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XESTOBERGSTEROL C, A NEW PENTACYCLIC STEROID FROM THE OKINAWAN MARINE SPONGE *IRCINIA* SP. AND ABSOLUTE STEREOCHEMISTRY OF XESTOBERGSTEROL A

JUN'ICHI KOBAYASHI,* HIDEKI SHINONAGA, HIDEYUKI SHIGEMORI,

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

AKEMI UMEYAMA, NOBORU SHOJI, and SHIGENOBU ARIHARA

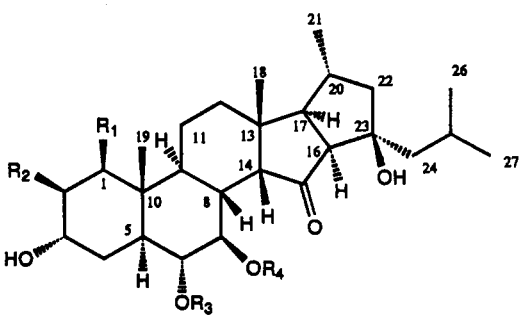
Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Tokushima 770, Japan

ABSTRACT.—A new pentacyclic steroid, xestobergsterol C [**1**], possessing a cis C/D ring junction, has been isolated together with two known compounds, xestobergsterols A [**2**] and B [**3**], from the Okinawan marine sponge *Ircinia* sp., and the structure determined on the basis of spectral data. Reexamination of the nmr data of xestobergsterols A [**2**] and B [**3**] resulted in revision of the configuration at C-23 and of the conformation of ring D in **2** and **3**. The absolute stereochemistry of xestobergsterol A [**2**] was established by the cd exciton chirality method.

Marine sponges have been a rich source of new types of steroids, typified by unique side-chain structures and unusual functionalization (1). During our studies on bioactive substances from marine organisms (2), we examined extracts of the Okinawan marine sponge *Ircinia* sp. and obtained a new pentacyclic steroid, xestobergsterol C [**1**], together with two known compounds, xestobergsterols A [**2**] and B [**3**] (3). In this paper we describe the isolation and structure elucidation of **1** and the revision of stereochemistry at C-23 and of the conformation of ring D in **2** and **3**. Furthermore, the absolute stereochemistry of xestobergsterol A [**2**] was established by the cd exciton chirality method.

The sponge *Ircinia* sp. was collected off Konbu, Okinawa Island, Japan, and kept frozen until used. The MeOH extract of the sponge was partitioned between EtOAc and H_2O, and the aqueous layer was subsequently extracted with *n*-BuOH. The *n*-BuOH-soluble portion was subjected to Si gel column chromatography ($CHCl_3$-*n*-BuOH-HOAc-H_2O, 1.5:6:1:1), followed by gel filtration on Sephadex LH-20 (MeOH) and C_{18} hplc (MeOH-H_2O, 75:25), to give xestobergsterol C (**1**, 0.00013%, wet wt) together with xestobergsterols A (**2**, 0.00013%) and B (**3**, 0.0004%).

Xestobergsterol C [**1**], a colorless powder ([α]D −18.6°), was shown to have the molecular formula, $C_{27}H_{44}O_6$, by hreims [*m/z* 464.3119 (M^+), Δ −1.9 mmu], indicating six degrees of



