Six New Diterpenoids from *Suregada multiflora*†

Ismet Ara Jahan,‡,§ Nilufar Nahar,‡ M. Mosihuzzaman,§ Farzana Shaheen,⊥ Atta-ur-Rahman,⊥ and M. Iqbal Choudhary*,⊥

Department of Chemistry, University of Dhaka, Dhaka, Dhaka-1000, Bangladesh, Bangladesh Council of Scientific and Industrial Research (BCSIR), Dhaka-1205, Bangladesh, and H.E.J. Research Institute of Chemistry, International Center for Chemical Sciences, University of Karachi, Karachi-75270, Pakistan

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Six new diterpenoids were isolated from a CH_2Cl_2−MeOH extract of the bark of *Suregada multiflora*. The structures were established on the basis of one- and two-dimensional NMR and other spectroscopic studies and chemical derivatizations. Two compounds, suregadolides C (**1**) and D (**2**), were identified as new diterpene lactones of two antipodal series, containing a cyclopropane ring bridging C-3 and C-4 of the basic abietane skeleton. Suremulide A (**3**) was found to be a new abietene diterpene lactone. Bannaringaolide A (**4**), a diterpene lactone, based on a novel carbon skeleton with a seven-membered ring, possibly formed by the rearrangement of the exocyclic C-17 in ring C of an *ent*-pimarane framework, has also been isolated. A kaurane triol, suremulol A (**5**), and a kaurane diol, suremulol B (**6**), were also identified as new metabolites.

The plant *Suregada multiflora* (A. Juss.) Baill. (syn. *Gelonium multiflorum*), known locally as "bannaringa", is distributed in the tropical and subtropical areas of Asia and Africa.[1] It is used as a purgative and in hepatic complaints in folkloric medicines.[1] Previous phytochemical studies on different parts of *S. multiflora* have resulted in the isolation of several diterpenoids,[2−7] flavonoids,[7,8] and triterpenoids.[9,10] An anti-HIV-[11−13] and anti-HSV-active[14] protein, GAP-31, has also been reported from the seeds of this plant.

Earlier we reported the isolation of two novel diterpene lactones, suregadolides A and B, from the CH_2Cl_2 soluble part of the crude bark extract (CH_2Cl_2−MeOH) of *S. multiflora.*[2] The crude (CH_2Cl_2−MeOH, 1:1) extract of *S. multiflora* exhibited selective cytotoxic activity in different human tumor cell lines.[2] Further work on *S. multiflora* bark has led to the isolation of six additional new diterpenes, namely, suregadolides C (**1**) and D (**2**), suremulide A (**3**), bannaringaolide A (**4**), and suremulols A (**5**) and B (**6**).

Results and Discussion

The IR spectrum of **1** showed an absorption maximum (1713 cm^{-1}) for an α,β-unsaturated γ-lactone.[2−5] The HREIMS of **1** afforded the M^+ at *m/z* 348.1905 ($C_{20}H_{28}O_5$). The ^1H and ^{13}C NMR spectra ($CDCl_3$+CD_3OD) of compound **1** indicated a rearranged abietane skeleton with signals for a lactone carbonyl (δ_C 177.6), a vinylic methyl (δ_H 1.85/δ_C 8.5),[3,5−7] two secondary hydroxyl-containing methines (δ_H 3.80/δ_C 69.9 and δ_H 4.83/δ_C 64.9), and one tertiary hydroxyl-bearing carbon (δ_C 76.6). The signals at δ_H 0.05/0.42 (H_2-18), δ_C 22.5 (C-18), δ_H 0.60 (H-3), δ_C 20.5 (C-3), and δ_C 16.9 (C-4) indicated the presence of a cyclopropane ring,[2,15] while the signals at δ_H 1.01 (δ_C 24.9) and 1.14 (δ_C 13.3) gave evidence for two more methyl groups in the molecule.

The ^1H NMR spectrum of **1** when recorded in C_5D_5N showed the signals for three hydroxyl protons (δ_H 7.73, 6.54, and 5.53), which disappeared when the spectrum was recorded with the addition of a few drops of D_2O. The spectrum of diacetate derivative (**1a**), obtained by acetylation of **1** with acetic anhydride in pyridine, further supported the presence of two secondary hydroxyl groups in the molecule, while the tertiary hydroxyl group, located at C-8, was confirmed from HMBC interactions.

The relative stereochemistry of **1** was deduced from NOE difference measurements (Figure 2), while the *trans* A/B ring junction was presumed on biogenetic grounds.[4] H-12 was inferred as α (pseudoaxial) and H-9 as β (pseudoaxial) from the coupling constants and multiplicities of their ^1H NMR signals (Table 1).[2,4,5] NOEs between H-12/H-11b, CH_3-20/H-11b, CH_3-20/CH_3-19, and CH_3-19/H-3 indicated the α-orientations of H-11b, CH_3-20, CH_3-19, and H-3, and thus the β-orientation of the cyclopropane ring. A NOE between H-18 *endo*/H-5 indicated the β-orientation of H-5. In turn, NOESY interactions between H-18 *endo*/H-5, H-5/H-6a, H-6a/H-7, H-7/H-14, and H-14/H-9 established β-orientations of H-7, H-14, and H-9. From a Drieding model, it was apparent that the NOEs between H-7/ H-9 and H-9/H-14 were only possible when the C-8 OH is α-oriented. The assigned stereochemistry for H-5, CH_3-20, and H-9 supported it being an abietane diterpene lactone skeleton of the *ent* (antipodal) series.[4,16] Accordingly, compound **1** was established as, 3,4,18β-cyclopropa-7α,8α,14α-trihydroxyabiet-13,15-en-16,12-olide, on the basis of 1D (^1H, ^{13}C, Table 1) and 2D NMR (COSY-45°, HMQC, HMBC) spectral data and spectral comparison with data of previously reported compounds.[2−5,15]

Compound **2** (*m/z* 348.1930, $C_{20}H_{28}O_5$) showed evidence for an α,β-unsaturated γ-lactone in the IR (1733^{-1} cm) and ^{13}C NMR spectra (δ_C 176.0). A vinylic methyl (δ_H 1.70/δ_C 8.2), two secondary hydroxyl methines (δ_H 3.62/δ_C 67.9 and δ_H 4.45/δ_C 71.4), and one tertiary hydroxyl-bearing carbon (δ_C 77.5) were also inferred from the NMR spectra. The signals at δ_H −0.17, 0.19/δ_C 21.7, δ_H 0.35/δ_C 15.7 and δ_C 18.6 indicated the presence of a trisubstituted cyclopropane ring and two other methyl groups (δ_H 0.72/δ_C 12.3 and δ_H 0.70/δ_C 23.1) in the molecule. The structure of **2** was deduced having a rearranged abietane skeleton with the

† Dedicated to the memory of Dr. M. Salar Khan, a renowned taxonomist of Bangladesh.

