aluminum-backed precoated plates of Si gel 60 F_{254}, 0.2 mm. Mass spectra were recorded on a VG-70SE mass spectrometer; IR, on a Perkin−Elmer 1000 FT-IR spectrometer; and UV spectra, on a Shimadzu UV-2101 UV−vis spectrometer. Optical rotations were measured with a Perkin−Elmer 241 polarimeter for solutions in $CHCl_3$ or CH_2Cl_2.

Collection, Extraction, and Isolation. The sponge *Cacospongia* sp. was collected at Little Barrier Island, New Zealand, in 1990, and kept freeze-dried until used. A voucher specimen is retained in the School of Biological Science, University of Auckland, P. R. B. ref. no. 5.11). The sponge (50.2 g) was extracted with MeOH (350 mL × 3), and the combined extracts were concentrated to give a residue that was extracted with CH_2Cl_2 (100 mL × 3). Solvent was removed from the combined extracts to yield a dark oil (2.1 g) that was flash chromatographed. The column was eluted with solvents of increasing polarity from hexane to EtOAc. Fractions 27−33, eluted with hexane−EtOAc (2:1), contained sesterterpenes as shown by a ^{1}H NMR survey. The solid mixture was washed with Me_2CO−hexane (1:1), and the insoluble portion was purified by preparative TLC (CH_2Cl_2−EtOAc, 23:2), R_f 0.55, and crystallized from Me_2CO to yield 12-*O*-desacetylfuroscalar-16-one (**1**) (6 mg). The soluble portion was purified by column chromatography. Elution with CH_2Cl_2−EtOAc (23:2) gave scalarolide, R_f 0.58, which crystallized from hexane−CH_2Cl_2 as needles (2.2 mg), mp 292−294 °C dec (lit.[3] >300 °C dec); $[\alpha]^{20}_D$ +25.9°(*c* 0.15) (lit.[3] + 24.9°); correct IR, ^{1}H and ^{13}C NMR[3]; HRMS $[M]^+$ 386.2815, calcd for $C_{25}H_{38}O_3$ 386.2821.

12-*O*-Desacetylfuroscalar-16-one (1): colorless needles, mp 287−288 °C, $[\alpha]^{20}_D$ +44.8°(*c* 0.13, CH_2Cl_2); UV (CH_2Cl_2) λ_{max} 260 nm (logϵ 3.95); IR (film) ν_{max} 3360, 2916, 1652, 1446, 1386, 1233, 1026, 758, 724 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; DEIMS *m*/*z* (rel int) 384 (68), 366 (4), 351 (12), 233 (12), 215 (16), 191 (27), 175 (10), 161 (18), 149 (100), 148 (62), 137 (8), 123 (26), 109 (12), 95 (17), 81 (21), 69 (29), 55 (27), 40 (52); HRMS $[M]^+$ 384.2670, calcd for $C_{25}H_{36}O_3$ 384.2664.

12-Desacetylfuroscalar-12,16-dione (3). The hydroxyketone (**1**) (4 mg) in Me_2CO (0.5 mL) was oxidized with Jones' reagent for 30 min at room temperature. The mixture was poured onto ice, extracted with ether, and the extract worked up to give the dione, mp 215−216 °C (lit.[6] 218−220°); $[\alpha]^{20}_D$ + 120.2°(*c* 0.01,) (lit.[6] + 124.5°); correct UV and IR spectra.[6]

References and Notes

(1) Part 17: *J. Nat. Prod.* **1995**, *58*, 940−942.
(2) Faulkner, D. J. *Nat. Prod. Rep.* **1997**, *14*, 259−302 and previous reviews of this series.
(3) Walker, R. P.; Thompson, J. E.; Faulkner, D. J. *J. Org. Chem.* **1980**, *45*, 4976−4979.
(4) Bergquist, P. R.; Cambie, R. C.; Kernan, M. R. *Biochem. Syst. Ecol.* **1990**, *18*, 349−357.
(5) Ragoussis, V.; Liapis, M.; Ragoussis, N. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2545−2551.
(6) Cafieri, F.; De Napoli, L.; Fattorusso, E.; Santacroce, C.; Sica, D. *Gazz. Chim. Ital.* **1977**, *107*, 71−74.
(7) Cimino, G.; Cafieri, F.; De Napoli, L.; Fattorusso, E. *Tetrahedron Lett.* **1978**, 2041−2044.

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