1 $R_1=R_3=R_4=H$, $R_2=OH$
2 $R_1=R_2=R_3=R_4=H$
3 $R_1=R_2=OH$, $R_3=R_4=H$
6 $R_1=R_2=H$, $R_3=R_4=p$-BrBz

unsaturation. An ir absorption (3400 cm^{-1}) indicated the presence of hydroxyl group(s). ^1H- and ^{13}C-nmr data (Table 1) of **1** revealed signals due to five methyls, six methylenes, twelve methines, and four quaternary carbons. The carbon resonance at δ_C 217.3 and the ir band at 1715 cm^{-1} indicated the presence of a carbonyl group in a five-membered ring. The ^1H-^1H COSY nmr spectrum revealed the presence of three partial structures, C-1–C-12, C-16–C-22, and C-24–C-27. The connectivity between rings A and B and the presence of Me-19 at C-10 in **1** were deduced from ^1H-^{13}C long-range couplings of Me-19 to C-1, C-5, C-9, and C-10 in the HMBC (4) spectrum (Table 1). A ketone carbonyl carbon at δ_C 217.3 was assigned to C-15 from HMBC correlations of H-14 and H-16 to C-15. HMBC correlations of Me-18 to C-12, C-13, C-14, and C-17 indicated the connectivity between rings C and D and the presence of Me-18 at C-13. The chemical shift of C-23 (δ_C 82.1) implied that an oxygen atom was attached to the carbon. HMBC correlations of H-16 and H-22 to C-23 and C-24 supported the presence of ring E and the connectivity between C-23 and the side-chain of C-24–C-27. Thus, the structure of xestobergsterol C was assigned as **1**.

The relative stereochemistry of **1** was elucidated on the basis of NOESY

TABLE 1. ^1H- and ^{13}C-Nmr Data of **1** in Pyridine-d_5.

Position	^1H[a]	*J* (Hz)	^{13}C[a]	m	HMBC (^1H)[b]	NOESY (^1H)
1α	1.95	dd (11.2, 3.0)	41.1	t	3,5,19	1β,2,5,9
β	2.12	m				1α,2
2	4.49	br s	71.4	d		1α,1β
3	4.54	br s	70.8	d	5	4α,4β
4α	2.85	d (13.4)	26.9	t	2	3,4β,5
β	2.41	dd (13.4, 12.0)				3,4α,6,19
5	2.58	dd (12.0, 9.6)	42.6	d	6,19	1α,4α,7,9
6	3.85	t (9.6)	75.6	d	7	4β,8,19
7	5.18	t (9.6)	75.2	d	6,8	5,9
8	2.08	m	38.8	d	7,9,14	6,11β,14,18,19
9	1.63	m	47.4	d	19	1α,5,7,12α
10			36.9	s	1,2,4,19	
11α	1.62	m	21.6	t	8,9	11β,12β
β	1.35	m				8,11α,12β
12α	1.14	m	38.6	t	18	9,12β,16
β	1.39	m				11α,12α,17
13			38.4	s	17,18	
14	3.51	br s	51.8	d	8,9,12,18	8,16,18,20
15			217.3	s	8,14,16,17	
16	2.72	d (10.0)	62.8	d	14,17,20,22,24	12α,14,17,24a,24b,25
17	1.70	t (10.0)	58.0	d	12,16,18,20,21,22	12β,16,20,21,22α
18	1.18	s	19.9	q	12,14,17	8,14,20
19	1.45	s	16.1	q	1,5,9	4β,6,8
20	2.63	m	34.8	d		14,17,18,21,22β,24b
21	1.09	d (6.3)	20.8	q	17,20,22	17,20,22α
22α	1.32	t (12.3)	52.4	t	16,17,20,21	17,21,22β
β	2.10	m				20,22α,24b
23			82.1	s	16,22	
24a	1.98	dd (14.2, 4.2)	52.0	t	16,22,25,26,27	16,24b,25,26,27
b	1.58	dd (14.2, 7.0)				16,22α,24a,25,26,27
25	2.20	m	24.9	d	26,27	16,24a,24b,26,27
26	1.04	d (6.7)	24.8	q	24,25	24a,24b,25
27	1.02	d (6.7)	25.2	q	24,25	24a,25

[a]δ in ppm.
[b]H coupled with C.

