

Cytotoxic Biscembranes from the Soft Coral *Sarcophyton glaucum*

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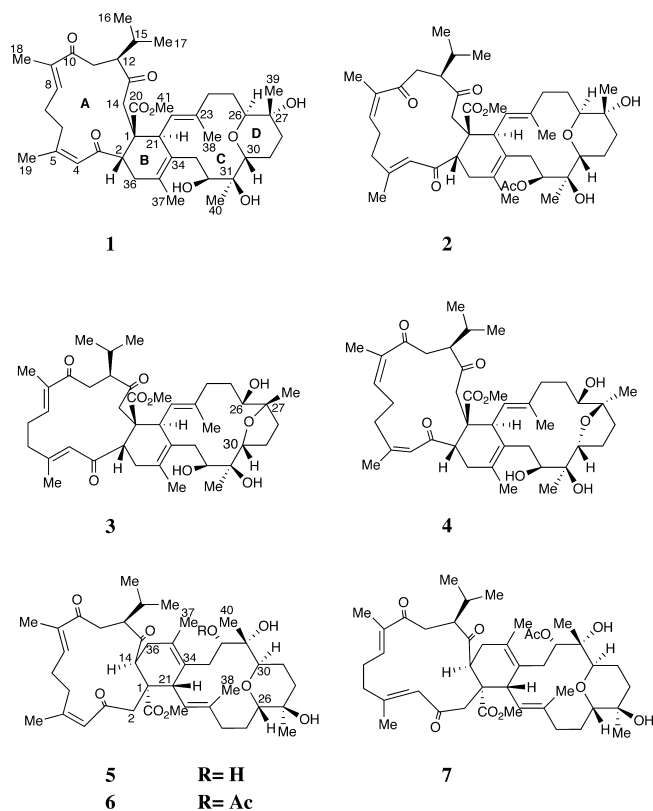
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Seven new tetracyclic biscembranes (**1–7**) have been isolated from the soft coral *Sarcophyton glaucum*. Four (**1–4**) may be formed biogenetically by a Diels–Alder reaction of $\Delta^{4(5)}$ and $\Delta^{8(9)}$ geometrical isomers of methyl sarcoate and $\Delta^{21(34)}$, $^{35(36)}$ dienes, including two with a tetrahydrofuran ring between C-27 and C-30 (**3, 4**), and three biscembranes (**5–7**) are probably derived from methyl sarcoate isomers with $\Delta^{1(14)}$, $^{4(5)}$, $^{8(9)}$ and a cembrane diene. Their structures were established on the basis of spectroscopic methods. Six of them (**1–5, 7**) exhibited weak cytotoxic activity against proliferation of human promyelocytic leukemia cells (HL-60).

The soft corals of the genus *Sarcophyton* (family Alcyoniidae) are well known as a rich source of cembrane dimers exhibiting a wide range of biological activities.¹ Nineteen kinds of unusual biscembranes have been isolated so far from *S. glaucum*, *S. tortuosum*, and *S. latum*.^{2–10} In the course of our studies of the bioactive cembrane constituents of the soft coral *Sarcophyton glaucum*, collected in Kagoshima Prefecture,^{11,12} Japan, we isolated four new cembranes, named bisglaucumlides A–D, with different double-bond geometries at C-4 and C-8.⁸ Bisglaucumlides C and D exhibited weak cytotoxicity against the growth of HL-60. Further investigation of the dichloromethane extract has led to the isolation of seven new biscembranes, bisglaucumlides E–K (**1–7**). We report the isolation and structure elucidation of these new compounds.

