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NEW CHLORINATED DITERPENES FROM THE GORGONIAN *JUNCEELLA GEMMACEA*

Hai-yin He and D. John Faulkner*

Scripps Institution of Oceanography (A-012F)
University of California, San Diego
La Jolla, California 92093-0212, USA

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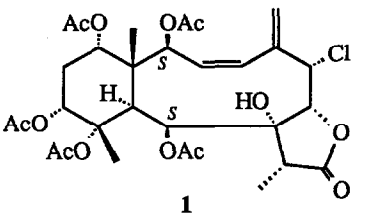
Abstract: The gorgonian *Junceella gemmacea* from Pohnpei, Micronesia, yielded six novel diterpenes (**3-8**) of the briarane class. The structures and relative configurations of gemmacolides A - F (**3-8**) were assigned on the basis of extensive NMR studies and the predominant conformations of **6** and **8** were determined by interpretation of NOEDS experiments.

The briaranes are a group of highly oxidized diterpenes that have been obtained from gorgonians, soft corals and sea pens.[1] The first compound in this series, briarein A (**1**), was isolated from the gorgonian *Briareum asbestinum*[2] and similar compounds, such as stylatulide (**2**),[3] were soon found in sea pens. Several species of *Junceella* from the South China Sea,[4,5] the Red Sea,[6] and the Great Barrier Reef[7] have been studied and all contained diterpenes of the briarane class. Three briarane diterpenes were isolated from *Junceella gemmacea* from Broadhurst Reef, Australia,[7] but none of these was found during the current investigation. In this paper we report the structures of six new diterpenes, gemmacolides A - F (**3-8**), from a Pohnpei collection of *Junceella gemmacea*.

The ethyl acetate soluble material from a methanolic extract of frozen *Junceella gemmacea* was chromatographed on silica and selected fractions were further purified by HPLC to obtain, in order of increasing polarity, gemmacolide B (**4**, 0.025% dry wt.), gemmacolide C (**5**, 0.01% dry wt.), gemmacolide A (**3**, 0.015% dry wt.), gemmacolide E (**7**, 0.01% dry wt.), gemmacolide F (**8**, 0.023% dry wt.), and gemmacolide D (**6**, 0.02% dry wt.).



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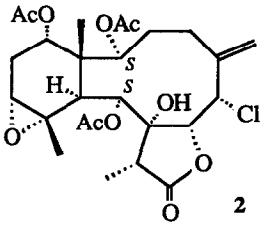

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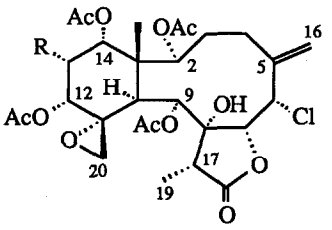
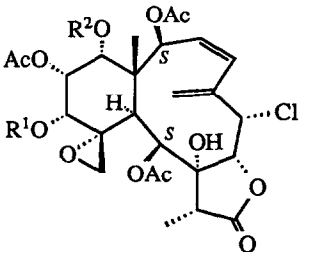
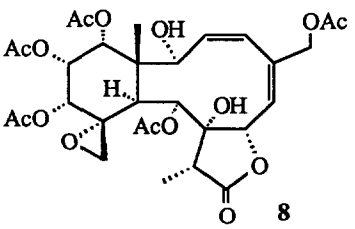


3 R = OAc
4 R = $OCOCH_2CH(CH_3)_2$
5 R = H



6 R^1 = H R^2 = Ac
7 R^1 = R^2 = H
10 R^1 = R^2 = Ac



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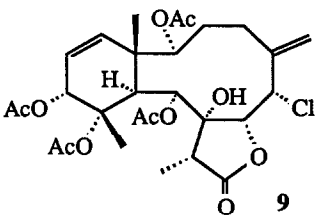

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Gemmacolide A (**3**) was isolated as a clear oil. The molecular formula, $C_{30}H_{39}ClO_{14}$, was established by high resolution mass measurement. Both the ^{13}C and ^1H NMR spectral data indicated the presence of five acetate groups on a diterpene carbon skeleton. The ^{13}C NMR signals at δ 146.6 (s) and 121.1 (t) and the ^1H NMR signals at 5.80 (br s, 1 H) and 5.51 (br s, 1 H) were assigned to an exocyclic methylene group and the ^{13}C NMR signal at 174.3 (s) was attributed to a γ-lactone (IR 1795 cm^{-1}). The ^1H NMR spectrum contained two mutually coupled signals at δ 2.94 (d, 1 H, J = 3.6 Hz) and 2.36 (d, 1 H, J = 3.6 Hz) that were appropriate for an exocyclic 11(20)-epoxide;[6] the corresponding ^{13}C NMR signals appeared at 56.7 (s)

