Sardisterol, A New Polyhydroxylated Sterol from the Soft Coral *Sarcophyton digitatum* Moser

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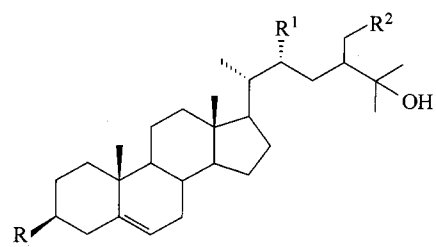
A new polyhydroxylated sterol, named sardisterol, was isolated from the soft coral *Sarcophyton digitatum* Moser. Its structure was determined as (22*R*, 24ξ)-methylcholest-5-en-3β, 22, 25, 28-tetraol-3-acetate on the basis of spectroscopic methods.

Keywords Soft coral, *Sarcophyton digitatum*, polyhydroxylated sterol

Polyhydroxylated sterols have been known to be the important secondary metabolites of corals, marine sponges.[1-7] Many of them showed cytotoxicity or antiinflammatory. In our continuing search to discover biologically active substances from marine organisms, a sample of soft coral *Sarcophyton digitatum* Moser was investigated and a new polyhydroxylated sterol (**1**), named sardisterol was isolated. Its structure was determined to be (22*R*, 24ξ)-methylcholest-5-en-3β, 22, 25, 28-tetraol-3-acetate by spectroscopic methods (Fig. 1).



1 R=OAc, R^1=R^2=OH
2 R=OAc, R^1=R^2=OAc

Fig. 1 Structures of sardisterol (**1**) and (22*R*)-methylcholest-5-en-3β, 22, 25, 28-tetraol-3, 22, 28-triacetate (**2**).

Compound **1** was obtained as colorless needles, m. p. 252—254℃. $[\alpha]_D^{20}$ − 6 (*c* 0.017, EtOH). Its molecular formula $C_{30}H_{50}O_5$ was established by the FAB MS [*m/z* 513 (M + Na)$^+$] and NMR data. The presence of one trisubstituted double bond, one primary hydroxyl group, one secondary hydroxyl group, one tertiary hydroxyl group and an acetoxy group were shown by the following ^{13}C NMR data δ 139.7 (s, C-5), 122.5 (d, C-6); 63.8 (t, C-28), 74.0 (d, C-22), 73.4 (s, C-25) and 73.9 (d, C-3) and the ^{1}H NMR data δ 5.37 (d, *J* = 5.3 Hz, 1H, H-6), 3.80—3.85 (m, 2H, H-28), 4.59—4.62 (m, 1H, H-3), 3.90—3.96 (m, 1H, H-22), 2.03 (s, 3H, CH_3COO), respectively. The ^{13}C NMR data from C-1 to C-19 were found to be in excellent agreement with those of (22*R*, 24ξ)-methylcholest-5-en-3β, 22, 25, 28-tetraol-3, 22, 28-triacetate (**2**)[8] suggesting that **1** possesses the same steroidal nucleus of **2** (Fig. 1). Therefore, all of the remaining three hydroxyl groups must be located at the side chain. The correlation between the protons Me-26 (δ 1.25), Me-27 (1.28) and H_2-28 (δ 3.83) with carbons at C-25 (δ 73.4) and C-24 (δ 49.6); between the proton Me-21 (δ 0.97) with carbons at C-20 (δ 43.0) and C-22 (δ 74.0) in HMBC spectrum (Fig. 2) revealed that these hydroxyl groups should be located at C-22, C-25 and C-28 positions in the side chain. The ^{13}C NMR data of **1** at C-25 (δ 73.4), C-27 (δ 28.6) and

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Table 1 ^{13}C NMR spectra data[a] of compound **1**[b] and **2**[8] (in $CDCl_3$)

position	1	2	position	1	2	position	1	2
1	38.1 t	38.2 t	11	21.0 t	21.1 t	21	12.4 q	13.0 q
2	27.9 t	27.8 t	12	39.7 t	39.7 t	22	74.0 d	77.9 d
3	73.9 d	74.0 d	13	42.7 s	42.8 s	23	27.7 t	25.2 t
4	37.0 t	37.1 t	14	56.2 d	56.3 d	24	49.6 d	46.4 d
5	139.7 s	139.7 s	15	24.4 t	24.4 t	25	73.4 s	72.8 s
6	122.5 d	122.6 d	16	27.7 t	27.2 t	26	28.6 q	28.4 q
7	31.8 t	31.9 t	17	53.4 d	53.1 d	27	27.7 q	27.2 q
8	31.8 d	31.8 d	18	11.9 q	11.9 q	28	63.8 t	66.0 t
9	50.1 d	50.1 d	19	19.3 q	19.4 q			
10	36.6 s	36.7 s	20	43.0 d	39.7 d			

[a]Spectra were recorded in $CDCl_3$ at 125 MHz; [b]Signals were assigned by DEPT, ^1H-^1H COSY and HMQC experiments.

C-28 (δ 27.7) to be identical with those of **2**[8] (Table 1) also confirmed a terminal structure of $(CH_3)_2C(OH)$ in the side chain. In addition, the MS fragments *m/z* (%) 129 (100) and 111 (56) of **1** strongly supported these deductions (Fig. 3).