* To whom correspondence should be addressed. Fax: +9221 9243190, 9243191. E-mail: hej@cyber.net.pk, zainaraa@digicom.net.pk.
‡ University of Dhaka.
§ Bangladesh Council of Scientific and Industrial Research.
⊥ University of Karachi.

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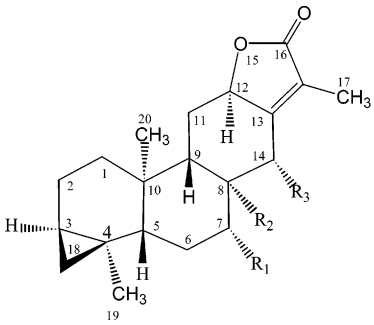
Chart 1



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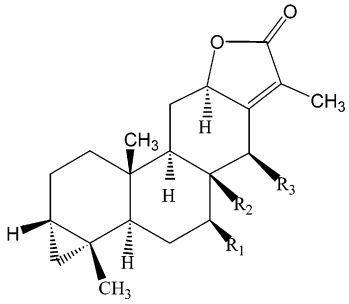
1a $R_1 = R_2 = R_3 = AcO$



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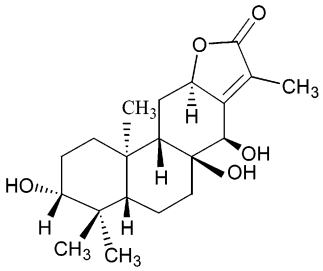
2a $R_1 = R_2 = R_3 =$ OAc



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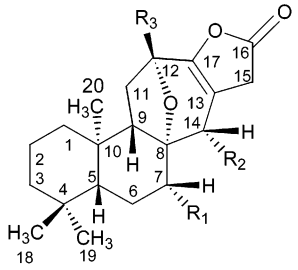
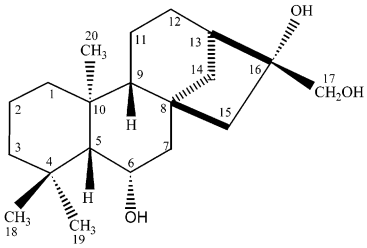


4 $R_1 = R_2 = R_3 = OH$
4a $R_1 = R_2 = R_3 = AcO$



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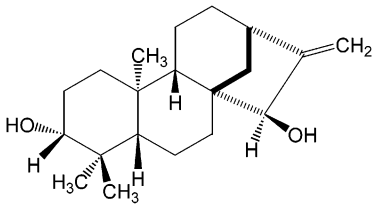

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aid of ^1H and ^{13}C ($CDCl_3$+CD_3OD, Table 1) NMR, COSY-45°, HMQC, HMBC, and NOE (Figure 2) studies and chemical derivatization.

NOE studies of compound **2** assisted in the assignment of relative stereochemistry at different stereogenic centers and indicated the abietane skeleton. The stereochemistry of H-12 (δ_H 4.54 ddd, J = 11.9, 6.0, 2.0 Hz) was deduced to be α (pseudoaxial) from a comparative study of chemical shifts, multiplicities, and coupling constants of the H-12 signal (Table 1) with structurally related compounds, namely, suregadolides A (δ_H 5.15, ddd, J = 12.0, 6.4, 1.6, Hz) and B (δ_H 4.18, ddd, J = 10.3, 5.5, 2.3 Hz)[2] and gelomulides A (δ_H 4.99, ddd, J = 12.9, 5.3, 2.1 Hz), F (δ_H 4.84, ddd, J = 13.0, 5.4, 2.1 Hz),[4] and H (δ_H 4.94, ddd, J = 12.3, 6.2, 2.0 Hz),[5] isolated from the same plant. The NOE between H-9 and H-12 suggested that H-9 was also α-oriented. The NOEs between H-9/H-5, H-9/H-7, H-9/H-12, H-9/H-14, and H-9/H-11b suggested the α-orientation of H-5, H-7, H-11b, and H-14 and therefore indicated the β-orientations of C-7 OH and C-14 OH. On the other hand, a strong NOE was observed between CH_3-20 and H-11a, which suggested the β-orientation of C-20 methyl group. The strong NOE interaction between H-18 *endo* and H-5 suggested the α-orientation of the cyclopropane unit. The Drieding model study and the observed NOE between H-7 and H-9 supported the β-orientation of OH-8 (Figure 2). The assigned stereochemistry of H-5, CH_3-20, and H-9 in compound **2** further supported a normal abietane diterpene lactone skeleton.

