Marine Terpenes and Terpeoids. IX.[1] Structures of Six New Cembranoids, Sarcophytols F, K, P, Q, R and S, from the Soft Coral *Sarcophyton glaucum*

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The structures of six new cembranoids, sarcophytol P (3a), sarcophytol R (4), sarcophytol S (5), sarcophytol Q (8a), sarcophytol K (11a), and sarcophytol F (14a), isolated from the soft coral *Sarcophyton glaucum*, were determined from the spectroscopic properties and by synthesis, or by analyses of their derivatives formed on storage in $CHCl_3$. Sarcophytol P (3a) was shown to be the 20-hydroxy derivative of the major component sarcophytol A (1a), and afforded the transannular cyclization product 6 on storage in $CHCl_3$ at room temperature, in the same way as 1a. Sarcophytol R (4) and sarcophytol S (5) were correlated to 1a by conversion of its 7*R*,8*R* (7a) and 7*S*,8*S* (7b) epoxide derivatives. Sarcophytol Q (8a) was shown to be a 1,4,14-trihydroxycembranoid, and was converted to the known ring-cleaved aldehyde 9. Sarcophytol K (11a) was a 13,14-dihydroxycembranoid having a 1*E*,3*Z*-diene moiety. The absolute configurations of 11a and its 1*Z*,3*E*- and 1*Z*,3*Z*-isomers sarcophytols B (2a) and J (13a) were determined by a circular dichroism study of their bis-*p*-dimethylaminobenzoate derivatives. Sarcophytol F (14a) was a 1*E* isomer of 1a and showed characteristic proton nuclear magnetic resonance spectral properties due to the restricted conformational interconversion. The structure was derived by characterizing two decomposition products, the same pentaene (15) and dihydrofuran (17) derivatives as those derived from 1a.

Keywords soft coral; *Sarcophyton glaucum*; cembranoids; sarcophytol F; sarcophytol K; sarcophytol P; sarcophytol Q; sarcophytol R; sarcophytol S

The remarkably wide range of biological activities of fourteen-membered cembranoid diterpenes[2] makes these compounds interesting targets for identification as natural products and for synthetic studies. The effective inhibition of the powerful tumor promotion system (dimethylbenzanthracene-teleocidin) in a two-stage carcinogenesis experiment on mouse dorsal skin[3] by the simple cembranoids sarcophytol A (**1a**)[4,5] and sarcophytol B (2a)[4,6] prompted us to re-examine the constituents of their original source, *Sarcophyton glaucum*, a ubiquitous soft coral in the coral reefs of Indo-Pacific coastal waters. In early work, eight new cembranoid derivatives, closely related to **1a** or **2a**, were isolated and their structures characterized.[6] Sarcophytols F (**14a**) and K (**11a**) were isolated at the same time, but their structures remained unclarified. The present report deals with the structures of sarcophytols P (**3a**), R (**4**), S (**5**) and Q (**8a**) which were isolated subsequently, together with those of **11a** and **14a**.

Sarcophytol P (**3a**), $C_{20}H_{32}O_2$, was found to be a monooxy derivative of **1a**. The proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra of **3a** showed typical signals due to the simple 14-hydroxy-1*Z*,3*E*,7*E*,11*E*-cembratetraene system (Experimental), as found in **1a**, but one of its methyl group was converted to a hydroxymethyl group (^{1}H-NMR, δ 4.04, 4.29). The mass spectrum (MS, *m/z* 304, 273) and ultraviolet (UV) spectrum (252 nm) supported this, but direct comparison of the ^{1}H-NMR spectra of **3a** and **1a** showed significant discrepancies as regards the chemical shifts of corresponding protons. This could be attributed to the presence of internal hydrogen bonding in **3a**, which influences the average conformation of the cembrane ring.[1,7] In contrast, the ^{1}H-NMR spectra of their acetates **1b** and **3b** showed close analogy concerning the protons at C-2,3,7 and C-14 to C-19; the maximum discrepancy was only 0.03 ppm. The hydroxylated methyl group was assigned to C-20, because the ^{13}C-NMR signal (δ 42.0) assigned to C-13 in **1b** was shifted, by the γ-effect, to upper-field (δ 37.2) in **3b**. The structure of **3a** was confirmed by its transannular cyclization as follows.

The crude cembranoid mixture of *S. glaucum* is stable and showed little detectable change at room temperature for two years, if a sufficient amount was kept tightly sealed in a flask. However, small amounts of purified samples, particularly those having a 14-hydroxy 1,3-diene system,

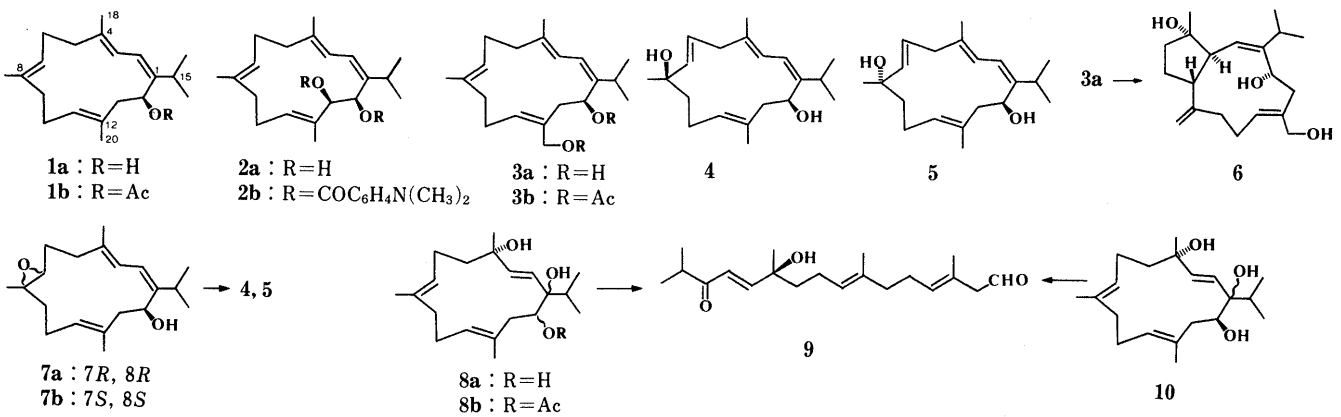
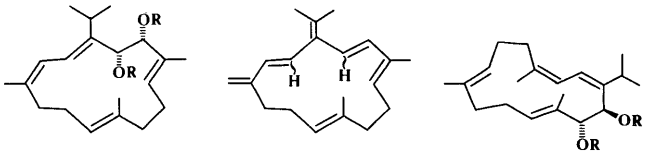