correlations (Figure 1) and ^{1}H-^{1}H coupling constants (Table 1). The NOESY spectrum showed cross-peaks of H-4β/Me-19, H-6/Me-19, and H-8/Me-19, and H-1α/H-5, H-7/H-5, and H-9/H-5, indicating a chair conformation for both the A and B rings and a trans- junction between rings A and B. The hydroxyl groups at C-2 and C-3 were assigned as being β- and α-oriented, respectively, judging from broad singlet proton signals at δ_H 4.49 (H-2) and 4.54 (H-3). The ^{1}H-^{1}H coupling constant between H-6 and H-7 (J=9.6 Hz) revealed the α- and β-configurations of hydroxyl groups at C-6 and C-7, respectively. The cis C/D ring junction was deduced from a NOESY correlation between H-14 and Me-18. NOESY correlations for H-16/H-24a, H-16/H-24b, and H-16/H-25 indicated that the C-24–C-27 side-chain was α-oriented, while NOESY correlations of H-9/H-12α, H-16/H-12α, and H-17/H-12β implied a chair conformation of ring C.

The structures of xestobergsterols A and B, first isolated from the Okinawan marine sponge *Xestospongia bergquistia*, were previously assigned as **4** and **5** (3), which are different from that of xestobergsterol C [**1**] in terms of the configuration at C-23 (α-OH on C-23 for **4** and **5**; β-OH on C-23 for **1**) and the conformation of ring C (boat form for **4** and **5**; chair form for **1**). All spectral data ([α]D, ^{1}H- and ^{13}C-nmr, ir, and eims) reported for xestobergsterols A and B (3), however, were identical with those of xestobergsterols A and B isolated from the sponge *Ircinia* sp. in the present study. This observation prompted us to reexamine the nmr data (Tables 2 and 3) of xestobergsterols A and B. Detailed analyses of ^{1}H-^{1}H COSY, NOESY, and HMQC spectra of xestobergsterol A required the assignments of the ^{1}H- and ^{13}C-nmr chemical shifts of C-2 and C-4 to be revised (δ_H 1.68 and 1.88 and δ_C 29.4 for C-2; δ_H 1.65 and 2.72 and δ_C 31.3 for C-

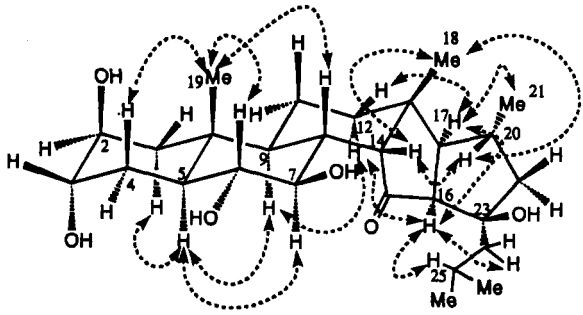


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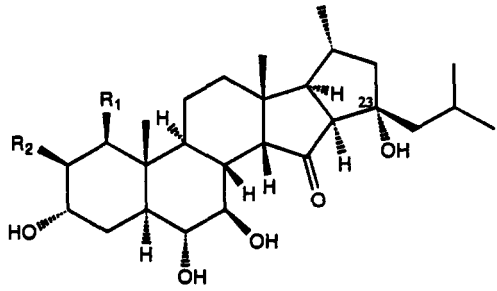
FIGURE 1. Relative stereochemistry of xestobergsterol C [**1**] (dotted arrows denote NOESY correlations).



4 R_1=R_2=H
5 R_1=R_2=OH

TABLE 2. ^{1}H- and ^{13}C-Nmr Data of **2** in Pyridine-d_5.