and 50.4 (t). The two remaining degrees of unsaturation require a bicyclic carbon skeleton. These data, together with the presence of a chlorine atom in the molecule, directed our attention toward the briarane class of diterpenes. One of the characteristics of the ^1H and ^{13}C NMR spectra of stylatulide (**2**) is that the H–6, C–6, H–7 and C–7 signals are unexpectedly broad.[3] This phenomenon is interpreted as being the result of slow interconversion of two conformers of the ten-membered ring.[3b,8,9] We observed the same phenomenon in the ^1H and ^{13}C NMR spectra of gemmacolide A (**3**) but we were concerned because the chemical shift of the C–7 signal in **3** was at δ 71.3 rather than at 78.0 , where it appears in stylatulide (**2**). Since the chemical shifts and particularly the coupling constants of the ^1H NMR signals assigned to the ten-membered ring protons in stylatulide (**2**) are almost identical to signals in the spectrum of gemmacolide A (**3**), we have assumed that the noted differences in the C–7 chemical shifts were due to the changes in the conformation of the 10–membered ring or to the presence of an exocylic C–11(20) epoxide in gemmacolide A (**4**) in place of the exocyclic olefin in stylatulide (**2**). It is interesting to note that in the ^{13}C NMR spectra of minabeins–2 and –3 (**9**),[8] which also have the same substitution pattern and stereochemistry in the ten-membered ring as stylatulide (**2**), it is the C–6 signal that is shifted more than 10 ppm upfield from its position in **2**. The ^1H NMR signals at δ 4.78 (dd, 1 H, J = 4,1 Hz), 5.22 (t, 1 H, J = 4 Hz), and 5.24 (dd, 1 H, J = 4,1 Hz) were assigned to H–12, H–13, and H–14, respectively. The small coupling between H–12 and H–14 is a W–coupling that requires both hydrogens to be equatorial. The 4 Hz couplings between H–13 and both H–12 and H–14 indicated that H–13 was probably an axial substituent and this situation was confirmed by an NOEDS experiment on the closely related molecule gemmacolide B (**4**).

Gemmacolide B (**4**) was obtained as a colorless oil of molecular formula $C_{33}H_{45}ClO_{14}$. The ^1H and ^{13}C NMR spectra indicated that gemmacolide B (**4**) contained four acetate esters and an isovalerate ester in place of the five acetate esters of gemmacolide A (**3**). Apart from the obvious differences in spectral data that result from replacing an acetate with an isovalerate ester, the ^1H and ^{13}C NMR spectra were almost identical. The ^{13}C NMR chemical shifts of the signals due to the bicyclic ring carbons in **4**, which was assigned by interpretation of the XHCORR experiment, differed from those of the corresponding signals in **3** by 0.1 ppm or less except for the C–10 and C–13 signals for which the difference was 0.3 ppm.

Table 1. ^{13}C NMR spectral data (50 MHz, $CDCl_3$) of stylatulide (**2**) and gemmacolides A – F (**3–8**).

