Marine Terpenes and Terpenoids. XIII.[1] Isolation of a New Dihydrofuranocembranoid, Sarcophytonin E, from the *Sarcophyton* sp. Soft Coral of Okinawa

Masaru KOBAYASHI* and Takumi HIRASE

Faculty of Pharmaceutical Sciences, Hokkaido University, Kita-ku, Sapporo 060, Japan. *Received June 3, 1991*

A new dihydrofuranocembranoid, sarcophytonin E (1a), was isolated from the *Sarcophyton* sp. soft coral of Chatan, Okinawa. The structure of 1a was derived from the spectroscopic data, and was confirmed by correlation with the known compound 16-deoxosarcophine (2a). Compound 1a was found to be converted, on storage, to the butenolide 3a. The proton nuclear magnetic resonance spectra of the 2-methoxy-2-trifluoromethylphenylacetic acid esters of 1a and 3a indicated that they are enantiomerically pure, and showed our previous assumption, that the cembranoids isolated from this soft coral are enantiomeric mixtures, to be incorrect.

Keywords soft coral; *Sarcophyton* sp.; cembranoid; dihydrofuranocembranoid; sarcophytonin E

Previously we isolated three new cembranoids, sarcophytonins B, C and D, together with the known compounds cembrene C, sarcophine (**2b**), 16-deoxosarcophine (**2a**) and sarcophytonin A (**4**), from the *Sarcophyton* sp. soft coral, collected off the coast of Chatan, Okinawa.[1,2] Subsequent study of the minor components of this soft coral resulted in the isolation of a new compound designated sarcophytonin E (**1a**). The proton and the carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra of **1a** showed signals due to the dihydrofuran ring (^{13}C-NMR, δ 78.3 (t), 127.8, 133.5 (each s), 83.7 (d); ^{1}H-NMR, δ 4.51, 2H, m, 5.58, 1H, m), in close analogy with those of sarcophytonin A (**4**, ^{13}C-NMR, δ 78.4, 127.2, 134.0, 84.1; ^{1}H-NMR, δ 4.48, 5.52).[3] Other signals due to the cembrane ring were also common between these two compounds except that one of the trisubstituted double bonds in **4** was converted to a terminal methylene and a secondary alcohol (^{13}C-NMR, δ 70.3 (d), 109.5 (t), 155.0 (s)). Sarcophytonin E monoacetate (**1b**) was found to be identical with the allylic alcohol monoacetate which was derived previously from 16-deoxosarcophine (**2a**) by hydrolysis, acetylation and dehydration.[2]

Dihydrofurano-type cembranoids are quite susceptible to autoxidation and afford degradation products, even during storage at -30 °C in the dark. In the preceding paper, we described in detail this autoxidation process, of which the conversion to the butenolide derivatives was the major pathway.[1] Probably, traces of peroxidic radical initiator impurities caused the formation of C-16 hydroperoxide, which, on dehydration, led to the butenolides. Purified sarcophytonin E was found, similarly, to give several oxidation products, of which the butenolide **3a** was the major product (*ca.* 40%, see Experimental).

The specific rotation ($+120°$) of the major component, sarcophytonin A (**4**), reported in the previous paper,[2] was different from that ($-92°$) of **4** which we first obtained from *S. glaucum* of Ishigaki Island, Okinawa.[3] This compound was subsequently reported as a deoxygenation product of several sarcophytonin A epoxides,[4,5] but the reported specific rotations varied considerably in both sign and magnitude ($+239°$ to $-210°$). Similarly, the specific rotation of 16-deoxosarcophine (**2a**), isolated from our Chatan material, was $+129°$ while the recorded values were diverse ($+157°$ to $-191°$).[4] These facts indicated that dihydrofuranocembranoid derivatives of this type exist in both (2*R*)- and (2*S*)-enantiomeric form and led us to conclude that our cembranoids, isolated from the Chatan material, and showing smaller magnitude of rotation, are composed of enantiomeric mixtures.[2] This time we prepared 2-methoxy-2-trifluoromethylphenylacetic acid (MTPA) esters (**1c**, **3c** and **3d**), in an attempt to determine the enantiomeric ratio of **1a** and **2a**. The (*S*)-MTPA ester **1c** was prepared by conversion of **2a** isolated from the soft coral used in this study. The (*S*)- and (*R*)-MTPA esters **3c** and **3d** were prepared from **3a** which was obtained by autoxidation of natural **1a**. However, examination of the ^{1}H-NMR spectra of these MTPA esters indicated that they consisted of single sets of signals corresponding to enantiomerically pure compounds, thus indicating that our previous assumption was incorrect. The large range of reported magnitudes of the specific rotations, at least for 16-deoxosarcophine (**2a**) and probably for sarcophytonin A (**4**), appears to be simply a result of inaccurate measurement.