Position	Compounds							
	2				**4**			
	^{1}H[a]	*J* (Hz)	^{13}C[a]	m	^{1}H[a]	*J* (Hz)	^{13}C[a]	m
1α	1.49	d (13.9)	33.1	t	1.50		33.1	t
β	1.76	dt (13.9, 1.9)			1.76			
2α	1.86	dd (12.8, 1.9)	29.4	t	2.72		31.3	t
β	1.70	dq (13.9, 1.9)			1.65			
3	4.37	br s	65.3	d	4.35		65.3	d
4α	2.77	dd (13.9, 1.9)	31.3	t	1.88		29.4	t
β	1.68	dt (13.9, 2.4)			1.68			
5	2.42	dt (12.5, 3.1)	42.4	d	2.36		42.4	d
6	3.63	dd (10.8, 9.0)	75.7	d	3.57	dd (10.0, 10.0)	75.7	d
7	5.11	dd (10.1, 9.2)	74.9	d	5.05	dd (10.0, 10.0)	74.9	d
8	2.00	dt (11.7, 3.8)	39.1	d	1.97		39.1	d
9	1.60	dt (13.6, 3.0)	46.5	d	1.57		46.5	d
10			36.9	s			36.9	s
11α	1.52	dd (13.9, 1.9)	21.5	t	1.54		21.5	t
β	1.23	dq (12.9, 3.0)			1.24			
12α	1.05	dt (13.9, 1.9)	38.6	t	1.06		38.6	t
β	1.39	dd (13.3, 2.0)			1.41			
13			38.4	s			38.4	s
14	3.50	br s	51.7	d	3.42		51.7	d
15			217.3	s			217.3	s
16	2.70	d (10.0)	62.8	d	2.70	d (9.5)	62.8	d
17	1.70	t (10.0)	58.0	d	1.72		58.0	d
18	1.16	s	19.9	q	1.18	s	19.9	q
19	0.89	s	12.8	q	0.89	s	12.8	q
20	2.62	m	34.9	d	2.63		34.9	d
21	1.10	d (6.3)	20.9	q	1.12	d (6.6)	20.9	q
22α	1.21	t (12.3)	52.3	t	1.33	dd (12.1, 12.1)	52.3	t
β	2.10	dd (12.3, 5.3)			2.12	dd (12.1, 5.9)		
23			82.2	s			82.2	s
24a.....	1.96	dd (14.3, 4.8)	52.0	t	1.98		52.0	t
b	1.55	d (14.3)			1.56			
25	2.20	septet (6.5)	25.0	d	2.19		25.0	d
26	1.04	d (6.7)	24.9	q	1.06	d (5.1)	24.9	q
27	1.02	d (6.7)	25.3	q	1.04	d (5.1)	25.3	q

[a]δ in ppm.

4). NOESY correlations observed for H-16/H-24a, H-16/H-24b, and H-16/H-25 of xestobergsterol A indicated that the C-24–C-27 side-chain was α-oriented on ring E. A chair conformation of ring C in xestobergsterol A was deduced from NOESY correlations of H-9/H-12α, H-11β/H-8, H-11β/H-12β, H-11β/H_3-18, H-12α/H-16, and H-12α/H-17. On the other hand, the chemical shift of H-11β (δ_H 2.21 for **5**) of xestobergsterol B was revised as δ_H 1.62 from its ^{1}H-^{1}H COSY and NOESY spectra. NOESY correlations observed for H-16/H-24a, H-16/H-24b, and H-16/H-25 of xestobergsterol B indicated that the C-24–C-27 side-chain was α-oriented on ring E. NOESY correlations of H-11β/H_3-19, H-12α/H-9, H-12α/H-16, H-12α/H-17, and H-12β/H-17 of xestobergsterol B revealed a chair conformation of ring C. Thus, the structures of xestobergsterols A and B were revised as **2** and **3**, respectively.

Since xestobergsterol A [**2**] possesses a 1,2-diol functionality at C-6 and C-7,

TABLE 3. ^{1}H- and ^{13}C-Nmr Data of **3** in Pyridine-d_5.

