Three New Sesquiterpenoids from the Aerial Parts of *Homalomena occulta*

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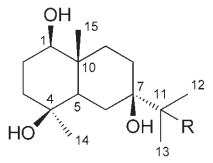
Three new eudesmane-type sesquiterpenoids, compounds **1**–**3**, and eight known constituents, including mucrolidin (**4**), 1β,4β,7α-trihydroxyeudesmane (**5**), 1β,4β,6β,11-tetrahydroxyeudesmane (**6**), oplodiol (**7**), bullatantriol (**8**), acetylbullatantriol (**9**), homalomenol (**10**), and maristeminol (**11**), were isolated from the aerial parts of *Homalomena occulta*. Their structures were determined by interpretation of spectroscopic and mass-spectrometric data, and their antimicrobial activities toward six different bacterial strains were tested. Most of the compounds showed weak antibacterial activities in an agar-diffusion assay.

Introduction. – *Homalomena occulta* (LOUR.) SCHOTT, belonging to the Araceae family, is widely distributed in southern China [1]. Its dried rhizomes are famous in traditional Chinese medicine (TCM), as recorded in the pharmacopoeia of China, and have been used for several hundred years [2]. Previous studies on this plant concerned only the essential oil [3] and a description of its chemical components [4]. So far, no extensive pharmacological study of *H. occulta* has been performed, although the plant extract exhibits significant antibacterial activity. We reported before some antibacterial components from *Polygonatum kingianum* [5].

As a part of our ongoing search for new biologically active constituents, we investigated the aerial parts of *H. occulta*, which led to the isolation of eleven compounds, the three sesquiterpenoids **1**–**3** being new constituents. Herein, we report their structure elucidation as well as antibacterial properties.

Results and Discussion. – 1. *Structure Elucidation.* The aerial parts of *H. occulta* were extracted with 90% aqueous EtOH. The dried extract was partitioned between H_2O and AcOEt, and the AcOEt-soluble fraction was purified by repeated column chromatography on silica gel to afford the three new compounds **1**–**3**, as well as the known compounds mucrolidin (**4**), 1β,4β,7α-trihydroxyeudesmane (**5**), 1β,4β,6β,11-tetrahydroxyeudesmane (**6**), oplodiol (**7**), bullatantriol (**8**), acetylbullatantriol (**9**), homalomenol (**10**), and maristeminol (**11**).

Compound **1**, obtained as a colorless solid, had the molecular formula $C_{15}H_{28}O_3$ according to HR-TOF-MS (*m*/*z* 279.1928 ($[M+Na]^+$; calc. 279.1936)) and NMR analysis. The IR spectrum suggested the presence of OH groups (3442 and 1122 cm^{-1}).



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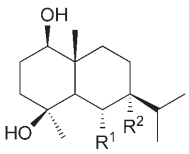
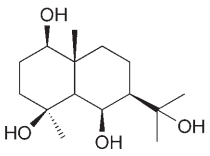
2 R = OH



4 R^1 = OH, R^2 = H
5 R^1 = H, R^2 = OH



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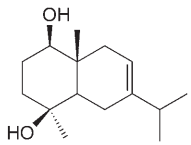

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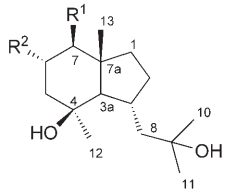
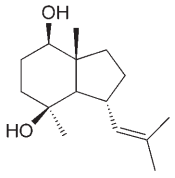


3 R^1 = OH, R^2 = OH
8 R^1 = OH, R^2 = H
9 R^1 = OAc, R^2 = H



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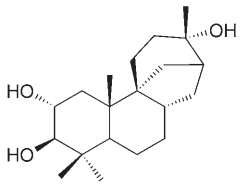

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The ^{1}H-NMR spectrum of **1** (*Table 1*) clearly displayed an oxygenated methine [δ(H) 3.12 (*dd*, J = 11.7, 4.1 Hz)] and two Me groups of an i-Pr moiety [δ(H) 0.82, 0.84 (J = 6.8 Hz each, 2 × 3 H)] at C(7). In the homonuclear ^{1}H,^{1}H-COSY spectrum of **1**, the

Table 1. *^{1}H- and ^{13}C-NMR Data of* **1** *and* **2**. At 500/125 MHz, resp., in $CDCl_3$; δ in ppm, J in Hz. Eudesmane atom numbering.