Chart 1

were rather unstable. The major decomposition proceeds first by epoxidation at the C-3 double bond, probably assisted by the C-14 hydroxyl group, followed by side reactions. This was initially regarded as troublesome but later proved to be often quite useful. Thus, the major components sarcophytols A (**1a**), B (**2a**), G and E, having a common 14*S*-hydroxy-1*Z*,3*E*,7*E*,11*E*-tetraene moiety, were found to be converted *via* the 3*S*,4*S*-epoxide to a *trans*-fused [9.3.0]cyclotetradecane system, simply by keeping them in $CHCl_3$ at room temperature for 7—20 d.[1] The yields are modest, the highest being that of **1a** (42%), but this transannular cyclization is a common feature of such triene systems. The ^{1}H-NMR spectrum of **3a** showed the presence of nuclear Overhauser effect (NOE) between H-3 and H-14 (17%) and indicated that the relative dispositions of the carbons C-1 to C-5 and C-14 to C-18 are roughly the same as in **1a**.[6] Treatment of **3a** in $CHCl_3$ at room temperature for 9d indeed gave the bicyclic system **6** in 10% yield. Its ^{1}H-NMR spectrum showed the H-2 signal at δ 5.03 (d, J=10.0 Hz) and H-18 at 1.09 (s). The appearance of exo-methylene protons (δ 4.79, 4.90, H-19), and retention of the hydroxymethyl group in **6**, indicate that the position of the hydroxymethyl of **3a** is C-20. The absolute configuration of **3a** at C-14 was shown, by Horeau determination,[8] to be *S*, the same as those of the cembranoids hitherto isolated from *S. glaucum*. The stereochemistry of **6** at C-3,4,7 was deduced to be as shown in Chart 1, by analogy with those derived from 14*S*-hydroxy 1*Z*,3*E*,7*E*,11*E* cembranoids previously examined.[1]

Sarcophytol R (**4**) and sarcophytol S (**5**) were a diastereomeric pair of diols having the molecular formula $C_{20}H_{32}O_2$. The ^{1}H-NMR spectra suggested them to be also derivatives of **1a** having the same 1,3-diene moiety and C-14 hydroxyl group; the hydroxymethine at C-14 resonated at markedly low field (**4**, δ 4.64; **5**, 4.71) due to the deshielding effect of the diene, which is characteristic of this system.[6] Both **4** and **5** are allylic alcohols and showed signals of an *E*-disubstituted double bond (**4**, δ 5.57, d, J=15.5 Hz, 5.69, dt, J=15.5, 6.5 Hz; **5**, δ 5.56, d, J=15.5 Hz, 5.72, ddd, J=15.5, 7.5, 6.0 Hz) and a methyl group adjacent to an oxygen atom (**4**, δ 1.33, s; **5**, δ 1.29, s). Since both diastereomers of 12-hydroxy-Δ^{10} diols (sarcophytol G and sarcophytol D) are known and their structures were established by synthesis,[6,9] the remaining possibilities, on biogenetic grounds, are 8-hydroxy-Δ^6 isomers. This was proved in the same way as done for the structure elucidation of sarcophytols D and G, by treatment of the 7*R*,8*R*- (**7a**) and 7*S*,8*S*-epoxy (**7b**) derivatives of **1a**[5] with diphenyl diselenide-$NaBH_4$ followed by oxidative elimination with H_2O_2.[10] The resultant allylic alcohols from **7a** and **7b** were identical with sarcophytol R (**4**) and sarcophytol S (**5**), respectively.

Sarcophytol Q (**8a**), $C_{20}H_{34}O_3$, was a triol with an *E*-disubstituted double bond at C-2,3. Its spectroscopic properties (Experimental) were similar to but not identical with those of the triol **10**, which was previously obtained by mild acid treatment of the 3*S*,4*S*-epoxy derivative of sarcophytol A acetate (**1b**), followed by hydrolysis.[1,5] Chromic acid treatment of **10** has been shown to give a seco-aldehyde **9**, $[\alpha]_D$ −3.0°. The same treatment of **8a** was found to give **9**, $[\alpha]_D$ −3.8°, so that the configuration at C-4 of **8a** is the same as that of **10**. It is possible, though not certain, that **8a** was derived secondarily from the isomer of **1a** through



11a : R=H
11b : acetonide
11c : R=$COC_6H_4N(CH_3)_2$

12

13a : R=H
13b : R=$COC_6H_4N(CH_3)_2$

Chart 2

autoxidation during the isolation process. Various 4-hydroxy-Δ^2 cembranoid derivatives have been found in tobacco leaves.[11]