C#	2		3		4[a]		5		6[b]		7		8	
1	45.3	(s)	47.2	(s)	47.2	(s)	47.8	(s)	46.9	(s)	48.0	(s)	46.2	(s)
2	72.2	(d)	72.7	(d)	72.6	(d)	73.1	(d)	70.8	(d)	72.3	(d)	64.1	(d)
3	28.3	(t)	28.2	(t)	28.2	(t)	28.2	(t)	129.6	(d)	129.2	(d)	124.1	(d)
4	33.5	(t)	33.4	(t)	33.3	(t)	33.6	(t)	128.5	(d)	128.2	(d)	137.2	(d)
5	146.0	(s)	146.6	(s)	146.7	(s)	146.9	(s)	136.9	(s)	136.9	(s)	139.5	(s)
6	54.4	(bd)	53.7	(bd)	53.6	(bd)	53.6	(bd)	63.6	(d)	63.3	(d)	124.7	(d)
7	78.0	(bd)	71.3	(bd)	71.4	(bd)	71.8	(bd)	73.4	(d)	73.6	(d)	73.5[c]	(d)
8	81.6	(s)	81.1	(s)	81.2	(s)	81.2	(s)	80.6	(s)	80.7	(s)	81.5	(s)
9	81.3	(d)	81.4	(d)	81.3	(s)	81.1	(d)	78.5	(d)	78.6	(d)	78.8	(d)
10	51.6	(d)	51.4	(d)	51.1	(d)	51.5	(d)	48.0	(d)	48.0	(d)	44.4	(d)
11	58.9	(s)	56.8	(s)	56.8	(s)	57.5	(s)	59.1	(s)	59.5	(s)	57.9	(s)
12	59.6	(d)	73.6	(d)	73.5	(d)	73.5	(d)	74.6	(d)	75.8	(d)	74.7[c]	(d)
13	27.6	(t)	66.8	(d)	66.5	(d)	29.1	(t)	67.5	(d)	68.4	(d)	66.7	(d)
14	72.3	(d)	73.0	(d)	73.0	(d)	73.3	(d)	74.7	(d)	76.2	(d)	71.9[c]	(d)
15	13.9	(q)	14.2	(q)	14.1	(q)	14.0	(q)	14.4	(q)	14.0	(q)	12.9	(q)
16	121.6	(t)	121.1	(t)	121.0	(t)	121.2	(t)	116.8	(t)	116.8	(t)	65.0	(t)
17	43.1	(d)	35.3	(d)	35.2	(d)	35.5	(d)	31.5	(d)	30.8	(d)	32.8	(d)
18	174.7	(s)	174.3	(s)	174.4	(s)	174.6	(s)	175.5	(s)	175.5	(s)	175.1	(s)
19	6.6	(q)	6.0	(q)	5.9	(q)	5.9	(q)	8.3	(q)	8.3	(q)	6.3	(q)
20	22.1	(q)	50.4	(t)	50.4	(t)	50.3	(t)	48.8	(t)	48.9	(t)	49.2	(t)
Ac	170.8	(s)	171.3	(s)	171.3	(s)	171.0	(s)	170.0	(s)	170.5	(2s)	170.1	(2s)
	170.7	(s)	170.2	(s)	170.0	(s)	170.4	(s)	169.9	(s)	169.1	(s)	169.7	(3s)
	170.1	(s)	169.7	(s)	169.3	(s)	169.5	(s)	169.8	(s)				
			169.3	(2s)	169.1	(s)	169.4	(s)	169.6	(s)				
	21.1	(3q)	21.6	(q)	21.6	(q)	21.3	(q)	21.4	(q)	21.5	(q)	21.5	(q)
			21.2	(q)	21.1	(q)	21.2	(q)	21.2	(q)	21.2	(2q)	20.9	(2q)
			20.8	(q)	20.8	(q)	21.1	(q)	21.0	(q)			20.8	(q)
			20.6	(2q)	20.6	(q)	20.9	(q)	20.7	(q)			20.6	(q)
1'					171.7	(s)								
2'					42.6	(t)								
3'					24.9	(d)								
4'					22.3	(2q)								

[a]Assignments by HMBC.

[b]Assignments by COLOC (J = 8 Hz).

[c]Assignments may be interchanged.

Comparison of the ^{1}H NMR spectra of **3** and **4** revealed that the comparable signals for hydrogens attached to the diterpene skeleton differed by less than 0.02 ppm. This remarkable similarity can best be explained if an axial acetate group in **3** is replaced by an axial isovalerate in **4**, a difference that is compatible with the 0.3 ppm difference in the C–13 chemical shift. The position of the isovalerate ester was confirmed by analysis of HMBC data (J = 8 Hz) obtained at 500 MHz in 3:1 $CDCl_3$–C_6D_6 solution. The H–13 signal at δ 5.21, which could be differentiated from the H–14 signal at 5.24, was coupled to an ester carbon signal at δ 171.56, that was in turn coupled to the methylene signals of the valerate ester at 2.06. The stereochemistry of gemmacolide B (**4**) was determined by analysis of an NOEDS study, again using a 3:1 $CDCl_3$–C_6D_6 solution. Irradiation of the methyl signal at δ 1.15 (s, 3 H, H–15) caused an 8% enhancement of the H–14 signal at 5.24 and a 9% enhancement of the H–13 signal at 5.21, which is indicative of a 1,3-diaxial arrangement of H–13 and Me–15. The NOEDS data also confirmed the relative stereochemistry at all other centers in the molecule.