Position	Compounds							
	3				**5**			
	^{1}H[a]	*J* (Hz)	^{13}C[a]	m	^{1}H[a]	*J* (Hz)	^{13}C[a]	m
1	4.31	br s	77.0	d	4.29		77.0	d
2	4.46	br s	76.2	d	4.46		76.2	d
3	4.65	br s	70.6	d	4.64		70.6	d
4α	2.87	d (13.8)	26.3	t	2.85		26.3	t
β	2.38	dt (13.8, 2.6)			2.36			
5	2.63	dt (11.9, 2.7)	42.0	d	2.60		42.0	d
6	3.93	t (9.5)	75.0	d	3.92		75.0	d
7	5.15	t (9.5)	74.9	d	5.15		75.0	d
8	2.12	dt (11.2, 2.6)	39.4	d	2.12		39.4	d
9	2.06	dt (11.7, 2.6)	48.3	d	2.01		48.3	d
10			43.4	s			43.5	s
11α	3.00	dt (13.7, 2.6)	25.0	t	2.98		25.0	t
β	1.64	dq (13.7, 2.6)			2.21			
12α	1.21	dt (13.7, 2.6)	39.1	t	1.21		39.1	t
β	1.46	dt (13.7, 2.6)			1.46			
13			38.1	s			38.1	s
14	3.56	br s	52.0	d	3.54		52.0	d
15			217.5	s			217.6	s
16	2.71	d (10.0)	62.8	d	2.73	d (10.3)	62.8	d
17	1.68	t (10.0)	57.9	d	1.71	dd (10.3, 10.3)	58.0	d
18	1.22	s	20.0	q	1.22	s	20.0	q
19	1.50	s	10.0	q	1.49	s	10.0	q
20	2.62	m	34.7	d	2.63		34.7	d
21	1.08	d (6.3)	20.8	q	1.10	d (5.9)	20.8	q
22α	2.09	dd (12.6, 5.9)	52.4	t	2.10		52.4	t
β	1.30	t (12.3)			1.33	dd (12.5, 12.5)		
23			82.1	s			82.2	s
24a.....	1.96	dd (14.0, 4.7)	52.0	t	1.98	dd (13.9, 5.1)	52.0	t
b	1.57	dd (14.1, 6.8)			1.60	dd (13.9, 6.6)		
25	2.21	septet (6.5)	24.9	d	2.21		25.0	d
26	1.04	d (6.6)	24.8	q	1.06	d (8.1)	24.9	q
27	1.03	d (6.6)	25.2	q	1.04	d (8.1)	25.3	q

[a]δ in ppm.

the cd exciton chirality method (5) was applied to determine the absolute stereochemistry. The ^{1}H-^{1}H coupling constant (J=9.6 Hz) between H-6 (δ_H 5.23) and H-7 (δ_H 6.45) in the 6,7-bis-*p*-bromobenzoate derivative [**6**] of **2** indicated that the two *p*-bromobenzoate groups were trans diequatorially disposed. The cd data {cd [θ] +5600 (232 nm), 0 (240 nm), and −57000 (251 nm)} of **6** showed negative exciton chirality, indicating that the absolute stereochemistries at C-6 and C-7 were both *R*. Thus, the absolute stereochemistry of xestobergsterol A [**2**] was elucidated as indicated. Xestobergsterols B [**3**] and C [**1**] are considered to possess the same absolute configurations as that of xestobergsterol A [**2**], because these steroids may be generated through the same biosynthetic pathway.

Xestobergsterol C [**1**] is a new steroid possessing five carbocyclic rings and a cis C/D ring junction like xestobergsterols A [**2**] and B [**3**]. This is the first isolation of novel steroids from a sponge of the genus *Ircinia*. Xestobergsterols C [**1**] and A [**2**] exhibited cytotoxicity against L-1210 murine leukemia cells with IC_{50} values of 4.1 and

4.0 μg/ml, respectively; xestobergsterol B [**3**] was not significantly cytotoxic (>10 μg/ml).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were recorded on a Jasco DIP-370 digital polarimeter. Uv and ir spectra were taken on Jasco Ubest-35 and Jasco Report-100 infrared spectrometers, respectively. ^{1}H- and ^{13}C-nmr spectra were recorded on JEOL JMN GX-270 and EX-400 and Bruker ARX-500 spectrometers in pyridine-d_5. The residual pyridine resonances at δ_H 7.19 and δ_C 123.5 were used as internal references for ^{1}H- and ^{13}C-nmr spectra, respectively. HMBC experiments were performed on a Bruker ARX-500 spectrometer, with 2K data points in the F2 domain and 256 increments, and optimized for $^{2-3}J_{H/C}$=10 Hz. NOESY experiments were made with a mixing time of 0.8 sec. Eims spectra were obtained on a JEOL JMS DX-303 spectrometer operating at 70 eV.