The MTPA esters **3c** and **3d** were expected to reveal the absolute configuration of the (+)- and (−)-16-deoxosarcophine, which were assigned originally from the interpretation of the circular dichroism (CD) data of the butenolide derivative (+)-sarcophine.[6,7] In principle, the plane which involves the C-7 carbinyl methine and the ester carbonyl group is supposed to bisect the average plane of the cembrane ring, and affords $\Delta\delta$'s having opposite sign for the chemical shifts of the protons in the

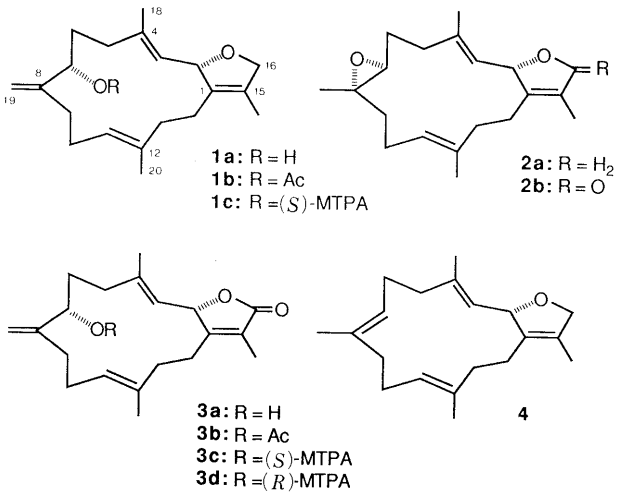

Chart 1

two segments.[8] In fact, even **3c** and **3d** exhibited small but distinctly different patterns of ^{1}H-NMR spectra, the $\Delta\delta$'s were observed for protons at C-2, C-3, and C-11 all having positive sign (+0.011, +0.091, and +0.021 ppm, respectively), so the attempted confirmation of the absolute configuration was unsuccessful. Apparently, the characteristic conformational movement of the cembrane ring makes the straightforward application of the MTPA method inappropriate for these compounds.

Experimental

Melting points were determined on Kofler hot stage and are uncorrected. Optical rotations were determined in $CHCl_3$ on a JASCO DIP-370 digital polarimeter. NMR spectra were determined in $CDCl_3$ solution on a JEOL JMN GX-400 spectrometer at 400 MHz (^{1}H) and on a JEOL JMN FX-90Q spectrometer at 22.5 MHz (^{13}C) with tetramethylsilane as an internal standard. Mass spectra (MS) were determined on a JEOL JMS D300 mass spectrometer. Chromatography was done by flash column chromatography[9] using silica gel (Wako gel C-300, 200—300 mesh, Wako Pure Chemical Industries).

Isolation of Sarcophytonin E (1a) The separation and purification of major known cembranoid derivatives from 20.9 g of the crude extract of the *Sarcophyton* sp. collected in October 1986 in Chatan, Okinawa, were described in the previous paper.[2] The cembranoid mixture obtained from the extract by chromatography with 15% ethyl acetate–hexane (250 mg) was used. It was separated into subfraction 1 (*ca.* 100 mg), which was composed of **2b**, and subfraction 2 (*ca.* 100 mg) with 2.5% Et_2O in $CHCl_3$. Subfraction 2 was purified with 2.5% Et_2O in $CHCl_3$ giving 84.2 mg of **1a**.

Sarcophytonin E (1a) Oil, $[\alpha]_D^{25}$ +120° (c=2.06). ^{1}H-NMR δ: 1.59, 1.65 (each 3H, br s, 17, 20-H_3), 1.82 (3H, br s, 18-H_3), 4.16 (1H, br d, J=10.5 Hz, 7-H), 4.51 (2H, m, 16-H_2), 4.90 (1H, br s, 19-H_2), 5.05 (1H, br t, J=7.0 Hz, 11-H), 5.07 (1H, br t, J=1.5 Hz, 19-H), 5.19 (1H, br d, J=10.5 Hz, 3-H), 5.58 (1H, m, 2-H). ^{13}C-NMR δ: C-1 (133.5), C-2 (83.7), C-3, 11 (125.0, 127.3), C-4 (138.9), C-5, 9, 13 (34.0, 36.3, 36.9), C-6, 10 (30.1, 32.1), C-7 (70.3), C-8 (155.0), C-12 (136.0), C-14 (24.7), C-15 (127.8), C-16 (78.3), C-17 (10.1), C-18, 20 (15.3, 15.5), C-19 (109.5). MS m/z: 302 (M^+), 287, 269, 243. High-resolution MS [Found (Calcd)] m/z: $C_{20}H_{30}O_2$ (M^+), 302.2273 (302.2245).

Sarcophytonin E Acetate (1b) Acetylation of **1a** by a usual method (Ac_2O–pyridine, room temperature, overnight) gave **1b** ($[\alpha]_D^{20}$ +90° (c=0.28)), which was identical with that ($[\alpha]_D$ +86°) prepared from 16-deoxosarcophine **2a**,[2] by direct comparison of their ^{1}H-NMR spectra and thin-layer chromatographic (TLC) behavior.