Sarcophytol K (**11a**), $C_{20}H_{32}O_2$, was a geometrical isomer of sarcophytol B (**2a**) and sarcophytol J (**13a**, 1*Z*,3*Z*) and showed common UV (254 nm) and MS (M^+, m/z 304) spectroscopic data. It was labile, compared wth **2a**, and on prolonged storage in $CDCl_3$, the ^{1}H-NMR sample of **11a** was converted partly into the hexaene **12**, having *E*- and *Z*-disubstituted double bonds, by serial dehydration of the two hydroxyl groups. ^{1}H-NMR studies of **11a** showed the presence of a 13,14-glycol group and 1,3-diene moiety but there were significant differences as compared with **2a** and **13a**. The H-14 signal was unaffected by the 1,3-diene and appeared at the normal position (δ 4.08 or 4.16, each d, J=9.5 Hz) in contrast to those of **2a** (δ 4.73, dd, J=8.0, 2.0 Hz) and 13a (δ 4.79, dd, J=9.5 and 2.0 Hz). Instead, H-15 is located in the deshielding region of the 1,3-diene and is shifted by *ca.* 0.4 ppm to lower field (δ 2.96, sept, J=7.0 Hz) than those of **2a** and **13a**. The ^{13}C-NMR chemical shift of one the olefinic methyl groups (δ 22.1 or 23.8) together with an up-field-shifted C-5 signal (δ 31.8) indicated that the geometry of the 3,4-double bond is *Z*, as found in **13a** (C-5, δ 31.0; C-18, δ 23.2 or 23.5 or 26.4).[6,12] The ^{1}H-NMR experiment of **11a** revealed the 1*E*,3*Z* geometry, since significant NOEs were observed between H-3 (δ 6.22, br d, J=11.5 Hz) and H-15 (9%), and between H-3 and H-18 (δ 1.82, d, J=1.0 Hz, 5%). Irradiation at H-2 (δ 6.08, d, J=11.5 Hz) caused NOEs at one of the hydroxymethine groups (δ 4.16) and a multiplet at δ 2.20, supposed to be due to one of the C-5 methylene protons. The vicinal coupling constant of the 13,14-hydroxymethine protons (9.5 Hz) indicate the *anti*-disposition of these two protons. This coupling constant was retained in the acetonide **11b** (9.0 Hz) and indicated that little conformational change had occurred in the cembrane ring on going from the glycol **11a** to the acetonide **11b**. The relation of the two hydroxy groups is thus nearly *gauche* to each other, and the preferred partial conformation of **11a** could be represented as A or B in Fig. 1, or their enantiomer. The circular dichroism (CD) study of the bis-*p*-dimethylaminobenzoate **11c** showed 13*R*,14*R* configuration from the typical pattern of split Cotton curve due to the negative dibenzoate chirality,[13] with $[\theta]^{15}$ −160000 (324 nm) and $[\theta]^{15}$ +112000 (299 nm) (Fig. 2). Similarly, sarcophytol B (**2a**) and sarcophytol J (**13a**), whose relative configuration had been postulated to be 13*R*,14*R* from the spatial arrangements of C-1 to C-5 and C-13 to C-18 (Fig. 1),[6] were examined by CD; they showed closely related split Cotton curves in virtually the same positions as in the case of **11c** (Fig. 2). Thus, these three compounds (**2a**, **11a**, **13a**) bear the same absolute configurations at C-13,14, which is reasonable on

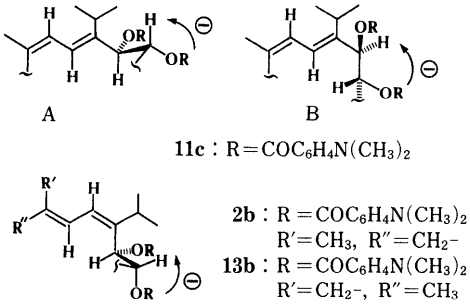


Fig. 1. Illustration of the Negative Chirality of the Bis-*p*-dimethylaminobenzoates **2b**, **11c** and **13b**

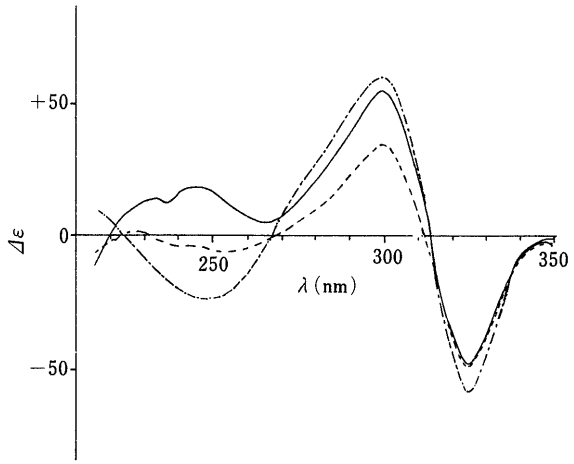


Fig. 2. CD Spectra of **2b**, **11c** and **13b**
2b,——; **11c**, – – –; **13b**, —·—.

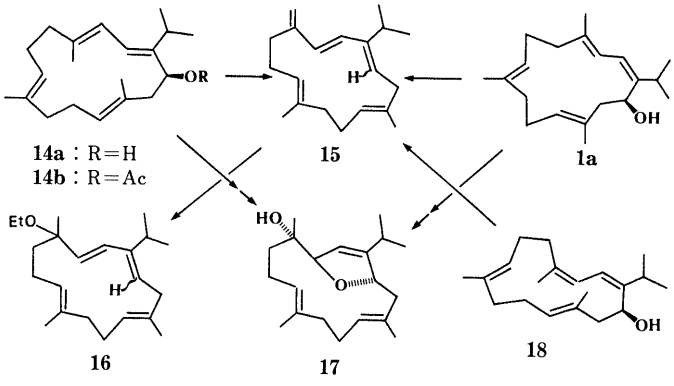


Chart 3

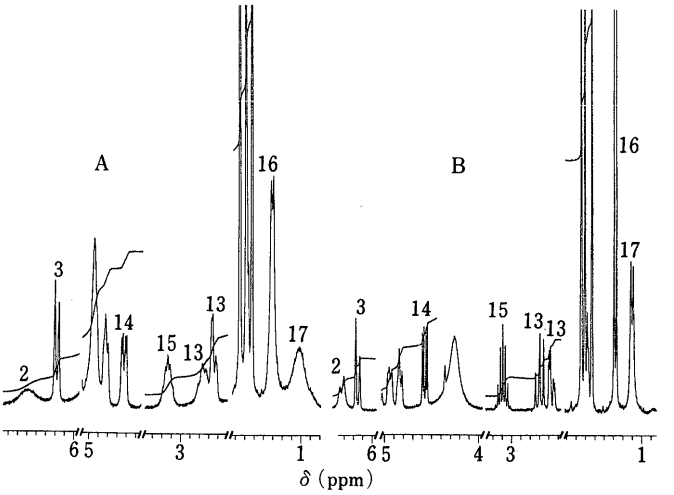


Fig. 3. Partial ^{1}H-NMR Spectra of Sarcophytol F (**14a**) in C_5D_5N, at 27 °C (**A**) and 70 °C (**B**)

biogenetic grounds.

