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Bisabosquals, Novel Squalene Synthase Inhibitors

II. Physico-chemical Properties and Structure Elucidation

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The squalene synthase inhibitor bisabosqual A was isolated from the culture broth of *Stachybotrys* sp. RF-7260, and its structure was determined on the basis of spectroscopic methods including detailed 2D NMR analyses. The structures of bisabosquals B, C and D isolated from *Stachybotrys ruwenzoriensis* RF-6853 were determined by spectroscopic methods and chemical reactions. The absolute stereochemistry of bisabosquals A, B and D was determined by X-ray crystallographic analysis. They have novel *cis*-fused tetracyclic structures with a bisabolane-type sesquiterpene and phenol moieties.

We have isolated bisabosquals A, B, C and D as novel squalene synthase inhibitors from *Stachybotrys* and elucidated their unique structures with a bisabolane-type sesquiterpene and *cis*-fused tetracyclic moieties. In the preceding paper[1], we described their taxonomy, fermentation, isolation and biological activities. In this paper, we describe the physico-chemical properties and structure elucidation of bisabosquals.

Results

Physico-chemical Properties

The physico-chemical properties of bisabosquals A (**1**), B (**2**), C (**3**) and D (**4**) are summarized in Table 1. These compounds were soluble in methanol, chloroform, EtOAc and acetone, but insoluble in *n*-hexane and water. The IR spectrum of **1** showed the absorption bands characteristic of hydroxyl (3597 cm^{-1}), conjugated carbonyl (1673 cm^{-1}) and aromatic (1619 cm^{-1}) groups. The UV spectra of **1** and **4** indicated the existence of the same chromophore in both compounds.

Structure Elucidation of Bisabosqual A

The molecular formula of bisabosqual A (**1**) was determined to be $C_{23}H_{28}O_5$ on the basis of HR-LSIMS and ^{13}C NMR data. The ^{13}C and ^{1}H NMR spectra of **1** revealed the presence of a deuterium exchangeable proton, four methyl groups, four methylene groups, seven methine groups and eight quaternary carbons. In addition, two of the methine groups were determined to be aldehyde groups (δ 10.46; δ_C 188.27; $^{1}J_{(C,H)}$ 181.5 Hz, δ 10.36; δ_C 192.24; $^{1}J_{(C,H)}$ 182.5). The five aromatic carbons (δ_C 112.08, 117.31, 139.26, 155.71, 165.69) and a methine carbon (δ_C 113.67) indicated the presence of a penta-substituted aromatic ring moiety. ^{1}H-^{1}H COSY experiment indicated the partial structures represented by thick lines in Fig. 2. In addition to ^{1}H-^{1}H couplings, the prenyl moiety (C8-C13) was assigned on the basis of long-range ^{1}H-^{13}C correlations from both H_3-12 (δ 1.65) and H_3-13 (δ 1.59) to C-10 (δ_C 123.08) and C-11 (δ_C 132.47). Moreover, the remaining two singlets assignable to methyl groups suggested the groups to be linked to the quaternary carbons, which were thought to be linked to an oxygen atom based on the chemical shifts at δ_C 83.52 and δ_C 69.14. The key

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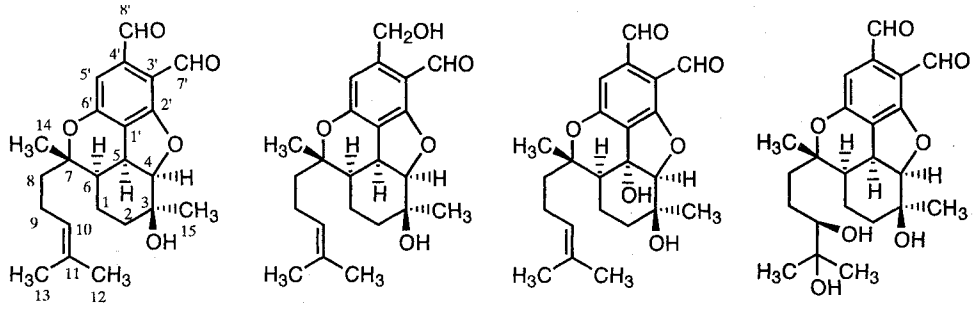
Fig. 1. Structures of bisabosquals A, B, C and D.