Bisglaucumlide E (**1**) was isolated as an amorphous powder and had a molecular formula of $C_{41}H_{60}O_9$, established by HRFABMS spectrometry (m/z 697.4314, $[M + H]^+$), which suggested a possible isomer of bisglaucumlide A. Comparison of the NMR data with those of bisglaucumlides A–D revealed the greatest similarities to the NMR data of bisglaucumlide C, except for the lack of an acetyl group in **1**. This was supported by the fact that the chemical shift of H-32 (δ 3.55, 1H, overlapped) was shifted upfield by 1.46 ppm when compared with that of bisglaucumlide C. The relative configuration of **1** was elucidated by the similarity of the NOE spectrum to that of bisglaucumlide C: H-4 (δ 6.22, 1H, s)/H-2 (δ 3.94, 1H, d, $J = 8.7$ Hz), Me-19 (δ 1.92, 3H, br s), H-36b (δ 1.98, 1H, d, $J = 18.4$ Hz); H-7a (δ 2.57, 1H, dd, $J = 14.2, 8.7$ Hz)/Me-18 (δ 1.80, 3H, br s); H-7b (δ 2.13, 1H, overlapped)/Me-19; H-8 (δ 6.34, 1H, br t, $J = 7.3$ Hz)/H-6a (δ 3.86, 1H, m), H-11a (δ 3.06, 1H, dd, $J = 14.2, 8.7$ Hz), H-12 (δ 2.76, 1H, m), Me-19; COOMe (δ 3.54, 3H, s)/Me-16 (δ 0.89, 3H, d, $J = 6.7$ Hz), Me-17 (δ 0.92, 3H, d, $J = 6.7$ Hz), H-22 (δ 4.73, 1H, d, $J = 11.2$ Hz). Thus, the structure of **1** was depicted as shown and is the 32-desacetyl derivative of bisglaucumlide C.

Bisglaucumlide F (**2**) was obtained as an amorphous powder with the molecular formula $C_{43}H_{62}O_{10}$ and is an isomer of bisglaucumlides B–D. While resonances due to rings B, C, and D in the ¹H NMR spectrum were similar to those of bisglaucumlides B–D, only resonances due to the A ring were somewhat different from each other. In the ¹³C NMR spectrum, the *E* geometry at C-4 and the *Z* geometry at C-8 were evident from the chemical shifts of C-19 (δ_c 20.7) and C-18 (δ_c 21.5), respectively, the latter of which was



downfield shifted by 9.7 ppm when compared to that of bisglaucumlide C, which has an *E* geometry. This was also supported by the NOE correlations of Me-19 (δ 2.09, 3H, br s) to H-6a (δ 2.15, 1H, m) and of Me-18 (δ 2.01, 3H, br s) to H-8 (δ 5.62, 1H, t, $J = 8.0$ Hz). The major conformation of the A ring was confirmed by interpretation of the NOE correlations (Figure 1). Thus, Me-41 (δ 3.52, 3H, s) was correlated to H-2 (δ 3.69, 1H, d, $J = 8.5$ Hz), Me-16 (δ 0.79, 3H, d, $J = 6.9$ Hz), and Me-17 (δ 0.99, 3H, d, $J = 6.8$ Hz), indicating that H-2, the isopropyl group, and Me-41 were β -oriented. NOE correlations from H-4 (δ 5.66, 1H, s) to H-6a and H-7b (δ 2.40, 1H, m), H-8 to H-6b (δ 2.08, 1H, overlapped) and H-6a, Me-18 to H-11b (δ 2.08, 1H, overlapped), and H-11a (δ 3.05, 1H, dd, $J = 14.8, 10.9$ Hz) to Me-16 were observed. With respect to the configuration of rings B–D, it was established to be similar to those of bisglaucumlides B–D by the signal patterns and the coupling constants in the ¹H NMR spectrum and NOE

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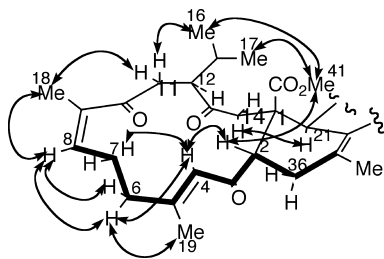


Figure 1. Selected NOE correlations of **2**.