Sarcophytol F (**14a**), $C_{20}H_{32}O$, was a geometrical isomer of **1a** whose 1*Z* double bond was converted to *E*, and afforded the monoacetate **14b**. It was isolated in our earlier work,[6] but its labile nature precluded structure determination. A purified sample of **14a** (a ^{1}H-NMR sample in $CDCl_3$ for instance) often decomposed overnight. It was found, later, to be sufficiently stable when kept as a pyridine solution. The spectral properties (Experimental) indicated the typical pattern of monohydroxy 1,3,7,11-cembratetraene as seen with sarcophytol A (**1a**) and sarcophytol N (**18**, 1*Z*,3*Z*),[6] but its ^{1}H-NMR spectra taken in $CDCl_3$, C_5D_5N (Fig. 3, **A**), or in C_6D_6 at room temperature, were characteristic. It showed the signals of H-2 and H-17 as a broadened envelope, and those of H-13,14,15,16 were also broadened, though to a lesser extent. The spectrum taken in C_5D_5N at 70 °C (Fig. 3. **B**) showed prominent sharpening of these signals but those of H-2 and H-17 were still broad. At −38 °C, the signals were better resolved than those at room temperature, and in particular, H-2 appeared as a doublet (J=11.5 Hz), sharper than that of H-3 (J=11.5 Hz) which has an allylic coupling with H-18. Thus, sarcophytol F (**14a**) apparently has severe steric hindrance which obstructs facile conformational interconversion, even at 70 °C, in contrast to other cembranoids isolated from *S. glaucum*.[4,6,9] The NOE which was observed between H-3 and H-15 indicated that the geometry at C-1 double bond is *E*. The ^{13}C-NMR spectrum of **14a** revealed the signals of three olefinic methyl groups at δ 14.2, 15.8 and 17.1, so that the geometries at C-3, C-7 and C-11 are *E*.[12] The intensity of the C-14 signal (δ 65.0) was quite weak and was not distinguishable by the INEPT method under the conditions employed.

The fragile nature of **14a** made the attempted derivatization unfruitful. The structure of **14a** was derived instead by analyzing the decomposition products of the initially purified material. After keeping **14a** in $CHCl_3$ for 24 h and 6 d, the mixture containing mostly decomposition products were separated by column chromtography. The least polar product **15**, formed after 24 h, was a conjugated triene and was identical with that obtained from **1a** and **18**.[6] Apparently the conjugated triene in the fourteen membered ring generates significant strain, and **15** was found to be converted to the ethyl ether **16**, derived by reaction with the stabilizer ethanol, when kept further in $CHCl_3$. Another major decomposition product was a dihydrofuran derivative **17**, which was also identical with that obtained from **1a**,[1,5] by direct comparison. This, together with the result obtained by Horeau determination, established the absolute configuration of **14a** at C-14 as S, the same as that of **1a** and **18**. Other polar products from **14a** were supposed to be the transannular cyclization products but the composition is more complex than those derived from the 1*Z*,3*E* isomers reported previously.[1] Formation of **17** indicates that the decomposition pathway of **14a** is similar to that of **1a**, triggered off by initial formation of the 3,4-

epoxide. Analysis of these transannular cyclization products, together with those derived from the 1*Z*,3*Z* derivatives **13a** and **18**, and the 1*E*,3*Z* derivative **11a**, is in progress.

Experimental

Infrared (IR) spectra were determined on a JASCO A102 spectrometer. UV spectra were determined on a Shimadzu UV-220 spectrometer. Optical rotations were determined in $CHCl_3$ on a JASCO DIP-4 digital polarimeter. NMR spectra were determined, unless otherwise specified, in $CDCl_3$ on a JEOL JMS GX-270 spectrometer at 270 MHz (^1H) and on a JEOL JNM FX-90Q spectrometer at 22.5 MHz (^{13}C) with tetramethylsilane as an internal standard. ^{13}C-NMR signals were assigned by using INEPT and by comparisons of chemical shift data with those of structurally related cembranoids.[4,6,9] Mass spectra were determined on a JEOL JMS D300 mass spectrometer. CD spectra were determined on a JASCO J-500A spectrometer. Chromatography was done by flash column chromatography[14] using silica gel (Wako gel C-300, 200—300 mesh, Wako Pure Chemical Industries). Horeau determination was done using gas chromatography and high performance liquid chromatography as reported previously.[6]

Isolation of Sarcophytols P (3a), R (4), S (5), and Q (8a) Chromatography fractions 63—95, obtained in a previous study and stored at −30 °C,[6] were used as the source material. They were unresolved complex mixtures containing known (sarcophytols B (**2a**), C, D, E, G, H, I, J (**13a**), O)[4,6,9] and unknown (sarcophytols P (**2a**), R (**4**), S (**5**), Q (**8a**), K (**11a**)) cembranoids, and the complete resolution of these compounds by a single column chromatography has not been possible. The R_fs of these compounds on thin-layer chromatography (TLC), in the order of ethyl acetate–hexane (1.5:4, twice), Et_2O–$CHCl_3$ (1:3.5) and 1.5% MeOH in $CHCl_3$ twice), are as follows: sarcophytol A (**1a**, 0.97, 0.90, 0.94); sarcophytol B (**2a**, 0.48, 0.42, 0.63); sarcophytol C (0.47, 0.32, 0.60); sarcophytol D (0.31, 0.32, 0.53); sarcophytol E (0.19, 0.12, 0.29); sarcophytol F (**14a**, 0.93, 0.88, 0.92); sarcophytol G (0.56, 0.47, 0.71); sarcophytol H (0.42, 0.43, 0.67); sarcophytol I (0.43, 0.39, 0.61); sarcophytol J (**13a**, 0.41, 0.35, 0.52), sarcophytol K (**11a**, 0.35, 0.33, 0.53); sarcophytol L (0.09, 0.02, 0.09); sarcophytol M (0.99, 0.93, 0.95); sarcophytol N (**18**, 0.94, 0.86, 0.92) sarcophytol O (0.21, 0.15, 0.32); sarcophytol P (**3a**, 0.25, 0.24, 0.43); sarcophytol Q (**8a**, 0.27, 0.20, 0.48); sarcophytol R (**4**, 0.34, 0.32, 0.59); sarcophytol S (**5**, 0.27, 0.24, 0.47). The new compounds (**3a**, **4**, **5**, **8a**) were isolated using the portions of the corresponding fractions by serial flash column chromatography, with slight modifications of the above three solvent systems.