Bisabosqual A (**1**) Bisabosqual B (**2**) Bisabosqual C (**3**) Bisabosqual D (**4**)

Table 1. Physico-chemical properties of bisabosquals A (**1**), B (**2**), C (**3**) and D (**4**).

	1	**2**	**3**	**4**
Appearance	pale yellow plates	colorless prisms	white powder	white powder
MP	108-109°C	151-153°C		
$[\alpha]_D$[a]	+37.2° (*c* 1.0, $CHCl_3$)	+25.6° (*c* 0.55, dioxane)	-49.7° (*c* 1.0, dioxane)	+29.7° (*c* 0.2, dioxane)
Molecular weight	384	386	400	418
Molecular formula	$C_{23}H_{28}O_5$	$C_{23}H_{30}O_5$	$C_{23}H_{28}O_6$	$C_{23}H_{30}O_7$
HR-LSIMS (m/z)				
calcd :	385.2005 (as $C_{23}H_{29}O_5$)	387.2169 (as $C_{23}H_{31}O_5$)	401.1962 (as $C_{23}H_{29}O_6$)	419.2069 (as $C_{23}H_{31}O_7$)
found :	385.2013	387.2169	401.1959	419.2072
UV λ_{max} nm (ε) in CH_3CN	225 (sh, 9,300) 254 (26,540) 310 (6,390) 340 (6,000)	237 (24,410) 285 (16,760) 320 (5,460)	215 (11,570) 244 (18,490) 295 (5,400) 343 (5,400)	254 (23,200) 309 (5,690) 340 (5,340)
IR ν_{max} cm^{-1} (KBr)	3597, 1673, 1619, 1452	3436, 1651, 1618, 1449	3433, 1681 ,1606, 1451	3434, 1684, 1618, 1453

[a] The $[\alpha]_D$ value of **1** was measured at 22°C, those of **2** and **4** at 25°C, and that of **3** at 23°C

connectivity of the above-mentioned fragments was derived from careful studies of its HMBC data as shown in Fig. 2. One of the singlet methyls at δ 1.46 (H_3-14) showed long-range ^1H-^{13}C correlations with C-6 (δ_C 35.94), C-7 (δ_C 83.52) and C-8 (δ_C 38.71). The other singlet methyl at δ 1.31 (H_3-15) showed long-range ^1H-^{13}C correlations with the methylene carbon C-2 (δ_C 34.93), the quaternary carbon C-3 (δ_C 69.14) and the oxymethine C-4 (δ_C 92.77). The substitution position of the aromatic ring was indicated by the NOE and long-range ^1H-^{13}C correlations as shown in Fig. 3. The above results established that **1** has a bisabolane-type sesquiterpene moiety. The linkage between the sesquiterpene moiety and the aromatic ring was derived from the long-range ^1H-^{13}C correlations of H-4 (δ 4.97) with C-1′ (δ_C 117.31) and C-2′ (δ_C 165.69) and those of H-5 (δ 3.66) with C-1′ and C-2′ (Fig. 2).

The relative stereochemistry of **1** was investigated by analyzing NOEs and ^1H-^1H coupling constants. The coupling constants between H-4 and H-5 and between H-6 (δ 2.05) and H-5 were 8.8 and 6.6 Hz, respectively, and NOEs were observed clearly between H_3-15 and H-4, and between H-4 and H-5. These findings indicated a *cis*-fused ring system. In addition to these, the key NOEs shown in Fig. 3 clarified the relative configuration of all asymmetric

Fig. 2. NOE and long-range ^{1}H-^{13}C correlations of bisabosqual A.

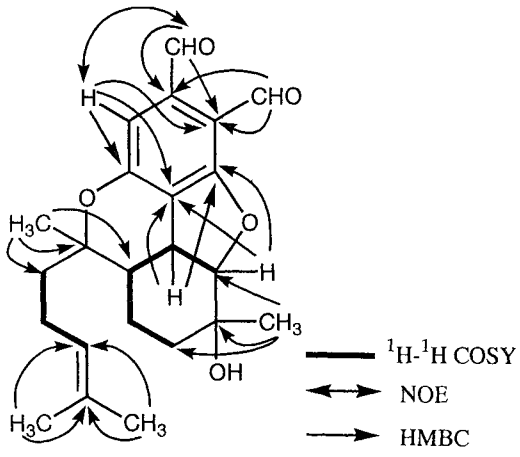


Fig. 3. Relative configuration of bisabosqual A and key NOE correlations.