Gemmacolide C (**5**) was obtained as a colorless oil of molecular formula $C_{28}H_{37}ClO_{12}$. The ^{1}H NMR spectrum contained four acetate signals and the ^{13}C NMR spectrum indicated that one of the acetate groups in **3** had been replaced by hydrogen in **5**. An analysis of the ^{1}H NMR spectrum revealed that the new methylene group was at C–13 giving rise to an isolated spin system with signals at δ 4.55 (dd, 1 H, J = 2.9, 1.8 Hz, H–12), 2.24 (m, 2 H, H–13), and 4.91 (t, 1 H, J = 2.9 Hz, H–14). In all other respects, the ^{1}H and ^{13}C NMR spectra of **3** and **5** are remarkably similar.

Gemmacolide D (**6**), which was isolated as a colorless oil, has the molecular formula $C_{28}H_{35}ClO_{13}$. The ^{1}H NMR spectrum contained four acetate signals at δ 2.18, 2.10, 2.05, and 1.98 (all s, 3 H) and, more significantly, two additional *cis*-oriented olefinic signals at δ 5.95 (br d, 1 H, J = 11.5 Hz, H–4) and 5.71 (dd, 1 H, J = 11.5, 9.7 Hz, H–3), the latter being coupled to the H–2 signal at 6.23 (d, 1 H, J = 9.7 Hz). The H–4 signal was also coupled by a very small coupling constant to one of the exocyclic methylene proton signals at δ 5.86 (br s, 1 H), the second signal being at 5.79 (br s, 1 H). These spectral features were reminiscent of those of the C–2 to C–5(16) portion of briarein–A (**1**) and, after further examination of the ^{1}H and ^{13}C NMR spectra, it was concluded that compounds **1** and **6** differed only in the substitution

pattern on the six-membered ring.

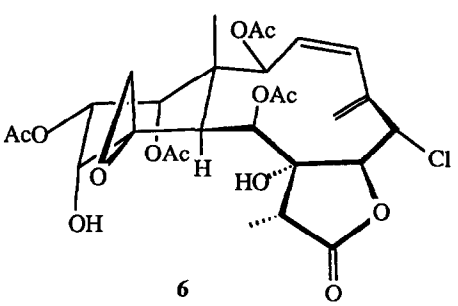
The ^{1}H NMR signals at δ 2.84 (d, 1 H, *J* = 2.9 Hz, H-20) and 2.77 (d, 1 H, *J* = 2.9 Hz, H-20) and ^{13}C NMR signals at 59.1 (s, C-11) and 48.8 (t, C-20) indicated that there was an exocyclic epoxide on the six-membered ring of gemmacolide D (**6**). The remaining signals at δ 2.65 (d, 1 H, *J* = 6.5 Hz, OH), 3.51 (br dd, 1 H, *J* = 6.5, 4 Hz), 5.08 (t, 1 H, *J* = 4.0 Hz) and 5.32 (br d, 1 H, *J* = 4 Hz) were assigned to a -CH(OH)-CH(OAc)-CH(OAc)- unit. Since irradiation of the H-20 signal at 2.77 caused a 10% nuclear Overhauser enhancement of the signal at 3.51, the substitution pattern and stereochemistry about the six-membered ring can be established. Additional NOEDS measurements (Table 2) allowed the full stereochemistry and conformation of gemmacolide D (**6**) to be defined as shown in Figure 1.

Gemmacolide E (**7**), which is also a colorless oil, has the molecular formula $C_{26}H_{33}ClO_{12}$. As expected from the molecular formula, gemmacolide E (**7**) has one less acetate group than gemmacolide D (**6**). With the exception of those differences that can be explained by the replacement of the acetate group at C-14 by a hydroxyl group, the ^{1}H and ^{13}C NMR spectra are almost identical. The H-12 signal at δ 3.59 (ddd, 1 H, *J* = 6.5, 3.2, 1.4 Hz) was coupled to a hydroxyl signal at 3.74 (d, 1 H, *J* = 6.5 Hz), to the H-13 signal at 4.95 (t, 1 H, *J* = 3.2 Hz), and to the H-14 signal at 3.80 (ddd, 1 H, *J* = 6.1, 3.2, 1.4 Hz), that was in turn coupled to a hydroxyl signal at 4.10 (d, 1 H, *J* = 6.1 Hz). Both **6** and **7** were treated with acetic anhydride in pyridine to obtain the same penta-acetate **10**, as indicated by TLC, ^{1}H NMR, and EIMS data.