Sarcophytol P (3a) Oil, $[\alpha]_D^{28}$ −66° (*c*=0.84). ^1H-NMR δ: 1.10, 1.11 (each 3H, d, *J*=7.0 Hz), 1.53 (3H, s), 1.75 (3H, d, *J*=1.0 Hz, H-18), 2.32 (1H, dd, *J*=14.5, 5.5 Hz, H-13), 2.52 (1H, dd, *J*=14.5, 6.0 Hz, H-13), 2.64 (1H, sept, *J*=7.0 Hz, H-15), 4.04 4.29 (each 1H, d, *J*=12.5 Hz, H-20), 4.88 (1H, t, *J*=5.5 Hz, H-14), 4.98 (1H, m), 5.15 (1H, dd, *J*=8.5, 3.5 Hz), 5.94 (1H, br d, *J*=11.0 Hz, H-3), 6.11 (1H, d, *J*=11.0 Hz, H-2). ^{13}C-NMR δ: C-1 (148.4), C-2,3 (119.4, 119.8), C-4,12 (136.6, 137.0), C-5,9 (38.1, 39.1), C-6,10 (23.8, 25.0), C-8 (133.9), C-11 (130.0), C-13 (43.9), C-14 (72.6), C-15 (27.7), C-16,17 (24.3, 24.7), C-18,19 (15.3, 17.3), C-20 (61.2). UV λ_{max}^{EtOH} nm (ε): 252 (14000). MS *m/z* 304 (M^+), 289, 286, 273, 261, 243, 137, 109. High-resolution MS [Found (Calcd)] *m/z*: $C_{20}H_{32}O_2$ (M^+) 304.2391 (304.2402). Acetylation (Ac_2O–pyridine) of **3a** gave **3b**, oil, $[\alpha]_D^{25}$ +210° (*c*=1.00). ^1H-NMR δ: 1.05, 1.06 (each 3H, d, *J*=7.0 Hz), 1.47 (3H, s), 1.73 (3H, br s), 2.02, 2.05 (each 3H, s), 2.48 (1H, sept, *J*=7.0, H-15), 4.40, 4.61 (each 1H, d, *J*=12.0 Hz, H-20), 5.00 (1H, br t, *J*=6.0 Hz), 5.40 (1H, br t, *J*=7.0 Hz), 6.06 (1H, dd, *J*=9.5, 4.5 Hz, H-14), 6.11 (1H, br d, *J*=11.5 Hz, H-3), 6.21 (1H, d, *J*=11.5 Hz, H-2). ^{13}C-NMR δ: C-1 (141.8), C-2,3 (121.5, 122.7), C-4 (137.5), C-5,9 (38.5, 39.8), C-6,10 (24.4, 26.7), C-7 (125.1), C-8 (134.0), C-11 (132.7), C-12 (129.4), C-13 (37.2), C-14 (72.2), C-15 (27.9), C-16,17 (24.0, 25.0), C-18,19 (15.6, 16.3), C-20 (63.3), OAc (20.9, 21.3, 170.0). UV λ_{max}^{EtOH} nm (ε): 252 (22000). MS *m/z*: 388 (M^+), 328, 313, 286, 268, 253, 243, 137, 109.

Transannular Cyclization of 3a A solution of **3a** (17 mg) in $CHCl_3$ (1 ml) was kept at room tempeature for 9 d. After evaporation of the solvent, the residue was subjected to column chromatography with MeOH–$CHCl_3$ (1:100) to give 1.6 mg of **6**, oil, $[\alpha]_D^{17}$ −18° (*c*=0.32). ^1H-NMR δ: 1.08, 1.13 (each 3H, d, *J*=7.0 Hz), 1.09 (3H, s, H-18), 3.97, 4.49 (each 1H, d, *J*=14.0 Hz, H-20), 4.53 (1H, br d, *J*=9.0 Hz, H-14), 4.79, 4.90 (each 1H, br s, H-19), 5.03 (1H, d, *J*=10.0 Hz, H-2), 5.22 (1H, br dd, *J*=10.0, 6.5 Hz). MS *m/z*: 320 (M^+), 302, 287, 284, 259, 241, 217, 203, 193, 175, 161. High-resolution MS [Found (Calcd)] *m/z*: $C_{20}H_{32}O_3$ (M^+) 320.2365 (320.2352).

Sarcophytol R (4) Oil, $[\alpha]_D^{22}$ +12° (*c*=0.6, but contained persistent impurities so the value is not reliable). ^1H-NMR δ: 1.09, 1.11 (each 3H, d, *J*=7.0 Hz), 1.33 (3H, s, H-19), 1.61 (3H, d, *J*=1.0 Hz), 1.78 (3H, s), 2.35 (1H, dd, *J*=13.5, 6.0 Hz, H-13), 2.55 (1H, sept, *J*=7.0 Hz, H-15), 2.68, 2.78 (each 1H, dd, *J*=17.0, 6.5 Hz, H-5), 4.64 (1H, dd, *J*=6.0, 5.5 Hz, H-14), 5.31 (1H, br t, *J*=6.0 Hz, H-11), 5.57 (1H, d, *J*=15.5 Hz, H-7), 5.69 (1H, dt, *J*=15.5, 6.5 Hz, H-6), 6.00 (1H, br d, *J*=11.5 Hz, H-3), 6.08 (1H, d, *J*=11.5 Hz, H-2). MS *m/z*: 304 (M^+), 286, 271, 261, 243, 137. High-resolution MS [Found (Calcd)] *m/z* $C_{20}H_{32}O_2$ (M^+), 304.2390 (304.2402).