The structure of compound **2** was elucidated as 3,4,18α-cyclopropa-7β,8β,14β-trihydroxyabiet-13,15-en-16,12-olide and was named suregadolide D. The presence of

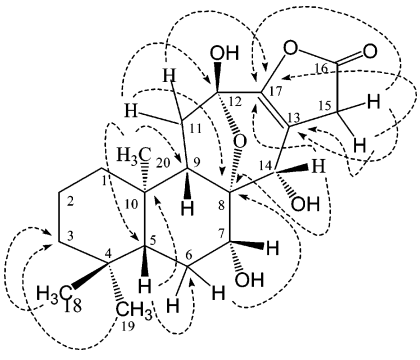
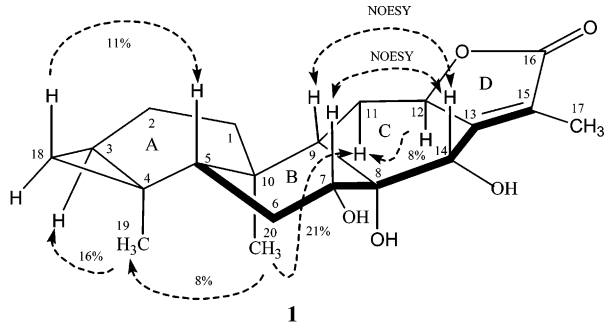


Figure 1. Important HMBC interactions for compound **4**.



1

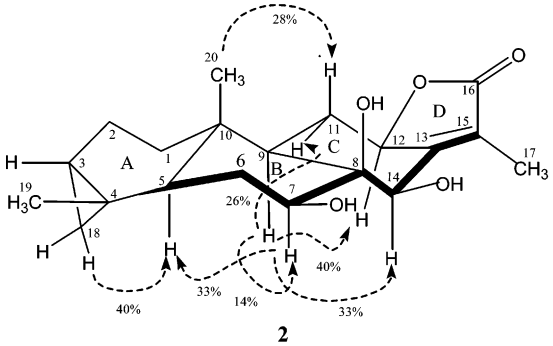


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Figure 2. Important NOE and NOESY interactions in compound **1** and NOE interactions in compound **2**.

Table 1. NMR Data ($CDCl_3$+CD_3OD) of Compounds **1**, **1b**, **2**, **2a**, and **3**

	1		**1a**	**2**		**2a**	**3**	
position	δ_H (J = Hz)	δ_C[a]	δ_H (J = Hz)	δ_H (J = Hz)	δ_C[a]	δ_H (J = Hz)	δ_H	δ_C[a]
1a	0.64 (m)	33.2 (t)		0.45 (m)	34.5 (t)	0.58 (m)	0.90 (m)	39.9 (t)
1b	1.40 (m)			1.30 (m)		1.35 (m)	1.82 (dt, 3.6)	
2a	1.60 (m)	19.8 (t)		1.45 (m)	18.8 (t)	1.49 (m)	1.45 (m)	27.0 (t)
2b	1.80 (m)			1.70 (m)		1.76 (m)	1.54 (m)	
3	0.60 (ddd, 9.0, 8.8, 6.1)	20.5 (d)	0.53 (m, $W_{1/2}$ = 9.5)	0.35 (ddd, 9.7, 7.0, 4.5)	15.7 (d)	0.45 (m, $W_{1/2}$ = 9.4)	3.12 (dd, 11.3, 5.0)	7 8.3 (d)
4		16.9 (s)			18.6 (s)			38.5 (s)
5	1.63 (dd, 13.7, 2.9)	43.3 (d)	1.40 (dd, 13.6, 2.9)	1.35 (dd, 14.3, 5.4)	42.2 (d)	1.30 (m)	0.82 (m)	5 4.2 (d)
6a	1.80 (dt, 13.1, 3.2)	29.6 (t)		1.60 (dt, 13.5, 3.5)	28.0 (t)		1.50 (m)	20.3 (t)
6b	2.08 (dt, 13.7, 2.5)			1.8 (dt, 13.5, 3.5)			1.54 (m)	
7a	3.8 (t, 3.0)	69.9 (d)	4.7 (m)	3.62(t, 3.0)	67.9 (d)	4.89 (t, s, 2.7)	1.47 (m)	41.7 (t)
7b			2.1 (s, Ac)			1.95 (s, Ac)	2.18 (dt, 2.7)	
8		76.6			77.5 (s)			74.0 (s)
9	1.2 (bd, 9.0)	42.5 (s)	1.22 (bd, 9.8)	1.1 (dd, 13.0, 2.6)	41.1 (s)	1.28 (dd, 13.4, 2.6)	1.43 (bd, 7.9)	56.1 (s)
10		37.3 (d)			35.4 (d)			38.5 (s)
11a	1.38 (m, $W_{1/2}$ = 14.5)	27.9 (s)	1.32 (m)	1.24 (m, $W_{1/2}$ = 12.3)	28.5 (t)	2.23 (m)	1.47 (m)	28.4 (t)
11b	2 0.32 (dd, 13.0, 9.0)	29.3 (t)	2.28 (dd, 13.0, 7.6)	2.02 (ddd, 12.0, 6.4, 2.8)		1.25 (m)	2.36 (dd, 12.2, 7.0)	
12	5.46 (ddd, 11.3, 7.6, 1.8)	79.4 (d)	5.48 (m)	4.54 (ddd, 11.9, 6.0, 2.0)	79.1 (d)	4.55 (ddd, 11.0, 6.0, 1.8)	5.12 (ddd, 10.3, 8.4, 1.7)	77.3 (d)
13		164.0 (s)			162.5 (s)			163.0 (s)
14a	4.83 (m)	64.9 (d)	5.90 (bs)	4.45 (d, 1.8)	71.4 (d)	5.47 (bs)	4.28 (s)	71.9 (d)
14b			2.10 (s, Ac)			2.04 (s, Ac)		
15		126.0 (s)			122.2 (s)			122.0 (s)
16		177.6 (s)			176.0 (s)			176.0 (s)
17	1.85 (d, 2.0)	8.5 (q)	1.82 (d, 2.0)	1.70 (d, 1.7)	8.2 (q)	1.71 (d, 1.8)	1.75 (d, 1.7)	7.5 (q)
18 *endo*	0.054 (dd, 5.8, 3.8)	22.5 (d)	0.07 (dd, 5.4, 4.9)	−0.17 (dd, 5.8, 4.5)	21.7 (t)	0.16 (dd, 5.2, 4.7)	0.90 (s)	28.5 (q)
18 *exo*	0.42 (dd, 9.3, 4.0)		0.42 (dd, 9.3, 4.2)	0.19 (dd, 9.2, 4.6)		0.34 (dd, 9.3, 4.2)		
19	1.01 (s)	24.9 (q)	0.94 (s)	0.70 (s)	23.1 (q)	0.84 (s)	0.70 (s)	15.4 (q)
20	1.14 (s)	13.3 (q)	1.01 (s)	0.72 (s)	12.3 (q)	0.88 (s)	1.14 (s)	16.0 (q)