Gemmacolide F (**8**) has the molecular formula $C_{30}H_{38}O_{15}$. The most obvious difference between gemmacolide F (**8**) and all other compounds in this series was the lack of a chlorine atom and an exocyclic methylene group. These groups were replaced by an acetoxymethylene group [δ 4.78 (d, 1 H, *J* = 14.8 Hz, H-16), 4.73 (d, 1 H, *J* = 14.8 Hz, H-16), 65.0 (t, C-16)] and a trisubstituted olefin [δ 5.77 (dd, 1 H, *J* = 8.6, 1.4 Hz, H-6), 139.5 (s, C-5), 124.7 (d, C-6)]. The same type of replacement had previously been observed among the minor metabolites of *Stylatula* sp.,[3b] *Pteroides laboutei*,[10] and *Minabea* sp.[8] The H-2 signal at δ 4.47 (dd, 1 H, *J* = 9.7, 3.2 Hz) was coupled to an olefinic proton signal at 5.88 (dd, 1 H, *J* = 10.1, 9.7 Hz, H-3) and a hydroxyl signal at *circa* 2.10; it sharpened to a doublet (*J* = 9.7 Hz) on D_2O addition. With the hydroxyl group located at C-2, analysis of the ^{1}H and ^{13}C NMR spectra revealed that the

Table 2. Selected NOEDS data for gemmacolides D (**6**) and F (**8**).

6				**8**			
irradiate (H #)		observe (%nOe, H #)		irradiate (H #)		observe (%nOe, H #)	
1.25	(H-15)	5.71	(9, H-3)	1.06	(H-15)	5.88	(6, H-3)
		5.32	(7, H-14)			5.44	(6, H-14)
		5.08	(8, H-13)			5.12	(8, H-3)
1.27	(H-19)	3.05	(8, OH-8)	2.91	(H-20)	4.91	(6, H-12)
		2.83	(6, H-17)			3.46	(6, H-20)
2.68	(OH-12)	3.84	(6, H-10)	3.57	(H-10)	4.47	(9, H-2)
		3.51	(5, H-12)	4.73	(H-16)	5.77	(3, H-6)
2.77	(H-20)	3.51	(10, H-12)	4.80	(H-9)	3.46	(7, H-20)
		2.84	(9, H-20)			2.36	(4, H-17)
2.84	(H-20)	4.95	(17, H-9)	5.88	(H-3)	6.12	(3, H-4)
		2.77	(9, H-20)			1.06	(2, H-15)
3.05	(OH-8)	3.84	(3, H-10)	6.12	(H-4)	5.88	(4, H-3)
3.51	(H-12)	5.08	(7, H-13)			4.97	(4, H-7)
		2.77	(6, H-20)				
3.84	(H-10)	6.23	(7, H-2)				
		4.95	(2, H-9)				
		3.05	(3, OH-8)				
		2.68	(2, OH-12)				
4.79	(H-6)	5.95	(9, H-4)				
		5.10	(9, H-7)				
4.95	(H-9)	3.84	(2, H-10)				
		2.84	(10, H-20)				
5.87	(H-16)	6.23	(9, H-2)				



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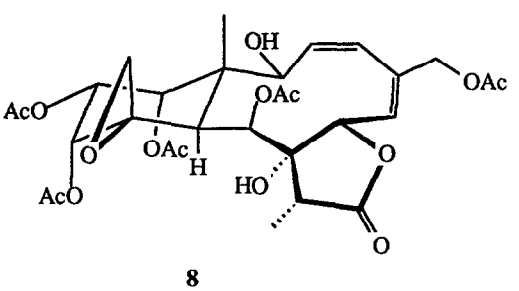

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Figure 1. The stereochemical projections of gemmacolides D (**6**) and E (**8**) based on NOEDS experiments.

five acetoxy groups must be positioned at C-9, C-12, C-13, C-14 and C-16. The substitution pattern and stereochemistry about the six-membered ring is the same as in gemmacolide A (**3**) but the chemical shift of the H-14 signal was shifted slightly downfield as a result of changing the substituent at H-2 from acetoxyl to hydroxyl. Analysis of a series of NOEDS measurements (Table 2) allowed the stereochemistry and conformation of gemmacolide F (**8**) to be determined as shown in Figure 1.

As has been observed previously for compounds in this series, the ^{1}H NMR spectra of gemmacolides D – F (**6**–**8**) in methanol-d_4 solution contained unusually broad signals due to slow conformational interconversion. We were able to improve the quality of the ^{1}H NMR spectra by recording them in a $CDCl_3$ solution that had been warmed to 50°C then cooled to room temperature, a treatment that appears to produce a dominant conformation.