ANIMAL MATERIAL.—The sponge *Ircinia* sp. (order Dictyoceratida, family Thorectidae) was collected at −15 m by scuba off Konbu, Okinawa Island, Japan, and kept frozen until used. The sponge is a medium-brown color after preservation with a slightly darker surface skin and a tough compressible texture. Further details of the sponge morphology and surface features could not be determined from the specimen provided. The sponge skeleton consists of filaments and fibers. The filaments are 5–7 μm wide and twined together into thick ropes. The primary fibers are fasciculate, cored with sandgrains in the central region of the sponge, and are orientated at right angles to the surface of the sponge. Some secondary fibers occur and do not appear to be cored by foreign material. There is abundant foreign material throughout the mesohyl. A voucher specimen (SS-717) was deposited at the Sir George Fisher Center, James Cook University, Townsville, Queensland, Australia.

EXTRACTION AND ISOLATION.—The sponge (0.75 kg) was extracted with MeOH (1 liter×2). The MeOH extract (44 g) was partitioned between EtOAc (500 ml×3) and H_2O (500 ml); the aqueous layer was subsequently extracted with *n*-BuOH (500 ml×3). The *n*-BuOH extract was evaporated under reduced pressure to give a crude residue (2.3 g), which was subjected to Si gel cc (2.8×36 cm) with $CHCl_3$-*n*-BuOH-HOAc-H_2O (1.5:6:1:1, 700 ml) and then MeOH (250 ml). The fraction eluting from 100 to 300 ml of the solvent system was subjected to Sephadex LH-20 cc (MeOH) followed by reversed-phase hplc (YMC-Pack AM-323 ODS, YMC Co., 10×250 mm; flow rate: 2.0 ml/min; ri detection: MeOH-H_2O, 75:25) to afford xestobergsterols B (**3**, 3.0 mg, R_t, 18.4 min), C (**1**, 1.0 mg, R_t, 24.8 min), and A (**2**, 1.0 mg, R_t, 67.2 min).

Xestobergsterol C [**1**].—A colorless powder; $[\alpha]^{22}_D$ −18.6° (*c*=0.38, MeOH); ir (KBr) ν max 3400 (OH), 1715 (C=O, ketone), 1620 cm^{-1}; ^{1}H- and ^{13}C-nmr data, see Table 1; ^{1}H-^{1}H COSY correlations (pyridine-d_5, H/H) 1α/2, 1β/2, 1β/3, 2/4α, 3/4α, 3/4β, 4α/5, 4β/5, 5/6, 6/7, 7/8, 8/9, 8/14, 9/11β, 11α/12α, 12β/14, 16/17, 17/20, 20/21, 20/22β, 20/22α, 22α/22β, 24a/24b, 24b/25, 25/26, 25/27; HMBC and NOESY correlations, see Table 1; eims *m/z* 464 (M^+); hreims *m/z* 464.3119 (M^+, calcd for $C_{27}H_{44}O_6$, 464.3138).