Position	**1**		**2**	
	δ(H)	δ(C)	δ(H)	δ(C)
1	3.12 (*dd*, J = 11.7, 4.1)	79.6 (*d*)	3.32 (*dd*, J = 11.5, 3.8)	79.3 (*d*)
2	1.81–1.83 (*m*), 1.51–1.54 (*m*)	26.8 (*t*)	1.90–1.93 (*m*), 1.55–1.58 (*m*)	26.8 (*t*)
3	1.67 (*dt*, J = 13.6, 3.2), 1.44 (*ddd*, J = 13.6, 13.0, 3.2)	39.3 (*t*)	1.67–1.70 (*m*), 1.55 (*dd*, J = 13.8, 5.0)	39.7 (*t*)
4		71.2 (*s*)		71.5 (*s*)
5	0.95 (*dd*, J = 11.4, 4.1)	46.7 (*d*)	1.47 (*dd*, J = 11.6, 4.3)	44.7 (*d*)
6	1.84 (*ddd*, J = 13.2, 11.4, 2.8), 1.41–1.45 (*m*)	30.8 (*t*)	1.71 (*dd*, J = 13.0, 11.6), 1.60–1.62 (*m*)	26.2 (*t*)
7		74.3 (*s*)		75.8 (*s*)
8	1.78–1.80 (*m*), 1.40–1.43 (*m*)	26.5 (*t*)	1.47–1.49 (*m*), 1.64–1.66 (*m*)	26.5 (*t*)
9	1.17–1.19 (*m*), 1.63–1.66 (*m*)	36.2 (*t*)	1.41–1.44 (*m*), 1.67–1.70 (*m*)	34.6 (*t*)
10		38.9 (*s*)		38.4 (*s*)
11	1.90–1.93 (*m*)	28.7 (*d*)		75.3 (*s*)
12	0.84 (*d*, J = 6.8)	15.8 (*q*)	1.26 (*s*)	24.7 (*q*)
13	0.82 (*d*, J = 6.8)	16.1 (*q*)	1.25 (*s*)	24.8 (*q*)
14	1.02 (*s*)	29.7 (*q*)	1.14 (*s*)	29.8 (*q*)
15	1.07 (*s*)	12.4 (*q*)	0.99 (*s*)	11.6 (*q*)

methylene H-atoms at δ(H) 1.81–1.83 and 1.51–1.54 coupled with the hydroxymethine at δ(H) 3.12 and with another CH_2 group at δ(H) 1.67 and 1.44, devoid of further coupling. These characteristic signals were in accord with an eudesmane-type sesquiterpene skeleton [6].

The ^{13}C-NMR signals at δ(C) 79.6 (*d*), 71.2 (*s*), and 74.3 (*s*) suggested that **1** had three OH functions. Two of them were placed at C(1) and C(4), respectively, based on HMBC correlations between Me(14) and C(1), and between Me(15) and C(4), respectively (*Fig. 1*). The remaining OH group was then attached at C(7), based on correlations of both Me(12) (δ(H) 0.84) and Me(13) (δ(H) 0.82) with C(7) (δ(C) 74.3) and C(11) (δ(C) 28.7). The OH group at C(1) was further placed in equatorial position (1β), according to the coupling constants for H–C(1) [δ(H) 3.12 (*dd*, J = 11.7, 4.1 Hz)] [7], and supported by the observed upfield shift of the angular Me(15) group (δ(C) 12.4) in the ^{13}C-NMR spectrum [8].