Sarcophytol S (5) Oil, $[\alpha]_D^{20}$ +57° (*c*=0.60). ^1H-NMR δ: 1.10, 1.11 (each 3H, d, *J*=7.0 Hz), 1.29 (3H, s, H-19), 1.62, 1.78 (each 3H, br s), 2.63 (1H, sept, *J*=7.0 Hz, overlapped with other signals), 4.71 (1H, t, *J*=6.2 Hz, H-14), 5.38 (1H, br t, *J*=5.0 Hz), 5.56 (1H, d, *J*=15.5 Hz, H-7), 5.72 (1H, ddd, *J*=15.5, 7.5, 6.0 Hz, H-6), 5.91 (1H, br d, *J*=11.5 Hz, H-3), 6.08 (1H, d, *J*=11.5 Hz, H-2). MS *m/z*: 304 (M^+), 286, 271, 243, 217, 203, 137. High-resolution MS [Found (Calcd)] *m/z*: $C_{20}H_{32}O_2$ (M^+), 304.2397 (304.2402).

Conversion of 7a to 4 Compound **7a** (26.1 mg) was dissolved in an isopropyl alcohol solution (3 ml) which was prepared by reducing diphenyl diselenide (20 mg) with $NaBH_4$ (5 mg) at room temperature. The mixture was refluxed for 20 h. The mixture was diluted with tetrahydrofuran (2 ml) and 0.3 ml of 30% H_2O_2 was added dropwise at 0 °C. The mixture was stirred at room temperature for 3 h, diluted with H_2O, and then extracted with Et_2O. After usual work-up, TLC examination of the product showed that the final H_2O_2 treatment had been incomplete. The mixture was dissolved again in a mixture of isopropyl alcohol (1.5 ml) and tetrahydrofuran (1.0 ml), then 30% H_2O_2 (0.3 ml) was added, and the whole was stirred at room temperature overnight. The mixture was extracted with Et_2O and the extract was worked up as usual. Column chromatography of the residue with ethyl acetate–hexane (2:8) gave 14.2 mg of **4**, $[\alpha]_D^{22}$ +19° (*c*=0.84), which was identical with sarcophytol R on the basis of comparisons of their ^1H-NMR and MS, and TLC behavior.

Conversion of 7b to 5 Compound **7b** (*ca.* 50 mg) was dissolved in an isopropyl alcohol solution (3 ml) which was prepared by reducing diphenyl diselenide (42 mg) with $NaBH_4$ (11 mg) at room temperature. It was found to be quite unreactive, and after refluxing for 17 h, most of the starting material remained unchanged. Diphenyl diselenide (126 mg) was reduced by $NaBH_4$ separately and added to the reaction mixture and the mixture was refluxed for 4 d. It was treated in the same way as above. Column chromatography of the residue with ethyl acetate–hexane gave 14.3 mg of **5**, $[\alpha]_D^{21}$ +58° (*c*=0.78), which was identical with sarcophytol S on the basis of comparisons of their ^1H-NMR and mass spectra, and TLC behavior.

Sarcophytol Q (8a) Oil, $[\alpha]_D^{26}$ +79° (*c*=4.18). ^1H-NMR (90 MHz) δ: 0.84 (6H, d, *J*=6.7 Hz), 1.32 (3H, s, H-18), 1.53 (3H, s), 1.76 (3H, s), 3.83 (1H, dd, *J*=10.0, 6.0 Hz, H-14), 5.05, 5.32 (each 1H, m), 5.62, 5.90 (each 1H, d, *J*=15.5 Hz, H-2,3). ^{13}C-NMR δ: C-1 (81.1), C-2 (129.1), C-3 (138.6), C-4 (74.5), C-5,13 (42.1, 42.9), C-6,10 (23.8, 24.1), C-7,11 (126.0, 126.5), C-8,12 (133.8, 134.4), C-9 (38.8), C-14 (71.8), C-15 (32.5), C-16,17,19,20 (15.1, 16.0, 17.8, 17.8), C-18 (30.7). MS *m/z*: 304 ($M^+ - H_2O$), 261, 243, 215, 139. High-resolution MS [Found (Calcd)] *m/z*: $C_{20}H_{32}O_2$ ($M^+ - H_2O$), 304.2400 (304.2402). Acetylation (Ac_2O–pyridine) of **8a** gave **8b**, oil, $[\alpha]_D^{27}$ +74° (*c*=1.60). ^1H-NMR δ: 0.73, 0.77 (each 3H, d, *J*=7.0 Hz), 1.35 (3H, s, H-18), 1.60, 1.76 (each 3H, s), 2.15 (3H, s), 2.44 (2H, d, *J*=3.5 Hz, H-13), 5.15 (1H, t, *J*=3.5 Hz, H-14), 5.32 (2H, m), 5.60, 6.00 (each 1H, d, *J*=15.5 Hz, H-2,3). ^{13}C-NMR δ: C-1 (80.6), C-2,7 (127.8, 129.5), C-3 (139.6), C-4 (74.2), C-5,13 (40.4, 44.8), C-6,10 (23.4, 24.4), C-8, 12 (133.3, 134.4), C-9 (38.7), C-14 (74.5), C-15 (33.4), C-16,17,19,20 (15.2, 16.0, 17.3, 17.6), C-18 (29.6), OAc (21.4, 170.6). MS *m/z*: 364 (M^+), 304, 261, 243, 226, 215.