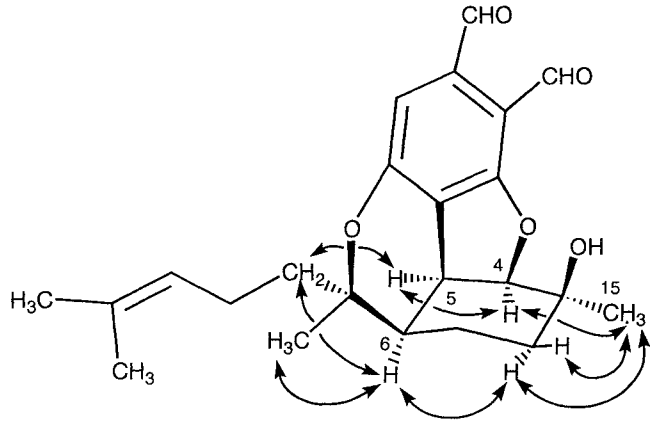


Table 2. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR spectral data of bisabosquals A and B.

	Bisabosqual A (1)[a]		Bisabosqual B (2)[b]	
Position	δ_C (ppm)	δ_H (ppm, J in Hz)	δ_C (ppm)	δ_H (ppm, J in Hz)
1	16.33 (t)	1.55 (m), 1.28 (m)	17.41 (t)	1.51 (m), 1.23 (m)
2	34.93 (t)	1.79 (m), 1.21 (m)	36.36 (t)	1.65 (m), 1.32 (m)
3	69.14 (s)		69.91 (s)	
4	92.77 (d)	4.97 (d, 8.8)	94.60 (d)	4.95 (d, 8.5)
5	33.27 (d)	3.66 (dd, 8.8 & 6.6)	34.26 (d)	3.64 (dd, 8.5 & 7.5)
6	35.94 (d)	2.05 (m)	37.27 (d)	2.13 (m)
7	83.52 (s)		84.35 (s)	
8	38.71 (t)	1.67 (m), 1.57 (m)	39.69 (t)	1.62 (m)
9	22.21 (t)	2.08 (m)	23.38 (t)	2.15 (m), 2.09 (m)
10	123.08 (d)	5.03 (m)	124.88 (d)	5.07 (m)
11	132.47 (s)		132.91 (s)	
12	25.57 (q)	1.65 (br.s)	25.88 (q)	1.65 (s)
13	17.63 (q)	1.59 (br.s)	17.70 (q)	1.59 (s)
14	22.11 (q)	1.46 (s)	22.59 (q)	1.43 (s)
15	29.53 (q)	1.31 (s)	29.45 (q)	1.26 (s)
1'	117.31 (s)		112.02 (s)	
2'	165.69 (s)		170.53 (s)	
3'	112.08 (s)		111.63 (s)	
4'	139.26 (s)		146.93 (s)	
5'	113.67 (d)	6.93 (s)	108.26 (d)	6.50 (s)
6'	155.71 (s)		158.44 (s)	
7'	188.27 (d)	10.46 (s)	189.62 (d)	10.12 (s)
8'	192.24 (d)	10.36 (s)	64.29 (t)	4.80 (s)
3-OH		1.55 (br.s)		

[a] Recorded in $CDCl_3$

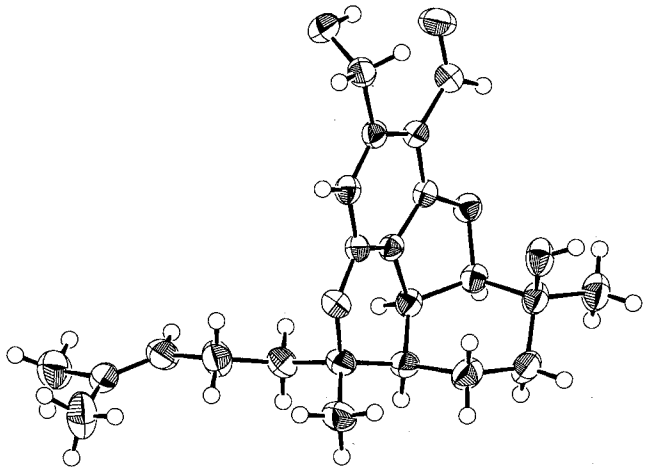
[b] Recorded in CD_3OD

carbons of **1**.