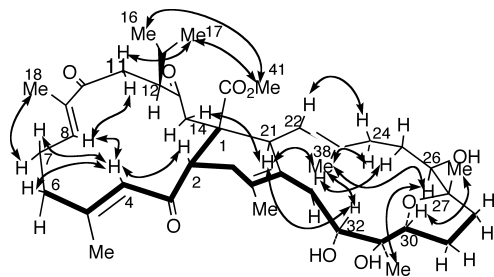


Figure 2. Selected NOE correlations of **3**.

experiments. This is the first report of the isolation of a biscebranone possessing 4*E* and 8*Z* geometries.

Bisglaucumlide **G** (**3**) was isolated as a viscous oil with the molecular formula $C_{41}H_{60}O_9$ and was isomeric with bisglaucumlides **A** and **E** (**1**). Though resonances due to rings **A** and **B** in the NMR spectra were similar to those of bisglaucumlide **A**, the carbon chemical shifts due to rings **C** and **D** were drastically shifted. Thus, the chemical shifts of C-26, C-27, and C-30 were found to be at δ 74.6, 84.8, and 87.6, respectively, while the corresponding signals in bisglaucumlide **A** were shifted at δ 85.1, 69.9, and 69.3, respectively. This implied the formation of an ether ring linkage between C-27 and C-30. The relative configuration of rings **A** and **B** was elucidated to be the same as those of bisglaucumlide **A** by the interpretation of the NOESY data, though an NOE correlation between H-2 (δ 4.02, 1H, d, $J = 8.0$ Hz) and the carbomethoxy methyl protons (δ 3.57, 3H, s, Me-41) was not observed. Thus, Me-41 indicated NOE correlations to Me-16 (δ 0.80, 3H, d, $J = 6.8$ Hz) and Me-17 (δ 0.96, 3H, d, $J = 6.8$ Hz), suggesting that the carbomethoxy group and the isopropyl group were situated on the same β face of the molecule. NOE correlations of H-4 (δ 6.05, 1H, br s) to H-2, H-6b (δ 2.30, 1H, m), H-7b (δ 2.41, 1H, overlapped), and H-8 (δ 6.24, 1H, m) were found. Furthermore, NOE correlations between H-7a (δ 2.53, 1H, overlapped) and Me-18 (δ 1.73, 3H, br s), between H-8 and H-11 (δ 3.45, 1H, dd, $J = 13.7, 5.7$ Hz), between H-12 (δ 2.54, 1H, overlapped) and H-14a (δ 3.30, 1H, d, $J = 19.1$ Hz), and between H-14b (δ 2.01, 1H, d, $J = 19.1$ Hz) and H-21 (δ 3.63, 1H, br d, $J = 11.0$ Hz) were observed. Therefore, this suggested that H-2 had a β -orientation and H-21 had an α -orientation. The relative configuration of rings **C** and **D** was also elucidated as depicted in Figure 2. NOE correlations between H-21 and H-32 (δ 3.49, 1H, m) suggested that H-32 was α -oriented. The Me-38 (δ 1.74, 3H, br s) showed NOE correlations to H-21, H-24b (δ 2.13, 1H, overlapped), and H-26 (δ 3.38, 1H, br d, $J = 6.8$ Hz), the latter of which was also correlated to Me-40 (δ 1.17, 3H, br s), indicating an α -configuration of H-26 and Me-40. NOE correlations of Me-39 (δ 1.15, 3H, br s) to H-30 (δ 4.06, 1H, t, $J = 7.4$ Hz) and H-28b (δ 1.65, 1H, overlapped) and of H-30 to H-28b suggested β -configurations of H-30 and Me-39. NOE correlations of H-22 (δ 5.26, 1H, d, $J = 11.0$ Hz) to H-24a (δ 2.46), H-25a (δ 1.89), and Me-41 were also observed. Therefore, bisglaucumlide **G** was assigned the structure shown for **3**. This is the third isolation of a biscebranone containing a tetrahydrofuran ring between C-27 and C-30.¹⁰