Experimental Section

Extraction and isolation: The gorgonian *Junceela gemmacea* (60 g, dry weight) was collected at Jokaj Pass, Kolonia, Pohnpei (-12 m) in April 1989 and was immediately frozen. The frozen tissue was extracted for two days with 1:1 methanol-ethyl acetate (2 x 600 mL). The combined extracts were evaporated under reduced pressure and the aqueous residue was extracted with ethyl acetate (3 x 150 mL). The organic extract was dried over Na_2SO_4 and the solvent evaporated to give a brown oil (0.62 g), which was chromatographed on a silica column using solvents of increasing polarity from hexane to ethyl acetate. The fractions eluted with mixtures of hexane-ethyl acetate (4:1 to 1:1) were combined and evaporated to obtain a clear oil (170 mg), which was separated by HPLC (EtOAc-hexane, 85:15) to obtain four fractions that were further purified by HPLC. Using EtOAc-Et_2O-hexane (1:5:1) as eluant, the first fraction yielded gemmacolide B (**4**, 15 mg, 0.025% dry wt.) and the second fraction was separated into gemmacolide C (**5**, 6 mg, 0.01% dry wt.) and gemmacolide A (**3**, 9 mg, 0.015% dry wt.). The third fraction was purified by reversed phase HPLC (MeOH-H_2O, 65:35) to obtain gemmacolide E (**7**, 6 mg, 0.01% dry wt.) and gemmacolide F (**8**, 14 mg, 0.023% dry wt.). The last fraction contained gemmacolide D (**6**, 12 mg, 0.02% dry wt.).

Gemmacolide A (3): Colorless oil, $[\alpha]_D$ = -2.0° (c = 0.2, $CHCl_3$); IR ($CHCl_3$) 3480, 1795, 1745 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.91 (br d, 1 H, *J* = 8.3 Hz, H-2), 5.80 (br s, 1 H, H-16), 5.71 (br s, 1 H, H-9), 5.51 (br s, 1 H, H-16), 5.24 (dd, 1 H, *J* = 4.0, 1.0 Hz, H-14), 5.22 (dd, 1 H, *J* = 4.0, 4.0 Hz, H-13), 4.84 (dd, 1 H, *J* = 4.0, 1.0 Hz, H-12), 4.61 (br d, 1 H, *J* = 2.9 Hz, H-6), 4.44 (br s, 1 H, H-7), 3.67 (br s, 1 H, H-10), 3.48 (s, 8-OH), 2.96 (q, 1 H, *J* = 6.8 Hz, H-17), 2.94 (d, 1 H, *J* = 3.6 Hz, H-20), 2.70 (m, 1 H, H-3), 2.45 (m, 2 H, H-4), 2.38 (d, 1 H, *J* = 3.6 Hz, H-20), 2.23 (s, 3 H), 2.07 (s, 3 H), 2.02 (s, 3 H), 2.01 (s, 3 H), 1.95 (s, 3 H), 1.64 (m, 1 H, H-3), 1.26 (d, 3 H, *J* = 6.8 Hz, H-19), 1.25 (s, 3 H, H-15); ^{13}C NMR (50 MHz, $CDCl_3$) see Table 1; CIMS, Obsd. *m/z* = 676.2336 $(M + NH_4)^+$, $C_{30}H_{43}O_{14}NCl$ requires *m/z* = 676.2372.

Gemmacolide B (4): Colorless oil, $[\alpha]_D$ = -5.5° (c = 0.44, $CHCl_3$); IR ($CHCl_3$) 3490, 1795, 1745 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.91 (br d, 1 H, *J* = 8.3 Hz, H-2), 5.78 (br s, 1 H, H-16), 5.71 (br s, 1 H, H-9), 5.51 (br s, 1 H, H-16), 5.24 (d, 1 H, *J* = 2.9 Hz, H-13), 5.24 (d, 1 H, *J* = 2.2 Hz, H-14), 4.86 (dd, 1 H, *J* = 2.9, 2.2 Hz, H-12), 4.61 (br d, 1 H, *J* = 2.9 Hz, H-6), 4.44 (br s, 1 H, H-7), 3.67 (br s, 1 H, H-10),

3.43 (s, 8-OH), 2.97 (q, 1 H, J = 6.8 Hz, H-17), 2.96 (d, 1 H, J = 3.6 Hz, H-20), 2.70 (m, 1 H, H-3), 2.45 (m, 2 H, H-4), 2.39 (d, 1 H, J = 3.6 Hz, H-20), 2.23 (s, 3 H), 2.08 (m, 2 H, H-2'), 2.06 (s, 3 H), 2.01 (s, 3 H), 2.00 (s, 3 H), 1.99 (m, 1 H, H-3'), 1.63 (m, 1 H, H-3), 1.26 (d, 3 H, J = 6.8 Hz, H-19), 1.25 (s, 3 H, H-15), 0.92 (d, 3 H, J = 6.5 Hz, H-4'), 0.91 (d, 3 H, J = 6.5 Hz, H-5'); ^{13}C NMR (50 MHz, $CDCl_3$) see Table 1; CIMS *Obsd.* m/z = 718.2825 $(M + NH_4)^+$, $C_{33}H_{49}O_{14}NCl$ requires m/z = 718.2842.