[a] Determined by DEPT and HMQC spectra.

diterpenoids of both the normal [suregadolide D (**2**)] and antipodal [suregadolide C (**1**)] series in the same species is an intriguing observation. However, the co-occurrence of diterpenoids of two antipodal series has been reported earlier from the plant *Oxystigma oxyphyllum* Harms.[17]

The IR spectrum of **3** ($C_{20}H_{30}O_5$, *m/z* 350.2093) showed the presence of hydroxyl group (3425 cm^{-1}) and lactone carbonyl (1739 cm^{-1}) functionalities. The ^1H NMR spectrum in C_5D_5N exhibited three hydroxyl proton signals at δ_H 7.73, 6.54, and 5.53, which disappeared when the spectrum was recorded with the addition of a few drops of D_2O. An extensive analysis of NMR data ($CDCl_3$+CD_3OD, Table 1) along with the 2D NMR spectra (COSY 45° and HMBC) showed that compound **3** has distinct similarities to the previously reported compound gelomulide I.[5] The relative stereochemistry of all the chiral centers of **3** were deduced from its NOESY spectrum as depicted in Figure 3. Compound **3** was therefore identified as 3α,8β,14β-trihydroxyabiet-13,15-en-16,12-olide and was named suremulide.

The novel compound **4** showed the presence of lactone C=O (1732 cm^{-1}) and hydroxyl (3596 and 3445 cm^{-1}) groups in its IR spectrum. The molecular formula, $C_{20}H_{28}O_6$, of **4** was inferred from the negative HRFABMS (*m/z* 364.4370) and supported with ^{13}C NMR data. The NMR data (C_5D_5N) also revealed the presence of three methyls [δ_H 0.76/δ_C 22.0, δ_H 0.87/δ_C 33.5, and δ_H 1.14/δ_C 15.8], two oxygen-containing methines (δ_H 4.60/δ_C 69.7 and δ_H 5.94/72.7), and two tertiary hydroxyl-bearing carbons (δ_C 79.9 and 105.0). The presence of two quaternary carbon signals (δ_C 79.9 and 105.0) indicated the presence of an ether functionality. The lactone carbonyl carbon resonated at δ_C 172.4. The ^{13}C NMR spectrum also showed the presence of four methylenes, two more methines, and five additional quaternary carbons in the molecule (Table 2).

The $^1H-^1H$ (COSY-45°) NMR spectrum of **4** showed that H_2-11 (δ_H 2.30 m/2.67 m) were coupled with a methine H-9 (δ_H 2.40, bd, J = 13.0 Hz). The H-5 signal (δ_H 1.99, bs) was found to be coupled with H_2-6 (δ_H 1.80, dd, J = 12.2, 3.0 Hz and δ_H 2.08, m). In turn H_2-6 was also coupled with an oxymethine proton (δ_H 4.60, bs). The nonequivalent C-15 methylene protons (δ_H 3.22, d, J = 8.7 Hz; δ_H 3.56, d, J = 8.6 Hz) exhibited only geminal couplings. This suggested that the C-15 methylene must be attached to two quaternary carbons, of which one may be an electron-withdrawing lactone carbonyl. This was further confirmed by the observed $^1H-^1H$ (TOCSY-100 ms) and HMBC interactions (Figure 1).

The presence of three hydroxyl groups was inferred from the signals at δ_H 8.75, 6.40, and 4.80, which disappeared when the spectrum was recorded in C_5D_5N with a few drops of D_2O. In the COSY-45° spectrum, the cross-peaks between H-14 (δ_H 5.94, d, J = 5.4 Hz) and the geminal OH-14 (δ_H 8.70, d, J = 5.8 Hz) and between H-7 (δ_H 4.60, bs) and OH-7 (δ_H 6.40, d, J = 3.6 Hz) were observed, which confirmed the presence of two secondary hydroxyl groups in the molecule. On acetylation of **4** in the usual manner, the triacetate **4a** was obtained.

The HMBC spectrum of **4** showed long-range heteronuclear couplings, which were used to determine the position of different functionalities in the molecule (Figure 1). The presence of an ether bridge between the C-12 (δ_C 105.0) and C-8 (δ_C 79.9) quaternary carbons was concluded from the HMBC spectrum. This linkage has also been reported earlier in a furanoheliangolide derivative, 4,5-dihydroniveusin A.[18] Accordingly, compound **4** could be assigned as a novel diterpene skeleton containing one lactone, three hydroxyls, and one tetrahydrofuran ring.