Bisglaucumlide **H** (**4**) was isolated as a viscous oil possessing the molecular formula $C_{41}H_{60}O_9$. The 1H NMR spectrum was similar to that of **3**, except that resonances due to the **A** ring were somewhat different. The Me-18 and Me-19 in the ^{13}C NMR resonated at δ_C 20.5 and δ_C 27.5, respectively, suggesting the 4*Z*,8*Z*-geometry, as for bisglaucumlide **C**. This was further supported by NOE correlations between Me-18 (δ 1.88, 3H, br s) and H-8 (δ 5.51, 1H, t, $J = 8.2$ Hz), and between Me-19 (δ 1.87, 3H, br s) and H-4 (δ 6.27, 1H, br s). The signal patterns and coupling constants due to rings **B**, **C**, and **D** in the 1H NMR spectrum were almost the same as those of **3**. Therefore, the structure of bisglaucumlide **H** was assigned as **4**.

Bisglaucumlide **I** (**5**) was obtained as a viscous oil with the molecular formula $C_{41}H_{60}O_9$. The 1H NMR spectrum was very similar to that of **1**; however, the signal patterns and the chemical shifts due to H-2 and H-14 were drastically changed (Table 1). In the HMBC spectrum (Figure 3), methylene protons (δ 2.35 and 3.15, AB, $J = 19.0$ Hz) and H-4 (δ 6.07, 1H, s) were correlated to C-3 (δ 199.6). H-12 (δ 3.08, 1H, m) and a proton at δ 3.89 (1H, d, $J = 7.9$ Hz) showed HMBC correlations to C-13 (δ 214.0). The latter proton was also correlated to C-35 (δ 128.6) and C-36 (δ 32.1). Therefore, the methylene protons and the δ 3.89 proton were assigned as H-2 and H-14, respectively. The configuration of the **A**–**B** ring juncture was determined as *cis* by the interpretation of the NOESY spectrum. Thus, an NOE between H-12 and H-14 indicated that both hydrogens were situated on the same α face of the molecule. The carbomethoxy methyl protons (δ 3.55, 3H, s) were correlated to H-22 (δ 4.70, 1H, br d, $J = 11.6$ Hz), suggesting that the carbomethoxy group had an α -orientation. The $\Delta^{4(5)}$ *Z* and $\Delta^{8(9)}$ *E* configurations were established by the chemical shifts of C-19 (δ 24.9) and C-18 (δ 11.3), respectively. The configurations of the chiral centers in rings **B**–**D** were confirmed to be the same as that of **1** by comparing the NMR data with those of **1**. Bisglaucumlide **I** was assumed to be biogenetically formed by the Diels–Alder reaction of methyl sarcophytoate isomer **8** with the diene **9**, as depicted in Figure 4.

Bisglaucumlide **J** (**6**) was isolated as an amorphous powder with the molecular formula $C_{43}H_{62}O_{10}$ and found to have a similar 1H NMR spectrum to that of **5** except for an additional acetyl group. The acetoxy group was determined to be positioned at C-32, and the chemical shift of H-32 (δ 5.06, 1H, d, $J = 11.4$ Hz) was downfield shifted by 1.51 ppm when compared to that of **5**. Therefore, the structure of bisglaucumlide **J** was shown as **6**.

Bisglaucumlide **K** (**7**) was isolated as an amorphous powder with the molecular formula $C_{43}H_{62}O_{10}$ and was an isomer of **6**. The signal patterns and chemical shifts of rings **B**–**D** in the 1H NMR spectrum were very similar to those of **5** and **6**. Resonances due to ring **A** were in good agreement with those of **3**, namely, the presence of *E* geometries at C-4 and C-8, which was confirmed by the chemical shifts of C-19 (δ 18.2) and C-18 (δ 11.2). The configuration of the chiral centers was determined to be the same as that of **6** on comparing the 1H , ^{13}C , and NOESY spectral data with those of **6**. Therefore, the structure of bisglaucumlide **K** was established to be **7**. The lack of several chemical shifts in the 1H and ^{13}C spectra and correlations in the HMQC and HMBC spectra was observed, which was probably due to a slow conformational interconversion of **7**.

The absolute configurations of the new compounds were shown in structures **1** and **3**–**7**, because the CD spectra of **1**, **4**, **5**, and **6**, and **3** and **7** were similar to those of bisglaucumlides **C** and **A**, respectively. It is assumed that **2** also has the same absolute configuration as the other compounds due to their biogenetic relationship.