Structure Elucidation of Bisabosqual B

The ^1H NMR spectrum of **2** was very similar to that of **1** except for the signal of H-8′. The H-8′ protons of **2** were observed at δ 4.80 in place of the corresponding aldehydic proton of **1**. From the results of HR-LSIMS and ^{13}C NMR, the molecular formula of **2** was established as $C_{23}H_{30}O_5$, and **2** was speculated to be the dihydro analogue of **1**. The NOE between H-5′ and H-8′ revealed the position of these substitutions. Treatment of **1** with $NaBH_4$ in THF afforded **2** along with other reduction products. The synthetic **2** was identical with natural **2** by comparison of the spectroscopic data including optical rotation. This result also revealed that **2** has the same strerochemistry as **1**. Moreover, the structure of **2** including the relative stereochemistry was confirmed by X-ray crystallographic analysis (Fig. 4).

Fig. 4. ORTEP drawing of **2**.



Structure Elucidation of Bisabosqual C

The molecular formula of **3** was established as $C_{23}H_{28}O_6$ by HR-LSIMS and ^{13}C NMR data. The molecular formula of **3** indicated the presence of one more oxygen atom compared with that of **1**. In the ^1H NMR spectrum of **3**, the signal due to H-4 (δ 4.78, s) was observed instead of the signal (δ 4.97, d) observed in **1** and the signal due to H-5 (δ 3.66) observed in **1** was absent. The ^{13}C NMR spectrum was almost a duplicate except for the C-5 signal (δ_C 71.06 in **3**, δ_C 33.27 in **1**). Therefore, the structure of **3** was suggested to be a 5-hydroxy analogue of **1**. The long-range ^1H-^{13}C correlations of H-6 with C-1, C-5 and C-1′, and of H-4 with C-1′ and C-2′ confirmed the structure of **3**. The NOEs between H_3-15 and H-4 and between H-4 and 5-OH indicated the relative stereochemistry of **3** was same as **1**.

Structure Elucidation of Bisabosqual D

The molecular formula of **4** was determined to be $C_{23}H_{30}O_7$ by HR-LSIMS and ^1H and ^{13}C NMR data. The ^1H NMR spectrum of **4** was similar to that of **1**, but the H-10 signal appeared upfield compared with that of **1**. The ^{13}C NMR data showed that C-10 and C-11 were oxygenated as shown by their chemical shifts (δ_C 78.47 and δ_C 73.16). These data indicated that **4** was a 10,11-dihydroxy analogue of **1**. In order to identify the structure of **4**, **1** was treated with microencapsulated osmium tetraoxide (MC OsO_4)[2]. The reaction gave a mixture of dihydroxy products. They were separated by preparative reversed phase HPLC. One of them was identified with natural **4** by HPLC analysis, ^1H NMR and optical rotation data, and the other was elucidated as an epimer of **4** at the C-10 position. This result showed that **4** has the same strerochemistry as **1**.

Absolute Stereochemistry

To determine the absolute stereochemistry of the bisabosquals, bisabosqual D (**4**) was converted to the bromo derivative (**5**). Treatment of **4** with $NaBH_4$ in THF gave the pentahydroxy compound. Reaction of the pentahydroxy compound with *N*-bromosuccinimide afforded the bromo derivative (**5**). Compound **5** was crystallized from *n*-hexane - acetone solution as colorless prisms. A single crystal X-ray diffraction analysis of **5** confirmed the absolute stereochemistry of bisabosquals except for bisabosqual C (Fig. 5).

Discussion

Four novel compounds, bisabosquals, have been isolated as squalene synthase inhibitors and their structures have been elucidated. Their structural relationships are described as follows. Bisabosqual B is a reductive analogue of bisabosqual A at the 8′-position. Bisabosquals C and D are oxidative analogues of bisabosqual A at the 5-position and the 10- and 11-positions, respectively. Both bisabosquals B and D were converted from bisabosqual A by chemical reactions.