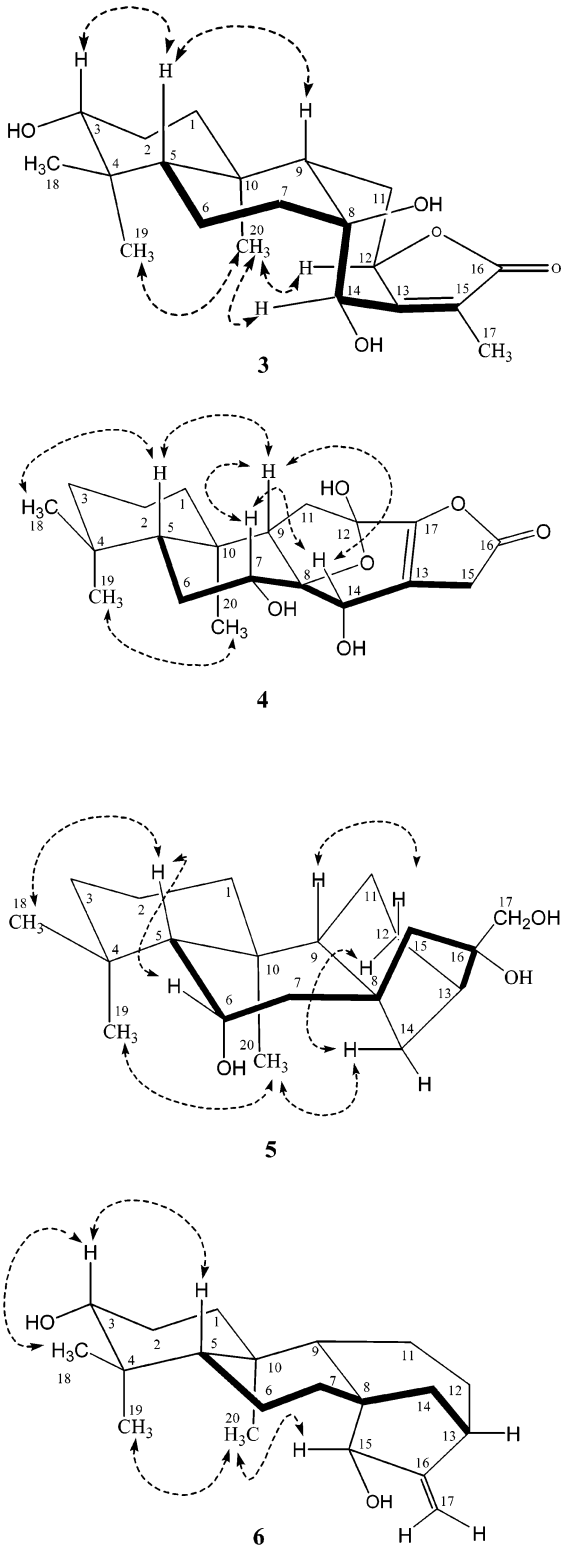

Figure 3. Important NOESY interactions for compounds **3**–**6**.

Compound **4** was determined as an *ent*-diterpenoid on biogenetic grounds,[16] and the stereochemistry of the ring A/B ring junction in **4** was deduced to be *trans*. The relative configuration of **4** was determined from its NOESY spectrum ($CDCl_3$+CD_3OD), as depicted in Figure 3. The interaction of the CH_3-20 methyl (δ_H 0.72) with the C-19 methyl (δ_H 0.68) protons suggested the α-orientation of the C-19 methyl and thus the β-orientation of the geminal C-18

Table 2. NMR Data of Compounds **4**, **4a**, **5**, and **6**

	4 ($CDCl_3$+CD_3OD)		**4** (C_5D_5N)		**4a** ($CDCl_3$+CD_3OD)	**5** ($CDCl_3$+CD_3OD)		**6** ($CDCL_3$)	
position	δ_H (J = Hz)	δ_C[a]	δ_H (J = Hz)	δ_C[a]	δ_H (J = Hz)	δ_H (J = Hz)	δ_C[a]	δ_H (J = Hz)	δ_C[a]
1a	0.75 (dt, 2.9, 11.2)	39.3 (t)	1.05 dt, 11.2, 2.9)	40.0 (t)		1.24 (m)	43.6 (t)	0.85 (m)	38.8 (t)
1b	1.47 (bd, 12.4)		1.67 (bd, 12.4)			1.35 (m)		1.85 (m)	
2a	1.20 (m)	18.3 (t)	1.34 (m)	18.8 (t)		1.45 (m)	18.2 (t)	1.62 (m)	27.7 (t)
2b	1.50 (m)		1.52 (m)			1.57 (m)		1.64 (m)	
3a	1.22 (m)	41.7 (t)	1.30 (m)	42.0 (t)		1.58 (m)	40.3 (t)	3.2 (dd, 11.5, 5.1)	79.0 (d)
3b	1.28 (m)		1.40 (m)			1.70 (m)			
4		33.0 (s)		33.8 (s)			33.5 (s)		39.2 (s)
5	1.30 (bs)	46.6 (d)	1.99 (bs)	47.0 (d)	1.49 (bs)	0.88 (m, $W_{1/2}$ = 3.4)	60.6 (d)	0.76 (bd, 12.6)	55.0 (d)
6a	1.57 (dd, 12.2, 3.0)	25.3 (t)	1.80 (dd, 12.2, 3.0)	26.8 (t)		3.74 (m, $W_{1/2}$ = 6.15)	69.9 (d)	1.30 (m)	18.1 (t)
6b	1.68 (m)		2.08 (m)		1.95 (s, Ac)			1.40 (m)	
7a	3.73 (bs)	68.5 (d)	4.60 (bs)	69.7(d)		1.65 (m)	52.1 (t)	1.45 (m)	35.2 (t)
7b			6.40 (OH, d, 3.6)			1.86 (m)		1.60 (m)	
8		79.1 (s)		79.9 (s)			44.6 (s)		47.5 (s)
9	1.48 (bd, 13.0)	45.3 (d)	2.40 (bd, 13.0)	46.1 (d)	1.76 (bd, 1.30)	0.75 (dt, 12.5, 3.7)	56.1 (d)	0.85 (dt, 12.5, 4.5)	55.0 (d)
10		37.2 (s)		38.0 (s)			40.9 (s)		38.8 (s)
11a	1.58 (m)	32.3 (t)	2.30 (m)	34.7 (t)		1.25 (m)	18.4 (t)	1.40 (m)	19.1 (t)
11b	2.01 (bd, 12.5, 2.6)		2.67 (m)			1.35 (m)		1.55 (m)	
12a		104.1 (s)	4.80 (OH, s)	105.0 (s)	2.02 (s, Ac)	1.62 (m)	26.0 (t)	1.55 (m)	32.7 (t)
12b						1.72 (m)		1.65 (m)	
13		127.3 (s)		128.0 (s)		1.98 (bs)	45.2 (d)	2.72 (bs)	42.3 (d)
14a	4.67 (d, 5.4)	71.8 (d)	5.94 (d, 5.4)	72.7 (d)	2.10 (s, Ac)	1.64 (m)	37.7 (t)	1.30 (m)	36.2 (t)
14b			8.70 (OH, d, 5.8)			1.88 (m)		1.87 (m)	
15a	2.60 (d, 6.1)	22.5 (t)	3.22 (d, 8.7)	24.6 (t)	2.40	1.45 (m)	53.0 (t)	3.79 (bs)	83.0 (d)
15b	2.45 (d, 6.0)		3.56 (d, 8.6)		2.50	1.55 (m)			
16		173.2 (s)		172.4 (s)			81.0 (s)		160.0 (s)
17a		162.3 (s)		162.8 (s)		3.56 (d, 11.2)	65.9 (d)	5.05 (bs)	108 (t)
17b						3.59 (d, 11.2)		5.15 (m)	
18	0.62 (s)	33.0 (q)	0.87 (s)	33.5 (q)	0.71 (s)	1.14 (s)	36.5 (q)	0.74 (s)	28.1 (q)
19	0.68 (s)	21.9 (q)	0.76 (s)	22.0 (q)	0.75 (s)	0.98 (s)	22.1 (q)	0.97 (s)	15.5 (q)
20	0.72 (s)	15.8 (q)	1.14 (s)	15.8 (q)	0.87 (s)	1.04 (s)	19.0 (q)	1.01 (s)	17.6 (q)