Bisglaucumlides **I**–**K** represent the second isolation of biscebranones probably derived from a methyl sarcoate isomer with a $\Delta^{1(14)}$, 4(5), 8(9) and $\Delta^{21(34)}$, 35(36) cembrane diene.⁹ The presence of a carbomethoxy group in biscebranones isolated so far

Table 1. NMR Spectral Data (400 MHz, CDCl₃) for 1–7^a

position	1		2		3		4		5		6		7	
	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)
1	48.0		47.2		48.1		50.1		47.6		48.1		48.1	
2	47.1	3.94 d (8.7)	46.2	3.69 d (8.5)	46.9	4.02 d (8.0)	45.4	3.63 br t (7.7)	49.3	3.15 d (19.0) 2.35 d (19.0)	49.3	3.10 d 19.2 2.69 d 19.2	50.2	2.92 br d (15.2) 2.56 br d (15.2)
3	201.7		202.6		205.0		202.2		199.6		198.9		196.9	
4	126.7	6.22 s	124.6	5.66 s	127.0	6.05 br s	125.4	6.27 br s	125.9	2.03 m	125.5	2.01 ^b	124.5	2.38 m
5	157.2		158.8		159.3		161.0		156.1	2.03 m	156.6	2.01 ^b	155.2	2.48 m
6a	30.2	3.86 m	39.2	2.15 m	39.6	2.41 ^b	35.0	2.79 dt (10.2, 2.9)	30.4	3.79 dt (12.5, 2.6)	30.7	3.80 dt (2.5, 12.8)	40.0	2.09 m
6b		2.07 ^b		2.08 ^b		2.30 m		1.97 ^b		2.51 m		2.21 m		2.55 m
7a	26.1	2.57 ^b dd (14.2, 8.7)	26.7	2.79 m	25.1	2.53 ^b	27.6	2.37 m	26.2	2.25 m	25.9	2.21 m	25.3	2.09 m
7b		2.13 ^b		2.40 m		2.41 ^b		2.10 m		6.40 t (7.5)		6.43 t (7.5)		6.61 br s
8	141.4	6.34 br t (7.3)	140.3	5.62 t (8.0)	141.4	6.24 m	132.4	5.51 t (8.2)	141.6		141.6		142.0	
9	138.3		134.9		137.9		138.6		137.2		136.9		138.1	
10	202.4		204.4		203.6		206.5		200.8		201.3		203.9	
11a	35.6	3.06 dd (14.2, 8.7)	37.0	3.05 dd (14.8, 10.9)	33.2	3.45 dd (13.7, 5.7)	40.0	3.12 dd (18.7, 9.2)	34.6	2.76 dd (15.7, 6.3)	34.6	2.80 dd (16.2, 5.1)		3.41 br s
11b		2.09 dd (14.2, 3.1)		2.08 ^b		2.01 dd (13.7, 5.1)		2.22 d (18.7)		2.61 dd (15.7, 5.7)		2.38 dd (16.2, 5.7)		1.86 ^b
12	55.7	2.76 m	53.9	2.80 dt (10.9, 3.3)	56.1	2.54 ^b	50.7	3.25 m	55.5	3.08 m	54.8	3.03 q (5.9)	59.0	1.86 ^b
13	212.2		211.0		210.7		211.0		214.0		212.6		212.5	
14a	48.8	2.38 d (19.30)	48.0	3.30 d (19.4)	47.4	3.30 d (19.1)	48.0	3.06 d (18.5)	45.7	3.89 d (7.9)	45.6	3.62 ^b	45.5	3.16 m
14b		3.04 d (19.3)		2.07 ^b		2.01 d (19.1)		1.91 m		2.22 m		2.15 ^b		2.16 m
15	29.5	2.01b	29.9	2.07 ^b	30.4	2.13 ^b	29.5	1.91 m	28.0	2.22 m	28.1	2.15 ^b	28.3	2.16 m
16	19.1	0.89 d (6.7)	18.0	0.79 d (6.9)	17.3	0.80 d (6.8)	18.8	0.79 d (6.8)	18.2	0.87 d (6.8)	18.4	0.87 d (6.7)	16.6	0.69 d (6.5)
17	20.8	0.92 d (6.7)	20.6	0.99 d (6.8)	20.5	0.96 d (6.8)	20.5	0.94 d (6.7)	21.1	0.89 d (6.7)	21.4	0.87 d (6.7)	21.8	1.06 br s
18	11.4	1.80 br s	21.5	2.01 br s	11.6	1.73 br s	20.5	1.88 br s	11.3	1.69 br s	11.2	1.73 br s	11.2	1.75 br s
19	24.5	1.92 br s	20.7	2.09 br s	18.7	2.09 br s	27.5	1.87 br s	24.9	1.92 br s	24.9	1.90 br s	18.2	2.26 br s