16-Oxosarcophytonin E (3a) A five-month-old sample of **1a**, stored in the dark at −30 °C, was found to have decomposed. The product was subjected to silica gel column chromatography with ethyl acetate–hexane (2:8), giving 14.6 mg of unchanged **1a** and 31 mg of **3a**. Oil, $[\alpha]_D^{20}$ +120° (c=0.60). ^{1}H-NMR δ: 1.62 (3H, s, 20-H_3), 1.84 (3H, t, J=1.5 Hz), 1.89 (3H, s), 4.09 (1H, br d, J=11.0 Hz, 7-H), 4.93, 5.07 (each 1H, s, 19-H_2), 5.00 (1H, d, J=10.0 Hz, 3-H), 5.12 (1H, br t, J=7.0 Hz, 11-H), 5.61 (1H, dq, J=10.0, 1.5 Hz, 2-H). ^{13}C-NMR δ: C-1 (162.9), C-2 (78.9), C-3 (121.5), C-4 (143.7), C-5, 9, 13 (33.9, 36.0, 36.8), C-6, 9 (30.0, 32.2), C-7 (70.5), C-8 (154.5), C-11 (125.9), C-14 (26.3), C-15 (122.9), C-16 (174.8), C-17 (9.0), C-18, 20 (15.5, 16.0), C-19 (110.0). MS m/z: 316 (M^+), 298, 283, 270, 255. High-resolution MS [Found (Calcd)] m/z: $C_{20}H_{28}O_3$ (M^+), 316.2028 (316.2039).

16-Oxosarcophytonin E Acetate (3b) Oil, $[\alpha]_D^{20}$ +83° (c=0.84). ^{1}H-NMR δ: 1.66 (3H, s, 20-H_3), 1.83 (3H, t, J=1.5 Hz), 1.91 (3H, s), 2.07 (3H, s, OAc), 4.85 (1H, d, J=10.0 Hz, 3-H), 4.89, 4.92 (each 1H, br s, 19-H_2), 5.16 (1H, br t, J=6.5 Hz, 11-H), 5.26 (1H, br d, J=10.5 Hz, 7-H), 5.59 (1H, dq, J=10.0, 1.0 Hz, 2-H). MS m/z: 358 (M^+), 316, 298, 283. High-resolution MS [Found (Calcd)] m/z: $C_{22}H_{30}O_4$ (M^+), 358.2163 (358.2144).

***(S)*- and *(R)*-MTPA Esters of 16-Oxosarcophytonin (3c and 3d) and *(S)*-MTPA Ester of Sarcophytonin E (1c)** (a) A solution of **3a** (7 mg) in CH_2Cl_2 (0.5 ml) was treated at room temperature with (*S*)-MTPA (30 mg), dicyclohexylcarbodiimide (DCC, 30 mg) and dimethylaminopyridine (10 mg) for 2 h. The mixture was charged on a column of silica gel. Elution with ethyl acetate–hexane (2:8) gave the (*S*)-MTPA ester (**3c**, 7.4 mg) as an oil, $[\alpha]_D^{20}$ −8° (c=1.47). ^{1}H-NMR δ: 1.675 (3H, s, 20-H_3), 1.870 (6H, s, 17, 18-H_3), 2.77 (1H, ddd, J=14.5, 11.5, 7.5 Hz), 3.504 (3H, d, J=1.5 Hz), 4.712 (1H, d, J=10.0 Hz, 3-H), 4.892, 4.933 (each 3H, s, 19-H_2), 5.204 (1H, br dd, J=7.5, 6.5 Hz, 11-H), 5.382 (1H, br d, J=10.5 Hz, 7-H), 5.578 (1H, dq, J=10.0, 1.5 Hz, 2-H).

(b) Treatment of 6 mg of **3a** with (*R*)-MTPA according to the same procedure as in (a) gave the (*R*)-MTPA ester (**3d**, 6 mg). Oil, $[\alpha]_D^{20}$ +30° (c=1.25). ^{1}H-NMR δ: 1.678 (3H, s, 20-H_3), 1.846, 1.880 (each 3H, s, 17, 18-H_3), 2.730 (1H, m), 3.495 (1H, d, J=1.0 Hz), 4.621 (1H, d, J=10.0 Hz, 3-H), 4.830, 4.870 (each 1H, br s, 19-H_2), 5.183 (1H, br dd, J=7.0, 6.5 Hz, 11-H), 5.344 (1H, br d, J=10.5 Hz, 7-H), 5.567 (1H, dq, J=10.0, 1.5 Hz, 2-H).

(c) Compound **1a** (0.2 mg) prepared from **2a** as described in a previous report,[2] was treated with (*S*)-MTPA according to the same procedure as in (a) to afford 0.2 mg of the (*S*)-MTPA ester (**1c**) as an oil, $[\alpha]_D^{21}$ −10° (c=0.040; due to the low concentration of the sample, this specific rotation is not reliable). ^{1}H-NMR δ: 1.66, 1.67 (each 3H, br s, 17, 20-H_3), 1.80 (3H, br s, 18-H_3), 2.55 (1H, m), 3.53 (3H, d, J=1.0 Hz), 4.51 (2H, br s, 16-H_2), 4.89, 4.91 (each 1H, br s, 19-H_2), 4.94 (1H, d, J=10.0 Hz, 3-H), 5.14 (1H, m, 11-H), 5.40 (1H, br d, J=10.5 Hz, 7-H), 5.54 (1H, m, 2-H).

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