[a] Determined from the DEPT and HMQC spectra.

methyl (δ_H 0.62). The NOESY interaction between the C-18 methyl and H-5 (δ_H 1.30) confirmed the β-orientation of H-5. NOESY interactions observed between H-9 (δ_H 1.48)/H-5, H-9/H-14 (δ_H 4.67), H-9/H-7 (δ_H 3.73), and H-14/H-7 indicated the β-orientations of H-9, H-14, and H-7. From the Drieding model study of the compound **4**, it was observed that the NOE interaction between H-9β/H-14β was only possible with a C-8α/C-12α ether link and thus a β-oriented OH-12. The structure of compound **4** was, therefore, determined to be 7α,14α,12β-trihydroxy-8,12α-epoxypimar-13,17-en-17,16-olide and was named bannaringaolide. Compound **4** represents a new diterpene skeleton with a seven-membered ring C, a rare feature in tricyclic diterpenes. Some examples of previously described diterpenoids with a seven-membered ring C include methyl verticoate[19] and strobic,[20] hispanonic, and hispaninic acids.[21]

Compound **5** ($C_{20}H_{34}O_3$, *m/z* 322.2090) showed the presence of one or more hydroxyl groups (3374 cm^{-1}) in its IR spectrum. The 1D NMR spectral data of **5** (Table 2) along with the 2D NMR spectra (COSY-45°, HMQC, HMBC) supported an *ent*-kaurane-6,16,17-triol skeleton as reported for corymbol, isolated from *Turbina corymbosa*[22] and *Calibrachoa parviflora*.[23] However the optical rotation, $[\alpha]_D^{25}$ −9° (*c* 0.0425, pyridine), of **5** was found to be different from the reported value of $[\alpha]_D^{25}$ −38° (pyridine),[23] which suggested that compound **5** might be a stereoisomer of corymbol. Corymbol has been reported as being a 6α,16β,17-triol.[23] Corymbol is an *ent*-kaurane diterpenoid where the C-20 methyl is α-oriented, H-5 is β, and H-6 is α. Compound **5** was also determined as an *ent*-diterpenoid on biogenetic grounds where the C-20 methyl is predicted to be α-oriented.[16] The relative stereochemistry at the important chiral centers of **5** was then deduced from its NOESY spectrum as depicted in Figure 6. The stereochemistry at H-6 was determined from the multiplicity and coupling constant observed for H-6 and from interactions found in its NOESY spectrum. In the ^{1}H NMR spectrum of compound **5**, H-6 showed a multiplet at δ_H 3.94 ($W_{1/2}$ = 6.15 Hz). This suggested the equatorial position of the H-6 proton and thus the axial position of the hydroxyl group. A strong cross-peak between H-5 and H-6 also supported the β-orientation of H-6. A Drieding model study of the compound indicated an equatorial proton at the C-6 position, which must be β-oriented, and thus an α-orientation of the hydroxyl proton. In corymbol, H-6 was reported as α (axial), while in compound **5**, H-6 was found to be β (equatorial) (Figure 3). The structure of compound **5** was elucidated as *ent*-kaurane-6β,16β,17-triol, an epimer of corymbol, and was named as suremulol A.

The IR spectrum of compound **6** ($C_{20}H_{32}O_2$, *m/z* 304.5290) showed a hydroxyl absorption (3361 cm^{-1}). The NMR spectral data ($CDCl_3$, Table 2) along with the COSY-45°, HMQC, and HMBC spectra of **6** supported the presence of a kaurene-3,15-diol, structurally related to *ent*-kaurene-3β,15β-diol[6] (euphoranginol),[24] *ent*-kaurene-3β,15α-diol,[25,27] and its enantiomer,[26] from *Elaeoselinum tenuifolium*. This suggested that compound **6** might be a stereoisomer of *ent*-kaurene-3β,15α-diol.