20	173.3		173.2		174.4		174.4		173.4		174.0		174.1	
21	41.1	3.64 ^b	40.2	3.42 br d (11.6)	40.6	3.63 br d (11.0)	46.9	3.30 br d (10.6)	40.3	3.58 br d (11.6)	40.9	3.63 ^b		3.29 m
22	124.7	4.73 d (11.2)	125.0	4.74 d (11.6)	125.7	5.26 d (11.0)	127.7	5.16 d (10.6)	125.0	4.70 d (11.6)	125.0	4.75 d (11.5)	123.9	4.90 d (10.8)
23	140.4		134.9		138.1		138.4		140.1		140.4		142.0	
24a	38.9	2.41 ^b	38.4	2.44 m	32.7	2.46 ^b	32.6	2.42 m	39.0	2.43 ^b	38.5	2.43 m	39.0	2.42 ^b
24b		1.86 ^b		1.85 dt (3.4, 13.7)		2.13 ^b		2.02 m		1.85 m		1.84 dt (3.0, 12.8)		1.84 ^b
25a	27.0	1.87 ^b	26.5	1.95 ^b	32.2	1.89 ^b	33.6	1.98 ^b	26.9	1.87 ^b	26.5	1.93 m	27.3	1.81 ^b
25b		1.56 ^b		1.55 dt (3.4, 13.7)		1.65 ^b		1.57 ^b		1.57 m		1.55 ^b		1.58 m at 27°
26	85.1	3.64 ^b	85.2	3.69 d (10.9)	74.6	3.38 br d (6.8)	73.2	3.39 br d (9.6)	85.0	3.65 d (8.9)	85.1	3.68 d (9.9)	85.1	3.67 br d (8.3)
27	69.9		69.8		84.8		84.7		69.9		69.8		69.8	
28a	31.9	1.69 ^b	31.6	1.68 ^b	36.4	2.09 ^b	36.2	2.23 ^b	31.8	1.69 ^b	31.5	1.68 ^b	31.9	1.69 ^b
28b		1.48 dt (4.3, 13.4)		1.49 dt (13.8, 4.5)		1.65 ^b		1.62 m		1.48 dd (13.7, 4.5)		1.49 dt (5.0, 13.9)		1.47 dt (14.1, 4.7)
29a	20.1	1.72 ^b	20.0	1.71 ^b	27.4	1.89 ^b	26.7	2.23 ^b	20.0	1.73 m	20.0	1.70 ^b	20.2	1.73 ^b
29b		1.57 ^b		1.59 m		1.89 ^b		1.77 ^b		1.57 ^b		1.57 ^b		1.61 m
30	69.3	3.65 m	69.2	3.64 br d (9.5)	87.6	4.06 t (7.4)	88.0	3.99 (10.1, 5.7)	69.4	3.64 d (12.7)	69.2	3.63 ^b	69.7	3.61 br d (10.1)
31	75.5		75.9		74.7		75.1		75.5		76.0		75.9	
32	71.0	3.55 ^b		5.07 br s	76.0	3.49 m	73.2	3.88 m	70.8	3.55 ^b	74.7	5.06 d (11.4)	74.7	5.02 br d (10.8)
33a	31.5	2.43 ^b	28.4	2.77 m	32.3	2.48 ^b	37.4	3.03b, m	31.4	2.44 ^b	28.6	2.71 ^b	29.2	2.76 br t (13.9)
33b		2.29 ^b		2.14 m		2.36 ^b		1.91, m		2.27 br d (13.7)		2.16 ^b		2.20 br d (13.9)
34	126.0		124.0		126.5		127.7		125.6		125.0		126.3	
35	127.6		127.5		129.3		128.1		128.6		126.9		128.5	
36a	32.3	2.96 dd (18.4, 8.7)	32.6	2.86 br dd (18.3, 8.3)	32.9	2.79 dd (18.3, 8.0)	33.1	2.32 dd (18.7, 7.7)	32.1	3.12 m	31.9	2.97 dd (18.7, 9.3)	34.3	
36b		1.98 d (18.4)		1.74 br d (18.4)		1.93 br d (18.3)		2.18 m		1.93 ^b		1.94 ^b		
37	20.0	1.69 br s	19.8	1.65 br s	19.6	1.68 br s	19.2	1.71 br s	19.8	1.69 br s	19.6	1.64 br s	19.7	1.66 br s
38	19.9	1.81 br s	19.9	1.94 br s	19.7	1.74 br s	20.8	1.86 br s	19.7	1.82 br s	19.9	1.98 br s	19.9	1.91 br s
39	25.6	1.12 s	25.4	1.11 s	19.3	1.15 s	19.5	1.15 br s	25.5	1.11 s	25.4	1.11 s	25.7	1.11 br s
40	18.9	1.33 s	18.7	1.15 s	21.4	1.17 br s	18.1	1.11 br s	18.8	1.31	18.7	1.13 s	18.8	1.14 s
41	51.2	3.54 s	51.0	3.52 s	51.5	3.57 s	51.1	3.56 s	51.3	3.55 s	51.1	3.53 s	51.4	3.54 s
Ac			20.9,		170.8	C-31, C-32 OH					20.6	1.99 s	20.9,	2.03 s
											170.6		170.5	