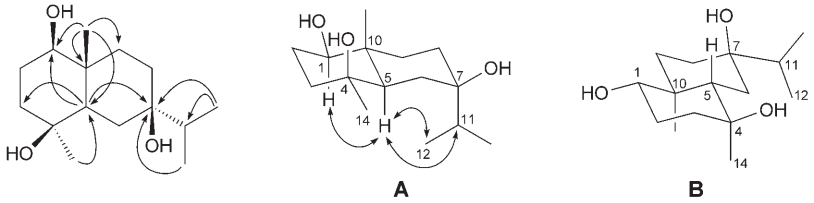

Fig. 1. *Key HMBC and ROSEY correlations for* **1**

Moreover, the relative configuration of **1** was found to correspond to **A** rather than **B** (*Fig. 1*), on the basis of the ^{1}H-NMR chemical shift of the angular Me(15) group, which is generally shifted downfield in a chair/chair conformation, compared with a chair/boat conformation [9]. The ^{13}C-NMR chemical shifts for C(4), C(10), and C(15) suggested a β-OH group at C(4), in accord with literature data [10–12], including an X-ray crystal structure of a related compound [10]. Further, ROESY correlations of H–C(5) [δ(H) 0.95 (*dd*, J = 11.4, 4.1 Hz)] with H–C(11) [δ(H) 1.90–1.93 (*m*)] and Me(12) [δ(H) 0.84 (*d*, J = 6.8)] indicated that the OH group at C(7) was in equatorial position, which further supported structure **A**. Thus, on the basis of the above evidence, the structure of compound **1** was determined as 1β,4β,7β-trihydroxyeudesmane.

Compound **2**, obtained as a colorless solid, was assigned the molecular formula $C_{15}H_{28}O_4$ by HR-TOF-MS (*m*/*z* 295.1883 ([M + Na]$^+$; calc. 295.1885)) and by analysis of its NMR data (*Table 1*). The EI mass spectrum of **2** showed the M^+ peak at *m*/*z* 272, suggesting an increase of 16 mass units compared to **1**. Careful investigation of the ^{1}H- and ^{13}C-NMR spectroscopic data showed that **2** had an additional OH group compared to **1**. Characteristic eudesmane signals were observed at δ(C) 79.3 (*d*), 71.5 (*s*), 75.8 (*s*), 38.4 (*s*), and 11.6 (*q*). The additional oxygenated quaternary C-atom resonated at δ(C) 75.3 (*s*), on the expense of the i-Pr methine at δ(C) 28.7 (*d*) (δ(H) 1.90–1.93 (*m*)) in **1**. An HMBC experiment displayed correlations of both Me(12) (δ(H) 1.26 (*s*)) and Me(13) (δ(H) 1.25 (*s*)) with δ(C) 75.3 (*s*) and 75.8 (*s*) (*Fig. 2*). So, the additional OH group was placed at C(11), and the structure of compound **2** was determined as 1β,4β,7β,11-tetrahydroxyeudesmane.

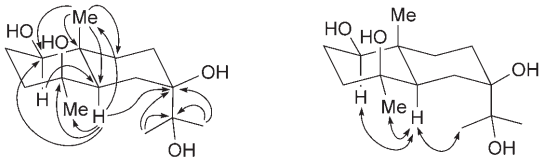

Fig. 2. *Key HMBC and ROSEY correlations for* **2**

Compound **3**, obtained as a colorless solid, had the molecular formula $C_{15}H_{28}O_4$ by HR-TOF-MS (*m*/*z* 295.1895 ($[M+Na]^+$; calc. 295.1885) and NMR analysis. The IR spectra showed the presence of OH groups (3425, 1067, 1023 cm^{-1}). The ^1H- and ^{13}C-NMR spectra of **3** (*Table 2*) revealed the presence of four Me, four CH_2, and four CH groups, as well as three quaternary C-atoms. Careful interpretation of its NMR and ^1H,^1H-COSY spectra indicated that **3** was an oppositane-type sesquiterpenoid [13]. The ^1H- and ^{13}C-NMR data of **3** were similar to those of bullatantriol (**8**), except that **3** contained a further oxygenated methine (δ(H) 3.80–3.84; δ(C) 69.2). In the ^1H,^1H-COSY spectrum, the hydroxymethine at δ(H) 3.00 (H–C(7)) coupled with another hydroxymethine at δ(H) 3.80–3.84, which indicated a 6-OH group. This was supported by HMBC correlations of the H-atom at δ(H) 3.80–3.84 with the C-atoms at δ(C) 83.8 (C(7)), 72.2 (C(4)), 48.5 (C(5)), and 47.0 (C(7a)). The coupling constant of H–C(7) (*d*, $J = 7.6$ Hz) showed that the OH groups at C(6) and C(7) were α- and β-oriented, respectively. The α-configuration of the 6-OH group was also evident form the key ROESY correlations of H–C(2)/Me(13) and of Me(13)/H–C(3) (*Fig. 3*). Therefore, the structure of **3** was determined as (1*R*,3a*R*,4*S*,5*S*,7*S*)-octahydro-1-(2-hydroxy-2-methylpropyl)-3a,7-dimethyl-1*H*-indene-4,5,7-triol, and given the trivial name *homalomentetraol*.