The C-20 methyl in structure **6** was deduced to be α-oriented on biogenetic grounds.[16] The relative stereochemistry was deduced on the basis of NOESY interactions, as shown in Figure 3. A Drieding model study and NOESY interactions between H-15 and H_3-20 agreed well with the α-orientations of C-8/C-13 in ring D of **6**. In the previously reported compound, *ent*-kaure-16-en-3β,15α-diol,[25,27] this fragment was found to be β-oriented. The structure of compound **6** was thus elucidated as 13α-*ent*-kaur-16-en-3β,15α-diol and was named suremulol B. Compounds **5** and **6** were identified as kaurane diterpenoids derived from two C-13 epimeric *ent*-pimaranes. The co-occurrence of diterpenoids of C-13 epimers from the same plant has also been reported.[26,28]

Experimental Section

General Experimental Procedures. The optical rotations were taken on a JASCO DIP-360 polarimeter. UV spectra were measured on a Hitachi UV-3200 spectrophotometer. IR spectra were recorded on a JASCO A-302 spectrophotometer. The ^{1}H NMR spectra were recorded on Bruker AM-400 and AMX 500 NMR spectrometers using a UNIX data system at 400 and 500 MHz, respectively. The ^{13}C NMR spectra were recorded on the same instruments at 100 and 125 MHz, respectively. The chemical shift (δ) values are in ppm with TMS as internal standard, and coupling constants (*J*) are in Hz. EIMS were recorded on a Varian MAT 311 mass spectrometer. HREIMS and FABMS measurements were performed on a JEOL JMS HX 110 mass spectrometer using glycerol as standard matrix. TLC was carried out on precoated Kieselgel 60 F_{254} aluminum sheets (Merck); spots were viewed at 254 and 366 nm stained by spraying with a solution of ceric sulfate in 10% H_2SO_4. Flash silica gel, 240−300 mesh, G_{254} (E. Merck) was used for the column chromatography.

Plant Material. The plant material (1.65 kg) was collected near Cox's Bazar, Chunati Game Reserve, Harbang Beat, Bangladesh, in April 1999. The plant was identified by the late Professor M. Salar Khan, Bangladesh National Herbarium (BNH), Dhaka, Bangladesh. A herbarium specimen of this plant was deposited at BNH (voucher no. DACB, accession no. 28004).

Extraction and Isolation. The air-dried bark of *S. multiflora* was ground into a powder and extracted with CH_2Cl_2−MeOH (1:1, 10 L × 3, 24 h). The resulting crude extract was concentrated to give a dark brown, thick liquid (115.8 g). The crude extract was then partitioned between CH_2Cl_2 and water, and a CH_2Cl_2-soluble extract (38.2 g) was thus obtained. The CH_2Cl_2-soluble part was then subjected to VLC over silica gel (600 g) and eluted with hexane, hexane−CH_2Cl_2 (9:1, 4:1, 3:2, 1:1, 2:3, 1:4), CH_2Cl_2, CH_2Cl_2−MeOH (100:1, 19:1, 9:1, 4:1, 3:2, 1:1), and MeOH (each 1.5 L) to yield 12 major fractions (SM-1−SM-12).

Fraction SM-8 (CH_2Cl_2−MeOH, 19:1, 6.5 g) was purified over a silica gel column (60 g) eluted with hexane and hexane−EtOAc and EtOAc, which yielded eight fractions (SM-8-1−SM-8-8). Further chromatography of fraction SM-8-6 (hexane−EtOH, 500 mg) over silica gel (10 g), eluted with a gradient of hexane−acetone and acetone, yielded six fractions (SM-8-6-1−SM-8-6-6). Fraction SM-8-6-1 (hexane−acetone, 3:1, 180 mg), on repeated column chromatography, afforded compound **1** (10 mg). Fraction SM-8-6-3 (hexane−acetone, 3:2, 150 mg) afforded compound **2** (8.0 mg) on column chromatography. Fraction SM-8-2 (300 mg, hexane−acetone, 2:3) was fractionated into five different fractions on a silica gel (5 g) column by eluting with hexane−EtOAc (9.5: 0.5, 9:1, 4:1, 3:2, 2:3) and EtOAc (each 200 mL). Fraction SM-8-2-2 (80 mg, 8.5:1.5) was purified over a silica gel column to yield compound **6** (10 mg, hexane−acetone, 9:1).

Fraction SM-10 (5.8 g, CH_2Cl_2−MeOH, 4:1) obtained from the first column was further fractionated into 12 fractions (SM-10-1−SM-10-12) by silica gel column chromatography (60 g), using gradients of hexane, hexane−EtOAc (9:1, 4:1, 2:3, 1:9), EtOAc, and EtOAc−MeOH (9.5: 0.5, 9:1, 8.5:1.5, 4:1, 1:4) (each 500 mL). Fraction SM-10-5 (700 mg), eluted by EtOAc−MeOH (9:1), was subjected to a silica gel column (14 g) to obtain 10 fractions (SM-1-5-1−SM-10-5-10), using gradient elution (CH_2Cl_2, CH_2Cl_2−MeOH (9.5:0.5, 9:1, 8.5: 1.5, 4:1, 3:2, 2:3, 1:4), each 300 mL). Fraction SM-10-5-2 (50 mg), obtained by elution with the solvent system CH_2Cl_2−MeOH (9:1), was purified on a silica gel column using CH_2Cl_2−MeOH (9.5:0.5), which yielded compound **5** (5 mg). Another fraction, SM-10-5-3 (250

mg, CH_2Cl_2–MeOH, 9:1), was purified on a silica gel column, affording compound **4** (10 mg, CH_2Cl_2–MeOH, 9.2:0.08). A final fraction, SM-10-4-3 (50 mg), eluted with CH_2Cl_2–MeOH (9.5:0.5) was purified on silica gel using CH_2Cl_2–MeOH (9.9: 0.1), which yielded compound **3** (4.0 mg).

The percent yields were 6.7×10^{-4} (**1**), 5.3×10^{-4} (**2**), 2.6×10^{-4} (**3**), 6.7×10^{-4} (**4**), 3.35×10^{-4} (**5**), and 6.7×10^{-4} (**6**). TLC: R_f values were as follows: compound **1**, 0.48 (CH_2Cl_2–MeOH, 24:1); **2**, 0.30 (CH_2Cl_2–MeOH, 24:1); **3**, 0.50 (CH_2Cl_2–MeOH, 9.9:0.1); **4**, 0.34 (CH_2Cl_2–MeOH, 9:1); **5**, 0.43 (CH_2Cl_2–MeOH, 9:1); **6**, 0.32 (CH_2Cl_2–MeOH, 10:0.5).