^aChemical shift values of ¹H NMR data and ¹³C NMR data are in ppm from TMS and CDCl₃ (δ 77.0), respectively. ^bOverlapping signals. ^cNot found.

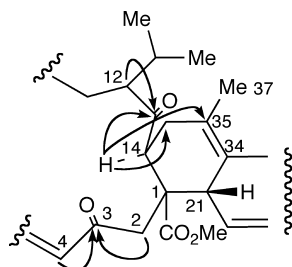


Figure 3. Selected HMBC correlations of **5**.

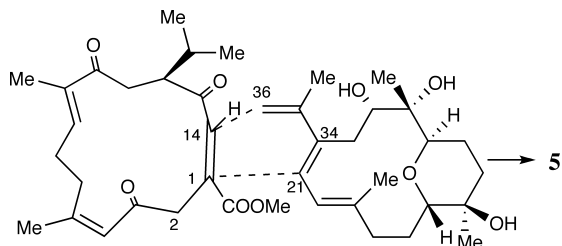


Figure 4. Probable biogenetic pathway for **5**.

from the ethanol,^{2,3} acetone,^{4,9,10} dichloromethane,⁵ and ethyl acetate⁶ extracts suggests that the carbomethoxy group of the new biscembranes **1–7** is not formed during the extraction process. Furthermore, the double-bond geometries did not change during the isolation procedures. Therefore, **1–7** are probably genuine natural products.

The cytotoxic activity of bisglaucumliides E–K against proliferation of human promyelocytic leukemia cells (HL-60) was examined, and they exhibited weak activity with the following IC₅₀ values: E (41.0 μM), F (13.3 μM), G (58.0 μM), H (47.8 μM), I (44.1 μM), K (29.8 μM).