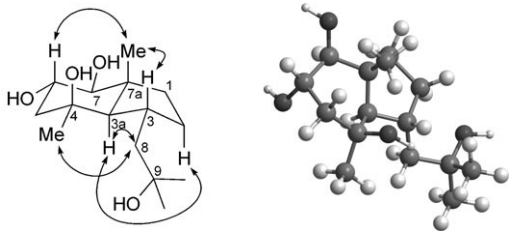

Fig. 3. *Key ROSEY correlations for* **3**

The known sesqui- and diterpenoidal compounds were identified as mucrolidin (**4**) [10], 1β,4β,7α-trihydroxyeudesmane (**5**) [12], 1β,4β,6β,11-tetrahydroxyeudesmane (**6**) [14], oplodiol (**7**) [15], bullatantriol (**8**) [12], acetylbullatantriol (**9**) [12], homalomenol (**10**) [12], and maristeminol (**11**) [16], by comparison of their physico-chemical, NMR, and MS data with those reported in the literature.

2. *Antibacterial Properties.* Compounds **1**–**11** were tested for their antibacterial properties against *Shigella flexneri*, *S. dysenteriae*, *S. sonnei*, *Mycobacterium tuberculosis*, α-hemolytic *Streptococcus*, and *Streptococcus pneumoniae* by means of the dose-dependent paper-disk diffusion method. The results, expressed in terms of

Table 2. *NMR Data of* **3** *and* **8**. At 500/125 MHz, resp., in $CDCl_3$; δ in ppm, J in Hz.

Position	**3**			**8**
	δ(H)	δ(C)[a])	HMBC (H→C)	δ(C)
1	1.46–1.50 (*m*)	38.5 (*t*)	2, 3, 3a, 12	27.3 (*t*)
2	1.24–1.28 (*m*)	34.4 (*t*)	1, 3, 3a	32.7 (*t*)
3	1.13–1.15 (*m*)	30.9 (*d*)	2, 8, 9	31.2 (*t*)
3a	1.02 (*d*, *J*=10.5)	58.9 (*d*)	3, 4, 7a, 13	58.5 (*d*)
4		72.2 (*s*)		71.5 (*t*)
5	1.88 (*dd*, *J*=13.6, 5.2)	48.5 (*t*)	3a, 4, 6, 7	40.5 (*t*)
	1.31 (*dd*, *J*=13.6, 11.5)		6, 7	
6	3.80–3.84 (*m*)	69.2 (*d*)	5, 7	38.6 (*t*)
7	3.00 (*d*, *J*=7.6)	83.8 (*d*)	1, 6, 7a, 12	79.4 (*d*)
7a		47.0 (*s*)		46.7 (*s*)
8	2.02 (*d*, *J*=10.2)	50.1 (*t*)	2, 3, 3a, 9	50.4 (*t*)
9		71.5 (*s*)		71.5 (*s*)
10	1.14 (*s*)	28.2 (*q*)	9, 11	28.6 (*q*)
11	1.15 (*s*)	30.9 (*q*)	10, 11	30.7 (*q*)
12	1.25 (*s*)	31.4 (*q*)	1, 7a, 7	31.1 (*q*)
13	0.95 (*s*)	15.0 (*q*)	3a, 4, 5	13.9 (*q*)

[a]) Recorded at 100 MHz.

minimal inhibitory amount (*MIA*; in μg/disk), are collected in *Table 3* relative to rifampicin as positive control. No such activities had been reported for these compounds before.

As can be seen from *Table 3*, the unsaturated eudesmane sesquiterpenoid **7** did not exhibit any antibacterial activity against the tested microbial strains. The sesquiterpe-

Table 3. *Antibacterial Activities of* **1**–**11** *towards Different Bacterial Strains.* All values were determined by the paper-disk method (see *Exper. Part*), and are expressed in terms of minimal inhibitory amount (*MIA*; in μg/disk).