p-BROMOBENZOYLATION OF XESTOBERGSTEROL A [**2**].—To a solution of xestobergsterol A [**2**, 5.5 mg, 0.012 mM] in CH_2Cl_2 (3 ml) was added *p*-bromobenzoyl chloride (40 mg, 0.18 mM), dimethylaminopyridine (3 mg), and triethylamine (2 ml). The mixture was stirred at room temperature for 12 h and then evaporated under reduced pressure. The residue was purified by a Si gel column (1.3×33 cm) with hexane-$CHCl_3$ (3:1) followed by a Si gel column (1.0×6.0 cm) with $CHCl_3$ to afford the tri-3,6,7-*p*-bromobenzoate of **2** (4.8 mg, 45%) and the bis-6,7-*p*-bromobenzoate of **2** (**6**, 0.5 mg, 5%), a colorless powder; uv (hexane) λ max (log ε) 244 (4.17) nm; cd (hexane) [θ] +5600 (232 nm), 0 (240 nm), and −57000 (251 nm); ^{1}H nmr ($CDCl_3$) δ 0.96 (3H, d, *J*=6.7 Hz, H_3-27), 0.98 (3H, d, *J*=6.7 Hz, H_3-26), 1.04 (3H, d, *J*=6.3 Hz, H_3-21), 1.08 (1H, m, H-12α), 1.12 (3H, s, H_3-18), 1.15 (1H, m, H-11β), 1.19 (1H, t, *J*=12.3 Hz, H-22α), 1.22 (1H, m, H-12β), 1.51 (3H, s, H_3-19), 1.43–1.82 (12H, m, H-1α, 1β, 2α, 2β, 4α, 4β, 9, 11α, 17, 20, 24b, and 25), 1.74 (1H, dt, *J*=8.9 and 2.1 Hz, H-24a), 1.86 (1H, dd, *J*=12.6 and 5.5 Hz, H-22β), 1.98 (1H, dt, *J*=9.6 and 3.5 Hz, H-8), 2.16 (1H, m, H-5), 2.23 (1H, m, H-20), 2.39 (1H, br s, H-14), 2.64 (1H, d, *J*=9.9 Hz, H-16), 4.18 (1H, br s, H-3), 5.23 (1H, t, *J*=9.6 Hz, H-6), 6.45 (1H, t, *J*=9.6 Hz, H-7), 7.43 (2H, d, *J*=8.5 Hz, *p*-bromobenzoate), 7.44 (2H, d, *J*=8.5 Hz, *p*-bromobenzoate), 7.67 (2H, d, *J*=8.5 Hz, *p*-bromobenzoate), 7.75 (2H, d, *J*=8.5 Hz, *p*-bromobenzoate); eims *m/z* 711, 713, and 715 [1:2:1, $(M-C_6H_{13}O\text{-}2)^+$, $(M-C_6H_{13}O)^+$, and $(M-C_6H_{13}O+2)^+$].

NOESY CORRELATIONS OF XESTOBERGSTEROLS A [**2**] AND B [**3**].—**2** (500 MHz, C_5D_5N, H/H) 1α/1β, 2α/2β, 2β/3, 2α/3, 2β/19, 3/4α, 4α/4β, 5/6, 5/7, 5/9, 6/7, 6/19, 7/8, 7/9, 8/11β, 8/14, 8/18, 8/19, 9/12α, 11α/11β, 11β/12β, 11β/18, 11β/19, 12α/12β, 12α/16, 12α/17, 14/18, 14/20, 16/17, 16/24, 16/24′, 16/25, 17/21, 18/20, 20/21, 21/22α, 22α/22β, 24a/24b, 24a/26, 24a/27, 24b/26, 24b/27, 25/26, 25/27; **3** (500 MHz, C_5D_5N, H/H)

1/5, 1/9, 2/3, 3/4β, 3/4α, 4α/4β, 4α/5, 4β/5, 4β/19, 6/7, 6/8, 6/19, 7/9, 8/11β, 8/14, 8/18, 8/19, 9/11α, 9/12α, 11α/12α, 11α/19, 11α/11β, 11β/19, 12α/12β, 12α/16, 12α/17, 12β/17, 14/18, 14/20, 16/17, 16/24, 16/24′, 16/25, 16/26, 16/27, 17/21, 17/22α, 18/20, 20/21, 20/22β, 21/22α, 22α/22β, 22α/26, 22α/27, 22β/26, 22β/27, 24a/24b, 24a/26, 24a/27, 24b/26, 24b/27, 25/26, 25/27.

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