Experimental Section

General experimental procedures, animal material, and initial extraction and isolation procedures have been previously reported.⁸

Isolation. Material (6.8 g) that eluted from a silica gel chromatography column with 1:19 MeOH–CH₂Cl₂ was chromatographed on silica gel using a gradient of MeOH and CH₂Cl₂. Elution with MeOH–CH₂Cl₂ (1:49) gave a crude fraction (184 mg), which was finally purified by HPLC (ODS) with CH₃CN–H₂O (1:1 to 3:2) to yield compounds **2** (2.7 mg), **6** (1.2 mg), and **7** (1.3 mg). After the fractions (694 mg) eluted with MeOH–CH₂Cl₂ (1:19), the material was repeatedly subjected to silica gel chromatography and then HPLC CH₃CN–H₂O (9:11 to 3:2) to give compounds **1** (2.8 mg), **3** (3.2 mg), **4** (1.2 mg), and **5** (1.3 mg).

Bisglaucumlide E (1): amorphous powder; [α]_D +66.7 (c 0.12, MeOH); UV (MeOH) λ_{max} (log ε) 230 nm (4.25); CD Δε₂₃₁ +3.2, Δε₂₅₂ –4.9; IR (film) ν_{max} 3503, 1732, 1709, 1661, 1615 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HRFABMS *m/z* 697.4314 [M + H]⁺ (calcd for C₄₁H₆₁O₉, 697.4316).

Bisglaucumlide F (2): amorphous powder; [α]_D +139 (c 0.30, MeOH); UV (MeOH) λ_{max} (log ε) 238 nm (4.17); CD Δε₂₃₈ –10.3; IR (film) ν_{max} 3459, 1734, 1713, 1678, 1613 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HRFABMS *m/z* 739.4423 [M + H]⁺ (calcd for C₄₃H₆₃O₁₀, 739.4421).

Bisglaucumlide G (3): viscous oil; [α]_D +125 (c 0.16, MeOH); UV (MeOH) λ_{max} (log ε) 232 nm (4.25); CD Δε₂₂₆ –3.4, Δε₂₄₇ +4.4; IR (film) ν_{max} 3482, 1732, 1715, 1669, 1607 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HRFABMS *m/z* 697.4318 [M + H]⁺ (calcd for C₄₁H₆₁O₉, 697.4316).

Bisglaucumlide H (4): viscous oil; [α]_D +133 (c 0.15, MeOH); UV (MeOH) λ_{max} (log ε) 237 nm (4.09); CD Δε₂₅₄ –6.7; IR (film) ν_{max} 3470, 1732, 1711, 1694, 1603 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HRFABMS *m/z* 697.4316 [M + H]⁺ (calcd for C₄₁H₆₁O₉, 697.4316).

Bisglaucumlide I (5): viscous oil; [α]_D +84 (c 0.05, MeOH); UV (MeOH) λ_{max} (log ε) 227 nm (4.30); CD Δε₂₂₅ +12.8, Δε₂₅₂ –8.4; IR (film) ν_{max} 3457, 1732, 1703, 1659, 1622 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HRFABMS *m/z* 697.4306 [M + H]⁺ (calcd for C₄₁H₆₁O₉, 697.4316).

Bisglaucumlide J (6): amorphous powder; [α]_D +33 (c 0.19, MeOH); UV (MeOH) λ_{max} (log ε) 231 nm (4.20); CD Δε₂₂₆ +9.6, Δε₂₅₀ –13.8; IR (film) ν_{max} 3485, 1732, 1713, 1691, 1620 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HREIMS *m/z* 738.4340 [M]⁺ (calcd for C₄₃H₆₂O₁₀, 738.4343).

Bisglaucumlide K (7): amorphous powder; [α]_D +95 (c 0.27, MeOH); UV (MeOH) λ_{max} (log ε) 231 nm (4.20); CD Δε₂₃₀ –5.2, Δε₂₄₉ +10.9; IR (film) ν_{max} 3468, 1709, 1680, 1620 cm^{–1}; ¹H and ¹³C NMR, see Table 1; HREIMS *m/z* 739.4426 [M + H]⁺ (calcd for C₄₃H₆₃O₁₀, 738.4421).

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