Compound	*Shigella flexneri*	*Shigella dysenteriae*	*Shigella sonnei*	*Mycobacterium tuberculosis*	α-Hemolytic *Streptococcus*	*Streptococcus pneumoniae*
1	n.a.[a])	400	n.a.	200	n.a.	n.a.
2	n.a.	n.a.	n.a.	300	450	400
3	n.a.	n.a.	n.a.	450	n.a.	n.a.
4	n.a.	250	400	300	450	450
5	n.a.	n.a.	300	250	350	n.a.
6	250	n.a.	450	250	n.a.	400
7	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
8	n.a.	n.a.	n.a.	350	n.a.	n.a.
9	n.a.	n.a.	n.a.	300	n.a.	n.a.
10	n.a.	n.a.	n.a.	450	n.a.	n.a.
11	n.a.	n.a.	300	400	350	250
Rifampicin[b])	1	1	1	1	1	1

[a]) Not active. [b]) Positive control.

noids with an oppositane framework (**3**, **8**, **9**, **10**) were only very weakly active against *M. tuberculosis*. Interestingly, the new eudesmane **1** with an α-configured i-Pr group was more active towards *M. tuberculosis* than its β-configured congeners **4**–**6**. However, the β-OH groups in **1** and **2** are probably not important in terms of activity.

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Experimental Part

General. Column chromatography (CC): silica gel (200–300 mesh; *Qingdao*) and *Sephadex LH-20*. TLC: precoated silica-gel plates (*Qingdao*). Optical rotations: *Horiba SEAP-300* polarimeter. IR Spectra: *Bio-Rad FTS* spectrophotometer, in cm^{-1}. NMR Spectra: *Bruker AM-400* or *DRX-500* spectrometers; in $CDCl_3$ soln.; δ in ppm rel. to Me_4Si, *J* in Hz. MS: *VG AutoSpec-3000* spectrometer; in *m*/*z* (rel. %).

Plant Material. The aerial parts of *Homalomena occulta* (Lour.) Schott were collected in Xishuangbanna (Yunnan Province, P. R. China) in July 2002. The plant material was identified by Dr. *Jian-Ying Xiang*. A voucher specimen (No. 200207X08) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, Yunnan 650204, P. R. China.

Extraction and Isolation. The air-dried aerial parts (4.8 kg) of *H. occulta* were extracted with 90% aq. EtOH at r.t. (2 ×). The solvent was evaporated below a temp. of 50°, and the resulting deep-brown waxy residue was suspended in H_2O, and extracted successively with AcOEt (3 × 2 l) and BuOH (3 × 2 l). The AcOEt-soluble material (128 g) was fractionated by CC (1.5 kg SiO_2; MeOH/$CHCl_3$ 1:100, 1:50, 1:20, 1:10) to afford several fractions. The first fraction (8.8 g) was purified by repeated CC (1. SiO_2, MeOH/$CHCl_3$ 1:100, 1:50; 2. *Sephadex LH-20*, MeOH/$CHCl_3$ 1:1) to afford **3** (18 mg), **5** (38 mg), **6** (42 mg), and **8** (865 mg). The second fraction (5.9 g) was purified by repeated CC (1. SiO_2, MeOH/$CHCl_3$ 2:100, 1:30; 2. *Sephadex LH-20*, MeOH/$CHCl_3$ 1:1) to afford **1** (1.202 g) and **2** (862 mg). The third fraction (1.8 g) was purified by repeated CC (1. SiO_2, MeOH/$CHCl_3$ 1:30, 1:20; 2. *Sephadex LH-20*, MeOH/$CHCl_3$ 1:1) to afford **4** (81 mg) and **7** (23 mg). The fourth fraction (2.1 g) was also purified by repeated CC (1. SiO_2, MeOH/$CHCl_3$ 1:20; 2. *Sephadex LH-20*, MeOH/$CHCl_3$ 1:1) to provide **9** (18 mg), **10** (38 mg), and **11** (42 mg).

1β,4β,7β-Trihydroxyeudesmane (=*(1*R,*4*S,*4a*R,*6*R,*8a*R*)-Decahydro-4,8a-dimethyl-6-(1-methylethyl)naphthalene-1,4,6-triol*; **1**). Colorless solid. $[\alpha]_D^{25} = +92.6$ ($c = 0.54$, $CHCl_3$). IR (KBr): 3442, 2925, 2854, 1382, 1122, 801, 568. ^{1}H- and ^{13}C-NMR: see *Table 1*. EI-MS: 256 (0.5, M^+), 238 (3, $[M - H_2O]^+$), 220 (6, $[M - 2\,H_2O]^+$), 213 (44, $[M - C_3H_7]^+$), 195 (100, $[M - C_3H_7 - H_2O]^+$), 177 (57, $[M - C_3H_7 - 2\,H_2O]^+$), 159 (31, $[M - C_3H_7O - 3\,H_2O]^+$), 135 (31), 123 (36), 107 (30), 71 (33). HR-TOF-MS (pos.): 279.1928 ($[M + Na]^+$, $C_{15}H_{28}NaO_3^+$; calc. 279.1936).