Chromic Acid Oxidation of 8a Jones' reagent (two drops) was added to a solution of **8a** (6.5 mg) in Et_2O (1 ml) at 0 °C and the mixture was stirred at room temperature for 10 min then worked up as reported.[5] Column chromatography of the neutral product mixture with $CHCl_3$–Et_2O (1:20) gave 3.9 mg of **9**, $[\alpha]_D^{25}$ −3.8° (*c*=0.78) (lit.,[5] −3.0°). It was shown to be identical with **9** prepared from **10** by direct comparisons of their ^1H-NMR and UV spectra, and TLC behavior (Et_2O–$CHCl_3$, 1:9).

Isolation of Sarcophytols K (11a) and F (13a) Isolation of these two compounds was done as reported previously, by repeated column chromatography of the crude extract of *S. glaucum*.[6]

Sarcophytol K (11a) Oil, $[\alpha]_D^{20}$ +20° (*c*=0.77). ^1H-NMR δ: 1.06, 1.18 (each 3H, d, *J*=7.0 Hz), 1.59, 1.61 (each 3H, s), 1.82 (3H, d, *J*=1.0 Hz, H-18), 2.96 (1H, sept, *J*=7.0 Hz, H-15), 4.08, 4.16 (each 1H, d, *J*=9.5 Hz, H-13,14), 4.94, 5.39 (each 1H, m), 6.08 (1H, d, *J*=11.5 Hz, H-2), 6.22 (1H, br d, *J*=11.5 Hz, H-3). ^{13}C-NMR δ: C-1,4 (138.9, 141.8), C-2,3,7 (122.3,

124.0, 124.4), C-5 (31.8), C-6, 10 (24.2, 24.6), C-8,12 (132.6, 132.7), C-9 (39.0), C-11 (130.9), C-13,14 (74.3, 80.3), C-15 (28.4), C-16,17,18 (22.1, 22.1, 23.8), C-19 (15.6), C-20 (11.3). UV λ_{max}^{EtOH} nm (ε): 254 (16000). IR ν_{max}^{neat} cm^{-1}: 3290, 850. MS *m/z*: 304 (M^+), 286, 271, 268, 261, 257, 243, 221, 215, 203, 187, 137, 109. High-resolution MS [Found (Calcd)] *m/z*: $C_{20}H_{32}O_2$ (M^+) 304.2402 (304.2402).

Sarcophytol K Acetonide (11b) Compound **11b** was prepared from **11a** by a usual method (acetone–hydrochloric acid). Oil, $[\alpha]_D^{22}$ −110° (*c*=0.40). ^{1}H-NMR δ: 1.18, 1.20 (each 3H, d, *J*=7.0 Hz), 1.44 (6H, s), 1.60, 1.67 (each 3H, s), 1.81 (3H, d, *J*=1.0 Hz), 2.87 (1H, sept, *J*=7.0 Hz), 4.21, 4.13 (each 1H, d, *J*=9.0 Hz, H-13,14), 4.91 (1H, br dd, *J*=7.5, 6.5 Hz), 5.25 (1H, m), 5.95 (1H, d, *J*=12.0 Hz, H-2), 6.25 (1H, br d, *J*=12.0 Hz, H-3). MS *m/z*: 344 (M^+), 329, 314, 301, 286, 271, 269, 253, 243, 225.

Bis-*p*-dimethylaminobenzoates of Sarcophytols B, K, J (2b, 11c, 13b) A mixture of **2a** (20 mg) and *p*-dimethylaminobenzoyl chloride (48 mg) in pyridine (0.2 ml) was heated at 85°C for 30 min, diluted with H_2O and Et_2O, and worked up as usual. Column chromatography of the evaporation residue with ethyl acetate–hexane (1:9) gave 8.7 mg of **2b**. Compounds **11c** and **13b** were prepared in a similar way. **2b**: ^{1}H-NMR δ: 1.01 (3H, d, *J*=7.5 Hz), 1.15 (3H, d, *J*=7.0 Hz), 1.46, 1.74, 1.76 (each 3H, s), 2.74 (1H, sept, *J*=7.0 Hz), 2.966 (6H, s), 2.972 (6H, s), 5.08, 5.57 (each 1H, m), 5.62 (1H, d, *J*=10.0 Hz, H-13), 6.30 (2H, s, H-2,3), 6.46 (1H, d, *J*=10.0 Hz, H-14), 6.53 (4H, dd, *J*=9.0, 2.0 Hz), 7.85 (4H, dd, *J*=9.0, 5.0 Hz). CD (*c*=1.67×10^{-5}, EtOH) $[\theta]^{15}$ (nm): −160000 (324.5), +190000 (299.5). UV λ_{max}^{EtOH} nm (ε): 311 (50000), 251 (17600), 234 (18000). **11c**: ^{1}H-NMR δ: 1.11, 1.20 (each 3H, d, *J*=7.3 Hz), 1.60, 1.75, 1.83 (each 3H, s), 2.95 (6H, s), 2.96 (6H, s), 5.00 (1H, br dd, *J*=7.0, 6.0 Hz), 5.63 (1H, m), 5.82, 5.98 (each 1H, d, *J*=10.5 Hz, H-13,14), 6.25 (1H, br d, *J*=11.5 Hz, H-3), 6.32 (1H, d, *J*=11.5 Hz, H-2), 6.51 (4H, dd, *J*=9.0, 4.5 Hz), 7.80 (4H, dd, *J*=9.0, 2.5 Hz). CD (*c*=1.67×10^{-5}, EtOH)$[\theta]^{15}$ (nm): −160000 (324), +112000 (299). UV λ_{max}^{EtOH} nm (ε): 311 (45000), 251 (16500), 234 (17000). **13b**: ^{1}H-NMR δ: 0.95, 1.17 (each 3H, d, *J*=7.0 Hz), 1.57, 1.69, 1.84 (each 3H, br s), 2.972, 2.965 (each 6H, s), 4.92, 5.42 (each 1H, m), 5.79, 6.42 (each 1H, d, *J*=10.5 Hz, H-13,14), 6.30 (1H, d, *J*=11.0 Hz, H-2), 6.41 (1H, br d, *J*=11.0 Hz, H-3), 6.53 (4H, dd, *J*=9.0, 2.0 Hz), 7.82 (4H, dd, *J*=9.0, 3.5 Hz). CD (*c*=1.67×10^{-5}, EtOH) $[\theta]^{15}$ (nm): −197000 (324.5), +200000 (300). UV λ_{max}^{EtOH} nm (ε): 310 (55000), 250 (sh, 19200), 234 (22400).