Gemmacolide C (5): Colorless oil, $[\alpha]_D$ = +13.8° (c =0.48, $CHCl_3$); IR ($CHCl_3$): 3490, 1795, 1740 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.97 (br d, 1 H, J = 8.3 Hz, H-2), 5.82 (br s, 1 H, H-16), 5.76 (br s, 1 H, H-9), 5.53 (br s, 1 H, H-16), 4.91 (t, 1 H, J = 2.9 Hz, H-14), 4.62 (br d, 1 H, J = 3.2 Hz, H-6), 4.55 (dd, 1 H, J = 2.9, 1.8 Hz, H-12), 4.45 (br s, 1 H, H-7), 3.70 (br s, 1 H, H-10), 3.44 (s, 8-OH), 2.96 (q, 1 H, J = 6.8 Hz, H-17), 2.83 (d, 1 H, J = 3.2 Hz, H-20), 2.72 (m, 1 H, H-3), 2.45 (m, 2 H, H-4), 2.36 (d, 1 H, J = 3.2 Hz, H-20), 2.24 (m, 2 H, H-13), 2.23 (s, 3 H), 2.01 (s, 6 H), 1.98 (s, 3 H), 1.61 (m, 1 H, H-3), 1.27 (d, 3 H, J = 6.8 Hz, H-19), 1.16 (s, 3 H, H-15); ^{13}C NMR (50 MHz, $CDCl_3$) see table 1; CIMS, Obsd. m/z = 618.2325 $(M + NH_4)^+$, $C_{28}H_{41}O_{12}NCl$ requires m/z = 618.2317.

Gemmacolide D (6): Colorless oil, $[\alpha]_D$ = +88.3° (c = 0.66, $CHCl_3$); IR ($CHCl_3$) 3700, 1780, 1740 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.23 (d, 1 H, J = 9.7 Hz, H-2), 5.95 (d, 1 H, J = 11.5 Hz, H-4), 5.86 (br s, 1 H, H-16), 5.79 (br s, 1 H, H-16), 5.71 (dd, 1 H, J = 11.5, 9.7 Hz, H-3), 5.32 (br d, 1 H, J = 4.0 Hz, H-14), 5.10 (d, 1 H, J = 3.6 Hz, H-7), 5.08 (t, 1 H, J = 4.0 Hz, H-13), 4.95 (d, 1 H, J = 2.9 Hz, H-9), 4.79 (d, 1 H, J = 3.6 Hz, H-6), 3.84 (br s, 1 H, H-10), 3.51 (br dd, 1 H, J = 6.5, 4.0 Hz, H-12), 3.05 (s, 8-OH), 2.84 (d, 1 H, J = 2.9 Hz, H-20), 2.83 (q, 1 H, J = 7.9 Hz, H-17), 2.77 (d, 1 H, J = 2.9 Hz, H-20), 2.68 (d, J = 6.5 Hz, 12-OH), 2.18 (s, 3 H), 2.10 (s, 3 H), 2.05 (s, 3 H), 1.98 (s, 3 H), 1.27 (d, 3 H, J = 6.5 Hz, H-19), 1.25 (s, 3 H, H-15); CIMS, Obsd. m/z = 632.2128 $(M + NH_4)^+$, $C_{28}H_{39}O_{13}NCl$ requires m/z = 632.2110.