1β,4β,7β,11-Tetrahydroxyeudesmane (=*(1*R,*4*S,*4a*R,*6*R,*8a*R*)-Decahydro-6-(1-hydroxy-1-methylethyl)-4,8a-dimethylnaphthalene-1,4,6-triol*; **2**). Colorless solid. $[\alpha]_D^{25} = +46.15$ ($c = 1.30$, $CHCl_3$). IR (KBr): 3425, 2974, 2939, 2875, 1460, 1435 1374, 1066, 1029, 939, 919. ^{1}H- and ^{13}C-NMR: see *Table 1*. EI-MS: 272 (4, M^+), 254 (1, $[M - H_2O]^+$), 236 (2, $[M - 2\,H_2O]^+$), 213 (30, $[M - C_3H_7O]^+$), 195 (100, $[M - C_3H_7O - H_2O]^+$), 177 (62, $[M - C_3H_7O - 2\,H_2O]^+$), 159 (35, $[M - C_3H_7O - 3\,H_2O]^+$), 135 (37), 123 (41), 107 (25), 97 (37), 55 (28). HR-TOF-MS (pos.): 295.1883 ($[M + Na]^+$, $C_{15}H_{28}NaO_4^+$; calc. 295.1885).

Homalomentetraol (=*(1*R,*3a*R,*4*S,*5*S,*7*S*)-Octahydro-1-(2-hydroxy-2-methylpropyl)-3a,7-dimethyl-1*H*-indene-4,5,7-triol*; **3**). Colorless solid. $[\alpha]_D^{25} = +30.30$ ($c = 0.65$, $CHCl_3$). IR (KBr): 3425, 2964, 2933, 2875, 1464, 1382, 1299, 1261, 1067, 1045, 1023, 831. ^{1}H- and ^{13}C-NMR: see *Table 2*. EI-MS: 272 (0.2, M^+), 254 (0.5, $[M - H_2O]^+$), 239 (70, $[M - Me - H_2O]^+$), 236 (8, $[M - 2\,H_2O]^+$), 229 (11), 218 (52, $[M - 3\,H_2O]^+$), 213 (35, $[M - C_3H_7O]^+$), 203 (20, $[M - Me - 3\,H_2O]^+$), 195 (50, $[M - C_3H_7O - 2\,H_2O]^+$), 123 (100), 81 (66), 59 (24). HR-TOF-MS (pos.): 295.1895 ($[M + Na]^+$, $C_{15}H_{28}NaO_4^+$; calc. 295.1885).

1β,4β,7α-Trihydroxyeudesmane (**4**). Colorless solid. $[\alpha]_D^{25} = -125.0$ ($c = 0.54$, $CHCl_3$). EI-MS: 238 (0.5, $[M-H_2O]^+$), 236 (3), 213 (50), 195 (100), 177 (66), 159 (37), 135 (35), 123 (41).

Bullatantriol (**8**). Colorless solid. $[\alpha]_D^{25} = +89.7$ ($c = 0.76$, $CHCl_3$). ^{13}C-NMR: see *Table 2*.

Antibacterial-Activity Assay. Antibacterial activities were determined against *Gram*-positive and *Gram*-negative bacteria by means of the paper-disk diffusion method [17]. Solns. of the test compounds in $CHCl_3$ were applied with a syringe to a paper disk (5 mm in diameter) at a single dose of 500 μg/disk. The disks were dried under a flow of air, and then put onto agar medium inoculated with the corresponding bacterial strain. After incubation for 10 h at 42°, the inhibition zones were analyzed. Then, the active compounds were resubjected to the same assay at ten different concentrations in the range 50–500 μg/disk. The results were expressed in terms of minimal inhibitory amount (*MIA*) (in μg/disk), rifampicin being used as pos. control (*MIA* = 1 μg/disk). The results are collected in *Table 3*.

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