Several structurally related compounds have been reported from *Stachybotrys* organisms. K-76[3],

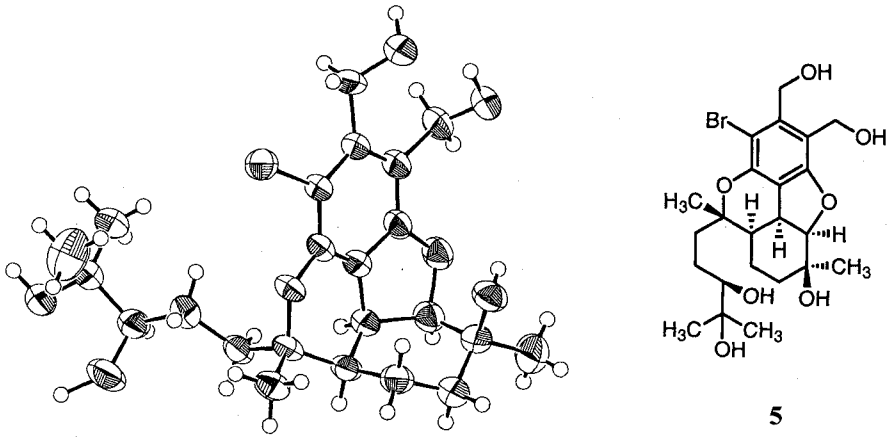
Table 3. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectral data of bisabosquals C and D in $CDCl_3$.

Position	Bisabosqual C (**3**)		Bisabosqual D (**4**)	
	δ_C (ppm)	δ_H (ppm, J in Hz)	δ_C (ppm)	δ_H (ppm, J in Hz)
1	18.02 (t)	1.60 (m), 1.19 (m)	16.36 (t)	1.56 (m), 1.28 (m)
2	34.16 (t)	1.75 (m), 1.36 (m)	34.89 (t)	1.79 (m), 1.23 (m)
3	70.19 (s)		69.24 (s)	
4	101.61 (d)	4.78 (s)	92.79 (d)	4.98 (d, 8.8)
5	71.06 (s)		33.12 (d)	3.72 (dd, 8.8 & 6.7)
6	41.05 (d)	2.31 (dd, 12.8 & 6.0)	36.05 (d)	2.05 (m)
7	85.38 (s)		83.59 (s)	
8	40.53 (t)	2.15 (m), 1.87 (m)	36.09 (t)	1.90 (m), 1.69 (m)
9	23.83 (t)	2.23 (m), 1.98 (m)	25.44 (t)	1.58 (m), 1.45 (m)
10	123.56 (d)	5.07 (m)	78.47 (d)	3.27 (br.d, 10.2)
11	132.08 (s)		73.16 (s)	
12	25.67 (q)	1.66 (br.s)	23.38 (q)[a]	1.19 (s)[b]
13	17.71 (q)	1.60 (br.s)	26.85 (q)[a]	1.22 (s)[b]
14	23.83 (q)	1.49 (s)	22.14 (q)	1.45 (s)
15	29.38 (q)	1.36 (s)	29.63 (q)	1.32 (s)
1'	117.98 (s)		117.46 (s)	
2'	166.14 (s)		165.73 (s)	
3'	112.55 (s)		112.40 (s)	
4'	141.28 (s)		139.29 (s)	
5'	113.59 (d)	6.91 (s)	113.69 (d)	6.93 (s)
6'	156.74 (s)		155.63 (s)	
7'	187.86 (d)	10.37 (s)	188.24 (d)	10.46 (s)
8'	192.29 (d)	10.35 (s)	192.32 (d)	10.37 (s)
3-OH		1.47 (br.s)		1.49 (br.s)
5-OH		2.78 (s)		
10-OH				2.37 (br)
11-OH				1.76 (br)

[a, b] Assignments may be interchanged

stachybotridial[4], stachybotramide[5], stachybocins[6], Mer-NF5003[7] and the F-1839 series[8] have a phenylspirodrimane moiety. Stachybotrin[9,10], staplabin[11] and the SMTP series[12,13] have a linear prenyl group and a chroman skeleton. They have in common a sesquiterpene moiety and an aromatic ring moiety in their structures. On the other hand, the bisabosquals have two unique structural features different from the known metabolites of *Stachybotrys* organisms. The first is a bisabolane skeleton as a sesquiterpene moiety. The second is that the bisabolane-type sesquiterpene connects to the aromatic ring *via* pyran and furan rings, which compose a *cis*-fused tetracyclic moiety. To our knowledge, this is the first report of the secondary metabolites from *Stachybotrys* organisms containing such a novel structure. This unique skeleton of bisabosquals attracts our interest from the viewpoint of their biogenesis.

Fig. 5. ORTEP drawing of **5**.