Gemmacolide E (7): Colorless oil; $[\alpha]_D$ = +56.0° (c = 0.25, $CHCl_3$); IR ($CHCl_3$) 3700, 3400, 1780, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.56 (d, 1 H, J = 9.7 Hz, H-2), 5.97 (br d, 1 H, J = 11.3 Hz, H-4), 5.83 (dd, 1 H, J = 11.3, 9.7 Hz, H-3), 5.79 (br s, 1 H, H-16), 5.60 (br s, 1 H, H-16), 5.10 (d, 1 H, J = 2.5 Hz, H-7), 4.95 (t, 1 H, J = 3.2 Hz, H-13), 4.92 (d, 1 H, J = 2.5 Hz, H-9), 4.78 (d, 1 H, J = 2.5 Hz, H-6), 4.10 (d, J = 6.1 Hz, 14-OH), 3.86 (br s, 1 H, H-10), 3.80 (ddd, 1 H, J = 6.1, 3.2, 1.4 Hz, H-14), 3.74 (d, J = 6.5 Hz, 12-OH), 3.59 (ddd, 1 H, J = 6.5, 3.2, 1.4 Hz, H-12), 3.11 (s, 8-OH), 2.83 (q, 1 H, J = 7.2 Hz, H-17), 2.83, 2.78 (d, 1 H, J = 3.6 Hz, H-20), 2.18 (s, 3 H), 2.17 (s, 3 H), 2.12 (s, 3 H), 1.24 (d, 3 H, J = 7.2 Hz, H-19), 1.13 (s, 3 H, H-15); FABMS, Obsd. m/z = 573.1765 $(M + H)^+$, $C_{26}H_{34}O_{12}Cl$ requires m/z = 573.1739.

Gemmacolide F (8): Colorless oil; $[\alpha]_D$ = −3.8° (c = 0.32, CHC_{13}); IR ($CHCl_3$) 3700, 1780, 1740 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.12 (br d, 1 H, J = 10.1 Hz, H-4), 5.88 (dd, 1 H, J = 10.1, 9.7 Hz, H-3), 5.77 (dd, 1 H, J = 8.6, 1.4 Hz, H-6), 5.44 (br d, 1 H, J = 3.6 Hz, H-14), 5.12 (t, 1 H, J = 3.6 Hz, H-13), 4.97 (dd, 1 H, J = 8.6, 1.8 Hz, H-7), 4.91 (br d, 1 H, J = 3.6 Hz, H-12), 4.80 (d, 1 H, J = 3.6 Hz, H-9), 4.78 (d, 1 H, J = 14.8 Hz, H-16), 4.73 (d, 1 H, J = 14.8 Hz, H-16), 4.47 (dd, 1 H, J = 9.7, 3.2 Hz, H-2), 3.57 (d, 1 H, J = 3.6Hz, H-10), 3.46, 2.91 (d, 1 H, J = 2.5 Hz, H-20), 2.36 (q, 1 H, J = 6.8 Hz, H-17), -2.20 (2-OH), -2.10 (8-OH), 2.17 (s, 3 H), 2.16 (s, 3 H), 2.10 (s, 3 H), 1.98 (s, 3 H), 1.17 (d, 3 H, J = 6.8 Hz, H-19), 1.06 (s, 3 H, H-15). CIMS, m/z = 656.2537 $(M + NH_4)^+$, $C_{30}H_{42}O_{15}N$ requires m/z = 656.2554.

Acetylation of Gemmacolides D (6) and E (7): A solution of gemmacolide D (**6**, 3.0 mg) in pyridine (0.1 mL) and acetic anhydride (0.1 mL.) was allowed to stand at room temperature for 10 hr. Ice-cold water (2 mL) was added to destroy the excess reagents and the resulting mixture was extracted with ethyl acetate. The extract was dried over anyhydrous sodium sulfate and the solvent evaporated to yield the penta-acetate (**10**, 2.9 mg) as an oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.24 (d, 1 H, J = 9.8 Hz), 5.96 (br d, 1 H, J = 11.5 Hz), 5.75 (m, 3 H), 5.24 (br d, 1 H, J = 3.3 Hz), 5.19 (t, 1 H, J = 3.7 Hz), 5.10 (br d, 1 H, J = 3.3 Hz), 4.91 (d, 1 H, J = 1.6 Hz), 4.85 (br d, 1 H, J = 3.7 Hz), 4.73 (d, 1 H, J = 3.3 Hz), 3.93 (br s, 1 H), 3.04

(s, 1 H), 2.90 (d, 1 H, J = 3.1 Hz), 2.88 (q, 1 H, J = 7.6 Hz), 2.71 (d, 1 H, J = 3.1 Hz), 2.17 (s, 3 H), 2.11 (s, 3 H), 2.06 (s, 3 H), 1.98 (s, 3 H), 1.95 (s, 3 H), 1.29 (s, 3 H), 1.22 (d, 3 H, J = 7.6 Hz); EIMS *m/z* 596 (M−OAc, 0.5), 553 (1.1), 539 (3.9), 537 (11), 477 (2.4), 459 (2.3), 399 (3.6), 253 (32), 191 (73), 149 (100).

Acetylation of gemmacolide E (**7**, 3.0 mg) under the same conditions gave the same penta-acetate **10** (2.8 mg), as indicated by TLC, ^{1}H NMR, and EIMS data.

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