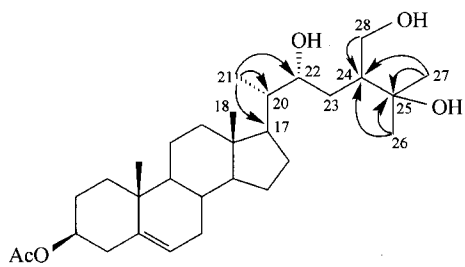

Fig. 2 Key HMBC correlation for **1**.

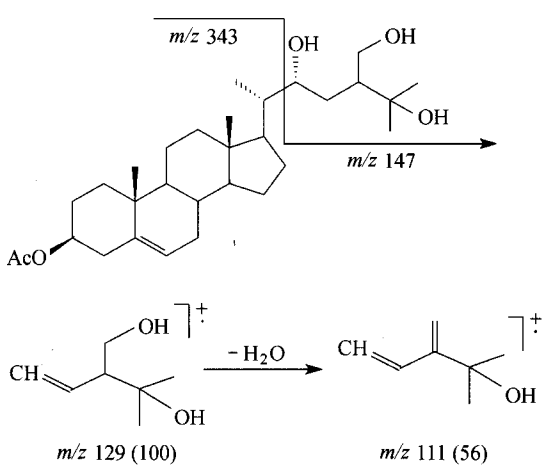

Fig. 3 Key MS fragmentation of **1**.

The stereochemistry of C-22 was determined to be *R* by comparing the ^{13}C NMR data with those of the model compounds, *i.e.* (22*R*)-cholest-5-en-3β,22-diol-3-benzoate and (22*S*)-cholest-5-en-3β, 22-diol-3-benzoate.[9] In conclusion, the structure of sardisterol (**1**) was determined to be (22*R*, 24ξ)-methylcholest-5-en-3β, 22, 25, 28-tetraol-3-acetate. (Fig. 1)

Experimental

General experimental procedures

^1H and ^{13}C NMR spectra were recorded with a Varian Unity INOVA spectrophotometer at 500 MHz in $CDCl_3$ and Py-d_5 using TMS as internal standard. IR spectra were recorded with a Nicolet 5-DX-FTIR spectrophotometer. MS spectra were obtained with Finnigan Mat TSQ 7000 and VG ZAB-HS mass spectrometers. Specific optical rotation was measured on PE-341 polarimeter.

Animal material

Soft coral *Sarcophyton digitatum* Moser was collected around Nansha Islands, China. A voucher specimen (No. 98-ns-22) is preserved in the Research Centre of Organic Natural Products, Zhongshan University.

Extraction and isolation

The fresh soft coral (500 g., after extracted and dried) was chopped to small pieces and extracted with 95% EtOH. After removal of solvent *in vacuo*, the residue was partitioned between 50% MeOH-petroleum ether. The aqueous MeOH solution was extracted by $CHCl_3$ and *n*-BuOH, respectively. The petroleum ether

extract (45 g) was chromatographied over Si gel 60 using *n*-hexane-EtOAc mixture of increasing polarity as eluting solvent system. Compound **1** (10 mg) was obtained as needle crystals from the *n*-hexane-EtOAc (1:1) eluted portion.

Compound 1 Colorless needles, m.p. 252—254℃, $[\alpha]_D^{20}$ −6(*c*, 0.017, EtOH); ^{1}H NMR ($CDCl_3$) δ: 5.37(d, *J* = 4.5 Hz, 1H, H-6), 4.59—4.62 (m, 1H, H-3), 3.90—3.96(m, 1H, H-22), 3.80—3.85 (m, 2H, H-28), 2.03 (s, 3H, CH_3COO), 1.28 (s, 3H, H-26), 1.25 (s, 3H, H-27), 1.02 (s, 3H, Me-19), 0.71 (s, 3H, Me-18), 0.97 (d, *J* = 6.5 Hz, 3H, Me-21); ^{1}H NMR (Py-d_5) δ: 5.35—3.59(m, 1H, H-6), 4.78—4.81 (m, 1H, H-3), 4.38—4.44 (m, 1H, H-22), 4.09—4.14 (m, 2H, H-28), 2.05 (s, 3H, CH_3COO), 1.50 (s, 3H, H-26), 1.49 (s, 3H, H-27), 1.25 (d, *J* = 6.5 Hz, 3H, Me-21), 0.99 (s, 3H, Me-19), 0.67 (s, 3H, Me-18); ^{13}C NMR spectra data: see Table 1; IR(KBr) ν: 3235, 1740, 1382, 1254, 1033 cm^{-1}; FABMS *m/z*: 513$[M+Na]^+$; EIMS *m/z* (%): 394 $[M-60-2H_2O]^+$, 301(10), 255(8), 147(14), 129(100), 111(56).

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9 Part of the ^{13}C NMR data of (22*R*)-cholest-5-en-3β,22-diol-3-benzoate: $\delta_{C\text{-}17}$ 53.2, $\delta_{C\text{-}20}$ 42.6, $\delta_{C\text{-}21}$ 12.5; and of (22*S*)-cholest-5-en-3β,22-diol-3-benzoate: $\delta_{C\text{-}17}$ 52.6, $\delta_{C\text{-}20}$ 40.3, $\delta_{C\text{-}21}$ 11.6, in Letourneux, Y.; Qui, K.-H.; Gut, M.; Lukacs, G. *J. Org. Chem.* **1975**, *40*, 1975.

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