5

Experimental

General

Melting points were obtained using a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were determined using the sodium D line on a Perkin-Elmer 241 polarimeter. UV spectra were measured on a Hitachi U-3410 spectrophotometer. IR spectra were recorded on a JASCO FT/IR-700 spectrometer. LSIMS and HR-LSIMS were obtained on a Hitachi M-90 instrument. FAB-MS and HRFAB-MS were obtained on a JEOL JMS-SX/SX 102A. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity-600, Varian XL-400 and Varian Gemini-300 spectrometers.

Reduction of 1

Compound **1** (50 mg) in THF (2 ml) was treated with $NaBH_4$ (1.2 mg) for 3 hours at −5°C. The reaction mixture was poured into iced water and extracted with EtOAc. The organic phase was washed with water and brine and then dried over anhydrous sodium sulfate. After the solvent was evaporated, the residue was purified by silica gel column chromatography (Silica gel 60, E. Merck, *n*-hexane-EtOAc=1 : 1) to give **2** (8 mg); synthetic **2**: $[\alpha]_D^{25}$ +26.2° (*c* 0.30, dioxane). The ^{1}H and ^{13}C NMR data of synthetic **2** were identified with those of natural **2**.

X-Ray Crystallographic Analysis of Bisabosqual B (2)

Colorless prismatic crystals of bisabosqual B (**2**), $C_{23}H_{30}O_5$, were grown from acetone solution. A single crystal with approximate dimensions of 0.35×0.35×0.35 mm was used for data collection. X-ray diffraction measurement were performed at 295 K on a Rigaku AFC7R diffractometer using graphite monochromated Cu-Kα radiation (λ=1.54178 Å) and rotating anode generator. Cell constants were obtained by least-squares refinement using the setting angles of 25 carefully centered reflections in the range 45°<2θ<50°. The crystal data are as follows: space group $P2_1$, a=5.8972(7) Å, b=21.330(1) Å, c=8.1072(8) Å, β=96.195(9)°, V=1013.8(2) Å^3, Z=2, Dcal=1.266 g/cm^3. The data were collected at a temperature of 295 K using the $\omega/2\theta$ scan technique to a maximum 2θ value of 140.2°. Scans of (1.84+0.3 tan θ)° were done at a speed of 16°/minute (in ω). Of the 2139 reflections collected, 1956 were unique. The data were corrected for Lorentz and polarization effects. The structure was solved by direct methods[14] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The positional parameters of H-atoms in the OH were refined, while the remainders were included in fixed positions. The final cycle of full-matrix least-squares refinement was based on 1931 reflections [$I>\sigma$(I)] and 259 variable parameters. Final R and weighted R values were 0.033 and 0.052, respectively. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.19 and −0.17 e/Å^3, respectively. All calculations were performed using the teXsan[15] crystallographic software package of Molecular Structure Corporation.

Dihydroxylation of 1

To a solution of **1** (40 mg) in 6 ml of acetone-CH_3CN-

water (1 : 1 : 1) was added *N*-methylmorpholine-*N*-oxide (13 mg), followed by MC OsO_4 (13 mg, 5 mol%). The resulting mixture was stirred for 20 hours at room temperature. After the reaction was completed, the catalyst was separated by filtration. After washing with MeOH, combined filtrates were concentrated under reduced pressure, diluted with brine, and extracted with EtOAc. The organic phase was dried over anhydrous sodium sulfate and evaporated. The residue was purified by HPLC using Symmetry C_{18} (19×150 mm, Waters), and developed with CH_3CN-water (15 : 85) to give **4** (10 mg) and a 10-epimer of **4** (11 mg). **4**: The ^1H NMR and HPLC analysis data were identified with those of natural **4**. **4**: $[\alpha]_D^{24}$ +30.6° (*c* 0.2, dioxane). 10-epimer of **4**: HR FAB-MS *m/z* 419.2059 (calcd *m/z* 419.2069 for $C_{23}H_{31}O_7$); $[\alpha]_D^{24}$ −29.6° (*c* 0.21, MeOH); ^1H NMR (300 MHz, $CDCl_3$) δ 1.18 (3H, s), 1.23 (3H, s), 1.31 (3H, s), 1.45 (3H, s), 1.2~1.9 (8H, m), 2.04 (1H, m), 3.25 (1H, br. d, *J*=8.7 Hz), 3.68 (1H, dd, *J*=7.2, 8.7 Hz), 4.97 (1H, d, *J*=8.7 Hz), 6.92 (1H, s), 10.34 (1H, s), 10.45 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 16.40, 22.12, 23.67, 25.47, 26.48, 29.54, 33.19, 34.85, 35.80, 36.36, 69.06, 73.00, 78.20, 83.23, 92.64, 112.17, 113.78, 117.18, 139.04, 155.37, 165.37, 188.07, 192.04.