1(15), 2ξ,4(18),7*E*,11*E*,13ξ-Cembrahexaene (12) Examination of the ^{1}H-NMR sample of sarcophytol K in $CDCl_3$, stored in a refrigerator for one month, indicated the formation of a small amount of nonpolar degradation product. Column chromatography of the mixture (*ca.* 15 mg) with hexane gave 2.3 mg of **12** as an oil, which contained a significant amount of hexane as a persistent impurity. ^{1}H-NMR δ: 1.53 (3H, d, *J*=1.0 Hz), 1.86, 1.91 (each 3H, s), 1.99 (3H, d, *J*=0.5 Hz), 4.96, 5.06 (each 1H, br s, H-18)), 5.05 (1H, m, H-7, overlapped with a signal at 5.06), 5.47 (1H, br t, *J*=8.8 Hz), 5.95, 6.53 (each 1H, d, *J*=11.0 Hz), 6.16, 6.60 (each 1H, d, *J*=15.5 Hz). MS *m/z*: 268 (M^+). The UV spectrum was not measured due to the facile decomposition.

Sarcophytol F (14a) Oil, $[\alpha]_D$ +57° (*c*=0.99). ^{1}H-NMR δ: 0.88 (3H, br, H-17), 1.11 (3H, d, *J*=7.0 Hz, H-16), 1.55, 1.59, 1.66 (each 3H, s, H-18,19,20), 2.98 (1H, br sept, *J*=7.0 Hz, H-15), 4.31 (1H, dd, *J*=10.5, 5.5 Hz, H-14), 4.72—4.85 (2H, m, H-7,11), 5.99 (1H, br d, *J*=11.0 Hz, H-3), 6.22 (1H, br, H-2). ^{13}C-NMR δ: C-1 (143.2), C-2,3 (122.3, 123.2), C-4 (138.1), C-5,9 (39.5, 39.8), C-6,10 (24.7, 25.1), C-7 (126.0), C-8 (133.1), C-11 (128.8), C-12 (129.8), C-13 (48.1), C-14 (65.0), C-15 (28.4), C-16,17 (20.9, 21.4), C-18,19,20 (14.2, 15.8, 17.1). UV λ_{max}^{EtOH} nm (ε): 255 (18800). IR ν_{max}^{neat} cm^{-1}: 3340, 885, 845, 825. MS *m/z*: 288 (M^+), 273, 270, 255, 245, 227, 137 (base peak), 109. High-resolution MS [Found (Calcd)] *m/z*: $C_{20}H_{32}O$ (M^+), 288.2442 (288.2453). Acetylation (Ac_2O–pyridine) of **14a** gave **14b**. ^{1}H-NMR δ: 0.91 (3H, br, H-17), 0.99 (3H, d, *J*=7.0 Hz, H-16), 1.55, 1.64, 1.67 (each 3H, s), 2.94 (1H, br sept, *J*=7.0 Hz, H-15), 4.71—4.86 (2H, m), 5.42 (1H, br dd, *J*=11.0, 3.5 Hz, H-14), 5.99 (1H, br d, *J*=11.5 Hz, H-3), 6.26 (1H, br, H-2).^{13}C-NMR δ: C-1,4 (137.8, 138.8), C-2,3,7 (122.3, 125.7, 125.9), C-5,9 (39.4, 39.7), C-6,10 (24.7, 25.0), C-8 (132.7), C-11 (129.6), C-12 (129.1), C-13 (44.4), C-15 (28.6), C-16,17 (20.9, 20.9), C-18,19,20 (14.1, 15.8, 16.7), OAc (21.4, 171.0).

Conversion of 14a to a Pentaene (15), a Tetraene Ethyl Ether (16) and a Dihydrofuran (17) Compound **14a** (13.8 mg) was dissolved in $CHCl_3$ (1 ml) and kept at room temperature for 24 h. Column chromatography of the mixture with hexane gave 3.9 mg of **15** as an oil, which was identical with **15** prepared previously,[5,6] from **1a** and **18**, by direct comparisons of their ^{1}H-NMR and mass spectra. The more polar fractions were combined and dissolved again in 1 ml of $CHCl_3$. Column chromatography of the mixture, after 5 d, with ethyl acetate–hexane (1:9) gave 0.95 mg of the dihydrofuran **17**, and an unidentified compound (2.0 mg), assumed to be a transannular cyclization product. Compound **17**, $[\alpha]_D^{17}$ −120° (*c*=0.19) (lit.,[5] $[\alpha]_D$ −133°) was identical with that prepared from **1a**, by comparisons of their ^{1}H-NMR and mass spectra, and TLC behavior. On prolonged treatment in $CHCl_3$ at room temperature for several days, the pentaene **15** was found to react with ethanol, contained in $CHCl_3$ as a stabilizer, giving an ethyl ether **16** as an oil. ^{1}H-NMR δ: 1.07, 1.09 (each 3H, d, *J*=7.0 Hz), 1.15 (3H, t, *J*=7.0 Hz, $-OC_2H_5$), 1.25 (3H, s, H-18), 1.49, 1.61 (each 3H, s), 2.53 (1H, sept, *J*=7.0 Hz), 2.66 (2H, br d, *J*=8.0 Hz, H-13), 3.36 (2H, q, *J*=7.0 Hz, $-OC_2H_5$), 4.82, 4.93 (each 1H, m), 5.45 (1H, t, *J*=8.0 Hz, H-14), 5.77, 5.90 (each 1H, d, *J*=16.5 Hz, H-2,3). MS *m/z*: 316 (M^+), 301, 273, 270, 255, 243, 233, 227, 137. UV λ_{max}^{EtOH} nm: 248.

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