Suregadolide C (1): white amorphous powder (10.0 mg); $[\alpha]_D^{25}$ −44° (*c* MeOH 0.048); UV (MeOH) λ_{max} (log ϵ) 218 (3.44) nm; IR ($CHCl_3$) ν_{max} 3504 (OH), 2922, 2864, 2557 (C–H), 1713 (α,β-unsaturated γ-lactone, C=O), 1684, 1449, 1385, 1216, 1133, 1059, 991 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$+CD_3OD), see Table 1; EIMS *m/z* 348 (82), 218 (100), 193 (49), 135 (58), 121 (97), 95 (66), 81 (53); HREIMS *m/z* 348.1905 ($C_{20}H_{28}O_5$, requires 348.1936).

Diacetate (1a). Compound **1** (6.0 mg) was acetylated with Ac_2O in pyridine (3:1) at room temperature for 24 h. Upon the usual workup and preparative TLC (hexane–acetone, 4:1, double development), **1a** (2.5 mg, R_f = 0.25, hexane–acetone, $[\alpha]_D^{25}$ −27° (*c* 0.095, $CHCl_3$) was obtained as a solid, amorphous powder: ^1H NMR ($CDCl_3$+CD_3OD), see Table 1; HREIMS *m/z* 432.2638 ($C_{24}H_{32}O_7$, requires 432.2670).

Suregadolide D (2): white amorphous powder (8.0 mg); $[\alpha]_D^{25}$ +49° (*c* MeOH, 0.038); UV (MeOH) λ_{max} (log ϵ) 225 (3.52) nm; IR ($CHCl_3$) ν_{max} 3326 (OH), 2925, 2864 (C–H), 1733 (α,β-unsaturated γ-lactone, C=O), 1517, 1446, 1381, 1283, 1092 1081, 983 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$+CD_3OD), see Table 1; EI MS *m/z* 348 (69), 330 (9), 193 (38), 123 (68), 121 (75), 55 (100); HREIMS *m/z* 348.1930 ($C_{20}H_{28}O_5$, requires 348.1936).

Diacetate (2a). Compound **2** (5 mg) was acetylated with Ac_2O in pyridine (3:1) at room temperature for 24 h. Usual workup and preparative TLC (hexane–acetone, 7.5:2.5 twice) afforded **2a** (2.3 mg, R_f = 0.20 in hexane–acetone): $[\alpha]_D^{25}$ +31° (*c* 0.035, $CHCl_3$); ^1H NMR ($CDCl_3$+CD_3OD), see Table 1; HREIMS *m/z* 432.2663 ($C_{24}H_{32}O_7$, requires 432.2670).

Suremulide (3): white amorphous powder (4.0 mg); $[\alpha]_D^{25}$ 33° (*c* 0.048, MeOH); UV (MeOH) λ_{max} (log ϵ) 220 (3.44) nm; IR ($CHCl_3$) ν_{max} 3415 (OH), 2925, 2857 (C–H), 1739 (α,β-unsaturated γ-lactone, C=O), 1648, 1553, 1460, 1090, 1026, 770 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$+CD_3OD), see Table 2; EIMS *m/z* 350 (40), 332 (14), 299 (9), 223 (19), 205 (11), 186 (16), 177 (54), 195 (68), 149 (50), 136 (60), 135 (73), 95 (61), 71 (57), 55 (100); HREIMS *m/z* 350.2093 ($C_{20}H_{28}O_5$, requires 350.2090).

Bannaringaolide A (4): white amorphous powder (10 mg); $[\alpha]_D^{25}$ +10.8° (*c* MeOH 0.048); UV (MeOH) λ_{max} (log ϵ) 227 (3.31) nm; IR ($CHCl_3$) ν_{max} 3596, 3445 (OH), 2931, 2846 (C–H), 1732 (α,β-unsaturated γ-lactone, C=O), 1688, 1378, 1200, 1076, 1000, 930 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$+CD_3OD), see Table 2; EIMS *m/z* M^+ not found, 341 (9), 310 (20), 297 (21), 227 (26), 123 (51), 109 (35), 83 (35), 69 (100); (−ve) HRFABMS *m/z* 364.4370 ($C_{20}H_{28}O_6$, requires 364.4364)

Triacetate (4a). Compound **4** (5.0 mg) was acetylated with Ac_2O in pyridine (3:1) at room temperature for 72 h. The usual workup and preparative TLC (CH_2Cl_2, thrice) afforded **4a** (2.5 mg, R_f = 0.20, CH_2Cl_2), $[\alpha]_D^2$ +3.1° (*c* 0.035, $CHCl_3$), as a solid amorphous powder: ^1H NMR ($CDCl_3$+CD_3OD), see Table 2; HREIMS *m/z* 490.5447 ($C_{20}H_{34}O_9$, requires 490.5464).

Suremulol A (5): white amorphous powder (5.0 mg); $[\alpha]_D^{25}$ −9° (*c* 0.028, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 202 (3.03) nm; IR ($CHCl_3$) ν_{max} 3374 (OH), 2923, 2852 (C–H), 1739, 1462, 1368, 1036 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$+CD_3OD), see Table 2; EIMS (*m/z*) 322 (1), 304 (5), 291 (100), 230 (39), 177 (8), 161 (6), 109 (17), 95 (21), 69 (26), 55 (20); HREIMS *m/z* 322.2090 ($C_{20}H_{34}O_3$, requires 322.2085).

Suremulol B (6): white amorphous powder (10.0 mg); $[\alpha]_D^{25}$ −14° (*c* 0.0425, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 202 (3.62) nm; IR ($CHCl_3$) ν_{max} 3361 (OH), 2927, 2867 (C–H), 1631, 1454, 1367, 1182, 1056, 1021, 996, 895, 756 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$+CD_3OD), see Table 2; EIMS *m/z* 304 (56), 286 (24), 271 (44), 253 (38), 135 (43), 121 (40), 107 (48), 105 (68), 91 (84), 55 (100); HREIMS *m/z* 304.5290 ($C_{20}H_{32}O_2$, requires 304.5185).

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Supporting Information Available: Proposal for the biogenesis of compounds **1**–**6** inclusive of five schemes. This material is available free of charge via the Internet at http://pubs.acs.org.

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