Bromo Compound (**5**)

Compound **4** (80 mg) in THF (10 ml) was treated with $NaBH_4$ (3.5 mg) for 2 hours at 0°C. The reaction mixture was poured into iced water and extracted with EtOAc. The organic layer was washed with water and dried over anhydrous sodium sulfate. After the solvent was evaporated, the residue was purified by silica gel column chromatography (Silica gel 60, E. Merck, EtOAc-MeOH=10 : 1) to give a pentahydroxy compound (55 mg). To an ice-cooled solution of the pentahydroxy compound (55 mg) in CH_2Cl_2 (10 ml) was added *N*-bromosuccinimide (25 mg). Two hours later, 10% aqueous sodium hydrogen sulfite (2 ml) was added to the reaction. The reaction mixture was stirred for 10 minutes and partitioned between organic and aqueous layers. The organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated. The residue was purified by silica gel column chromatography (Silica gel 60, E. Merck, EtOAc-MeOH=10 : 1) to give **5** (50 mg); HR FAB-MS *m/z* 500.1407 (calcd *m/z* 500.1410 for $C_{23}H_{33}O_7Br$); $[\alpha]_D^{24}$ −22.9° (*c* 0.30, MeOH); IR ν_{max} KBr cm^{-1}: 3400, 3200, 2973, 1633, 1484, 1432, 1365; ^1H NMR (300 MHz, CD_3OD) δ 1.13 (3H, s), 1.16 (3H, s), 1.26 (3H, s), 1.44 (3H, s), 1.2~1.9 (8H, m), 2.08 (1H, m), 3.14 (1H, dd, *J*=10.5, 1.5 Hz), 3.76 (1H, t-like), 4.70 (1H, d, *J*=15.3 Hz), 4.74 (1H, d, *J*=15.3 Hz), 4.80 (1H, d, *J*=8.4 Hz), 4.86 (2H, s); ^{13}C NMR (75 MHz, CD_3OD) δ_C 17.54, 22.76, 25.13, 25.65, 26.44, 29.63, 35.67, 36.26, 37.16, 37.43, 56.77, 61.77, 70.15, 73.68, 79.89, 84.36, 92.38, 103.18, 113.34, 115.67, 140.11, 149.19, 161.32.

X-Ray Crystallographic Analysis of Compound (**5**)

Colorless prismatic crystals of compound **5**, $C_{23}H_{33}O_7Br$, were grown from *n*-hexane-acetone solution. A single crystal with approximate dimensions of 0.20×0.20×0.15 mm was used for data collection. X-ray diffraction measurements were performed on a Rigaku AFC7R diffractometer using graphite monochromated Cu-Kα radiation (λ=1.54178 Å) and rotating anode generator. Cell constants were obtained by least-squares refinement using the setting angles of 25 carefully centered reflections in the range 59°<2θ<60°. Crystal data are as follows: space group *P*1, *a*=9.572(1) Å, *b*=11.305(1) Å, *c*=5.615(2) Å, α=102.83(1)°, β=92.34(2)°, γ=71.62(1)°, *V*=561.9(2) Å^3, *Z*=1, *D*cal=1.482 g/cm^3. The data were collected at a temperature of 295 K using the $\omega/2\theta$ scan technique to a maximum 2θ value of 140.3°. Scans of (1.78+0.3 tan θ)° were done at a speed of 16°/min (in ω). A total of 4421 unique reflections were collected. The linear absorption coefficient, μ, for Cu-Kα radiation is 28.5 cm^{-1}. An empirical absorption correction based on azimuthal scans of several reflections was applied which resulted in transmission factors ranging from 0.87 to 1.00. The data were corrected for Lorentz and polarization effects. The structure was solved by direct methods[14] and expanded using Fourier techniques. The absolute configuration of the compound was also determined based on anomalous scatterings of bromine atom. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in fixed positions. The final cycle of full-matrix least-squares refinement was based on 4421 reflections [*I*>0] and 279 variable parameters. Final *R* and weighted *R* values were 0.037 and 0.061, respectively. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.35 and −0.43 e/Å^3, respectively. All calculations were performed using the teXsan[15] crystallographic software package of Molecular Structure Corporation.

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